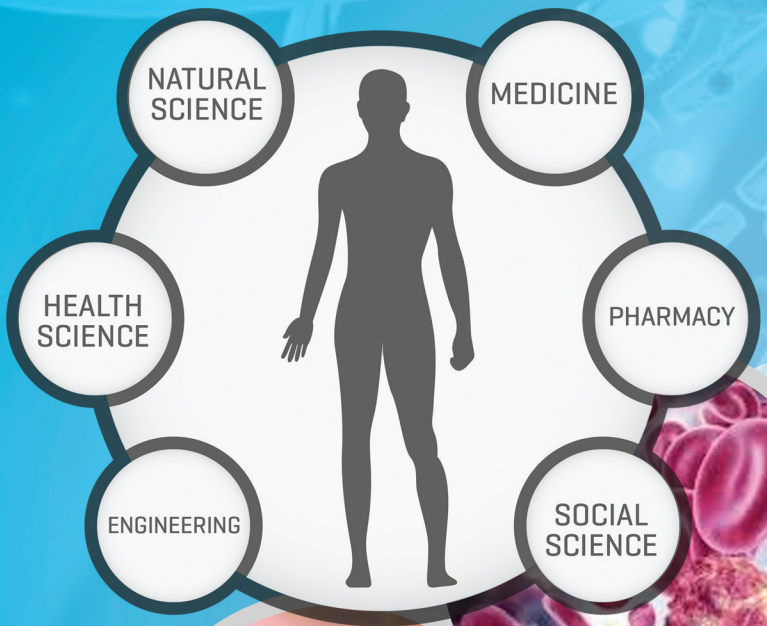
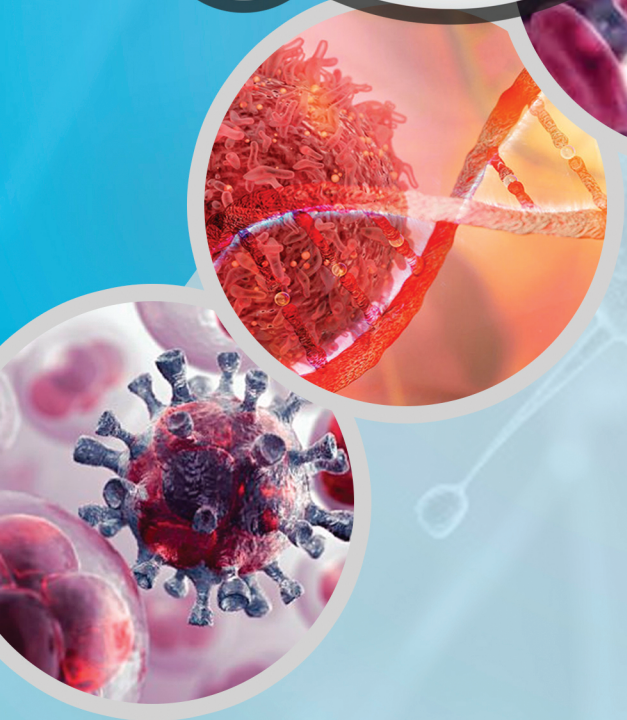
4. ULUSLARARASI KANSER GÜNLERİ (4. UKG)

4. INTERNATIONAL CANCER DAYS

CONGRESS BOOK





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SIVAS CUMHURIYET UNIVERSITY

4th INTERNATIONAL CANCER DAYS CONGRESS BOOK

Editors
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4th International Cancer Days Scientific Program
28-30 September 2023

Hour	28.09.2023 Thursday
09:00 09.30	Opening Ceremony
09:30 12:00	**Panel 1:** Opening Panel: Esat Korğalı ***Session Chairs*** *Esat Korğalı* *Hatice Özer* **1.** Epidemiology and Etiology: Ş. Reyhan Uçku **2.** Screening, early diagnosis: Gökhan Sönmez **3.** The Role of PSA in Prostate Cancer: Okan Doğan
12:00 13:30	Lunch
13:30 15:00	**Panel 2:** Diagnosis ***Session Chairs*** *İsmail Şalk* *Eda Erdiş* **1.** Multiparametric prostate MRI and PIRADS staging system: Mehmet H. Atalar **2.** Prostate Biopsy Methods: Abdullah Demirtaş **3.** Pathological Diagnosis of Prostate Cancer, Gleason, ISUP Grades: Selver Özekinci **4.** Nuclear medicine methods in the diagnosis of prostate cancer: Abdullah Hanif Bin Rosdi
15:00 15:15	Coffee Break
15:15 16:45	**Panel 3:** Treatment options in localized and locally advanced prostate cancer ***Session Chairs*** *Esat Korğalı* *Birsen Yücel* **1.** Active Monitoring and Focal Treatments: M. Öner Şanlı **2.** Surgical Treatment: Evren Süer **3.** Urinary Incontinence after surgery: Ömer Gülpınar
	Oral presentations
	29.09.2023 Friday
09:00 10:30	**Panel 4:** Radiotherapy and Hormonotherapy of Nonmetastatic Prostate Cancer ***Session Chairs*** *Esat Korğalı* *Fikret Erdemir* **1.** Radiation Oncology, Radiotherapy and Its Complications: Dicle Aslan **2.** Management of Sexual Complications in Prostate Cancer: Fikret Erdemir **3.** Treatment in Locally Advanced Prostate Cancer: Esat Korğalı
10:30 10:45	Coffee Break
10:45 12:45	**Panel 5:** Metastatic Disease ***Session Chairs*** *Zekiye Hasbek* *Birsen Yücel* **1.** Treatment of Hormone Naive Disease: Ersin Özaslan **2.** Treatment of Hormone-Resistant Disease: Nedim Turan **3.** Radionuclide Therapy in Castration-Resistant Prostate Cancer: Yasemin Şanlı
12:45 14:00	Lunch
14:00 15:30	**Panel 6:** Palliative Treatments in Bone Metastasis ***Session Chairs*** *Serdar Savaş Gül* *Eda Erdiş* **1.** Algology, Medical Treatment of Pain Palliation: İclal Özdemir Kol **2.** Radiation Oncology, Palliative Radiotherapy in Bone Metastasis: Gülhan Güler **3.** Nuclear Medicine, Radionuclide Therapies in Extensive Bone Metastasis: Nurhan Ergül **4.** Orthopedic Approach to Bone Metastases: Özhan Pazarcı
15:30 15:40	Coffee Break
15:40 16:40	**Panel 7:** Nursing Approaches to Psychosocial Problems in Prostate Cancer and Prostate Cancer from the Perspective of a Physiotherapist ***Session Chairs*** *Havva Tel* *Vehbi Ünal* **1.** Survival and Psychosocial Problems in Prostate Cancer: Havva Tel **2.** Nursing Care in Prostate Cancer: Nuriye Erbaş **3.** Prostate Cancer and Exercise Treatment: Aynur Otağ
	Oral presentations
	30.09.2023 Saturday
09:00 11:00	**Panel 8:** Pharmacological and Pharmaceutical Overview of Prostate Cancer ***Session Chairs*** *Bülent Saraç* *Sevgi Durna Daştan* **1.** Synthesis and Invitro Studies of New Peptides that Can Be Used in the Diagnosis and Treatment of Prostate Cancer: Bilge Şen **2.** New Biomarkers in Prostate Cancer: Tuba Çandar **3.** Gene Silencing Studies: Ercan Çaçan
10:30 10:45	Coffee Break
11:00 11:30	Closing Ceremony

ORAL PRESENTATION PROGRAM

RED HALL

28.09.2023 Thursday / 14:00-16:45

Session Chairs: *SÜLEYMAN KOÇ - HANDAN DEREBEYOĞLU*

ID 24	Gastrointestinal System Lymphomas: A Single Center Experience/ HATİCE TERZİ
ID 13	Fresh Frozen Plasma Plus Furosemide As A Potential Human Albumin Substitute In Cancer Patients In Resource-Limited Settings/ METIN YARICI
ID 25	Can Follicular Lymphoma, An Indolent Lymphoma, Be Aggressive?; A Case Report/ HATİCE TERZİ
ID 15	Can We Define A Measurable Laboratory Parameter Threshold To Initiate Cytokine Adsorption Therapy For Cancer Patients In The Intensive Care Unit?/ MEHMET EREN YÜKSEL
ID 22	Is Every Distant Organ Involvement Seen On Pet/Ct Imaging A Metastasis? Cases Report And Review Of The Literature/ ABDULKADİR SAFA

15:15-15:30 Tea-Coffee Break

ID 98	Characteristics And Survival Outcomes Of Gastric Cancer Patients Receiving Neoadjuvant Therapy / MUSTAFA KORKMAZ
ID 27	The Relationship Between Clinical And Histopathological Characteristics Of Patients With Breast Cancer And Bone Scintigraphy Results/ MUSTAFA GENÇ
ID 30	Diffuse Large B-Cell Lymphoma Of The Oral Cavity: A Case Report/ ŞÜKRAN ACIPINAR
ID 69	Partial Hydatiform Mole And Coexisting Alive Fetus In The Second Trimester Case Reports And Review Of The Literature/ HANDE YEŞİL ÇETİNKAYA

BLUE HALL

28.09.2023 Thursday / 14:00-16:45

Session Chairs: *ÇAĞLAR YILDIZ - SİNAN SOYLU*

ID 64	Rare Endometrial Tumor With Malignant Potential: Papillary Adenofibroma/ MUAZZEZ IŞIK SÖNMEZ
ID 34	Effects Of Molecular And Histological Characteristics On Prognosis In Synchronous Endometrial And Ovarian Cancer Cases/ FERAH KAZANCI (Online)
ID 55	Twin Pregnancy After Juvenile Type Granulosa Cell Tumor/ VİLDAN KILIÇ
ID 66	Diagnosis And Surgical Management Of Synchronous Colorectal Cancers: A Case Presentation And Discussion/ HAKKI COŞKUN
ID 68	Ten Year Analysis Of Ovarian Cancer In Sivas Cumhuriyet University Hospital Gynecology And Obstetrics Clinic/ SELİN MUTLU

15:00-15:15 Tea-Coffee Break

ID 92	Ten Years of Endometrial Cancer Cases Investigation of the Distribution According to Histological Types/ SÜMEYRA ALCALI
ID 26	Challenges In Diagnosing And Managing Insulinomas: Two Case Reports And Review Of The Literature/ EREN C MUTLU
ID 10	A Novel Block In Breast Cancer Surgery For Analgesia/ FATİH BALCI
ID 57	Delayed Diagnosis In A Mentally Motor-Retarded Girl: A Rare Case Of Giant Mucinous Cystadenoma/ ŞERİFE ÖZLEM GENÇ

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ID 47	Sarcoid-Like Reactions In Patients With Prostate Carcinoma: Can Mimic Metastasis On Oncologic Imaging/ GİZEM ISSIN
ID 97	Evaluation Of Mycosis Fungoides Cases; A University Hospital Experience/ SERKAN ÇELİKGÜN
ID 84	Small Cell Neuroendocrine Carcinoma Of The Cervix, Single-Center Experience/ PINAR KUBİLAY TOLUNAY
ID 89	Percutan Transtoracic Lung Biopsy; One Center Experience/ NİSA BAŞPINAR
ID 1	Cervical Cancer Screenings In Sivas: Covid-19 Pandemic Period, Before And After/ İREM AKOVA
ID 100	Investigation of the Hematologic Effect of Dexpanthenol (DXP) on 5-Fluorouracil (5-FU)-induced Bone Marrow Suppression in Rats/ HÜSEYİN ÖZEL

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15:45-17:00

Session Chairs: *HATİCE TEL AYDIN - NURİYE ERBAŞ*

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ID 71	Mental Status And Loneliness In Cancer Patients / ÖZGE KISAOĞLU
ID 74	Depression And Caregiving Burden In Caregivers Of Patients Receiving Chemotherapy Treatment/ ÖZGE KISAOĞLU
ID 85	Bibliometric Analysis Of Nursing Studies On Supportive Care Needs Of Cancer Patients/ DÖNE GÜNAY
ID 60	Evaluation Of People Who Died Of Prostate Cancer In Terms Of Risk Factors In Excavations From The Roman Age/ NİLGÜN ÖZBEY

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ID 23	The Relation Between Mediastinal Lymph Node Density And Radiotracer Uptake In Patients With Lung Cancer/ ENES GÜL
ID 61	The Importance Of Direct Laryngoscopy In Laryngeal Diseases/ AHMET AKSOY
ID 90	A Case-Based Approach To Medullary Thyroid Cancer/ EZGİ TANRIVERDİ

10:00-10:15 Tea-Coffee Break

ID 17	Punch Biopsy Results In Nasopharyngeal Pathologies/ ADEM BORA
ID 56	Colon Metastasis Of Breast Cancer Case Report/ YILDIRIMCAN DEMİRTAŞ
ID 83	Colonoscopy-Based Early Diagnosis Of Colorectal Cancer: A Single-Center Retrospective Study And Literatüre Review HÜSNÜ ÇAĞRI GENÇ

RED HALL

29.09.2023 Friday / 14:00-16:45

Session Chairs: *HATİCE ÖZER - HATİCE TERZİ*

ID 45 The Effect Of Prostate Biopsy And Periprostatic Nerve Block On Erectile Function/ YAGAN BALCI

ID 5 Tumor Suppressor Gene And Proto-Oncogene Mutations In Lung Cancer/ MALİK E. YILDIRIM

ID 3 Evaluation Of The Relationship Between Magnetic Resonance Imaging And Pathological Subtype In Renal Cell Cancers/ İRFAN ATİK

ID 59 Radiological Analysis Of Benign Lesions Mimicking Renal Tumours/ ESİN ÖLÇÜCÜOĞLU

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ID 46 Emergency Department Visits Due To Complications After Transrectal Ultrasound-Guided Prostate Biopsies A Four Year Retrospective Single-Center Study/ YAGAN BALCI

ID 52 Evaluation Of Treatment Response In Early Stage Renal Pelvis Tumors Introduction/ SERDAR ATA

ID 49 Exploration Imaging Biomarkers And Tissue Validation In Translational Neuro-Oncology/ YUSUF İÇER

ID 99 Biochemical Investigation Of The Protective Effects Of Dexpanthenol On 5-Fluorouracil-Induced Nephrotoxicity And Hepatotoxicity In Rats/ ŞEYMA TAŞTEMUR

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ID 43 The Relationship Between Bmi And Surgical Margin Positivity In Patients With Prostate Cancer/ MERCAN TAŞTEMUR

ID 12 Abdominal Ultrasonography And Colonoscopy Should Be Performed Before Inguinal Hernia Surgery To Identify Factors That Would Increase Intraabdominal Pressure/ MEHMET EREN YUKSEL

ID 40 A Rare Case Of Lung Adenocarcinoma In A Patient With Pulmonary Alveolar Proteinosis/ SELMA IŞIK

ID 72 Five-Year Survival And Related Factors In Elderly Lung Cancer Patients In Sivas Province/ SERKAN ÇELİKGÜN

10:00-10:15 Tea-Coffee Break

ID 76 Remission In Gallbladder Cancer With Olaparib And Pembrolizumab Treatment After Surgery: Case Report/ FAZİLET ÖZDİL ÇOŞKUN

ID 78 Assesment Of The Relationship Between Endometrial Cancer And Systemic Inflammation/ ŞERİFE ÖZLEM GENÇ

ID 75 Novel Variant In The Pten Gene Characterized By A Variable Phenotype Within The Family / HANDE KÜÇÜK KURTULGAN

ID 101 Bibliometric Analysis About Gastric Cancer/ AHMET FARUK GÜLDEŞ

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ID 29 In Vitro Evaluation Of The Effects Of Citrus Aurantium L. On Breast Cancer/ İPEK SÜNTAR

ID 35 Anti-Cancer Activities Of The New Triazine Compounds In Lung Cancer Cell (A549)/ SEDA MESCİ

ID 91 Antiproliferative Activity Investigation Of Malva Neglecta Wallr/ KEVSER TABAN

ID 93 Investigation Of Theoretical Activities Of Methanone Derivative Molecules Against Colon Cancer Proteins/ HÜLYA KÜBRA KILIÇ

15:00-15:15 Tea-Coffee Break

ID 94 Investigation Of Theoretical Activities Of Phenyldiazenyl Derivative Molecules Against Lung Cancer Proteins/ HÜLYA KÜBRA KILIÇ

ID 38 Examining The Interaction: Correlations Between Zinc, Copper, And Manganese Levels In Relation To The Risk Of Ovarian Cancer/ DENİZ BAKIR

ID 36 A Case Of Chronic Myeloid Leukemia With Thalassemia Trait Presenting With High Platelet/Eosinophil/Leukocyte Levels And Splenomegaly/ ALPARSLAN MERDİN

TURQUOISE HALL

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ID 50 Synthesis Of Diarylurea Derivative And Investigation Of Its Activity Against Insulin-Like Growth Factor (Igf) By In Silico Methods/ RUKİYE ÖZYAVAŞ

ID 51 In-Silico Prediction Of Toxicity Parameters Of Some Conventional And New-Generation Anticancer Drugs Used In Prostate Cancer Treatment/ MUSTAFA TUĞFAN BİLKAN

ID 77 Investigation Of Theoretical Activities Of Triazole Derivative Molecules Against Prostate Cancer Proteins/ AZRA HASPOLAT

ID 79 Investigation Of Theoretical Activities Of Aminophenyl Derivative Molecules Against Endometrial Cancer Proteins AZRA HASPOLAT

ID 87 The Effect Of Compound B-84 Containing Azomethine Group On Nqo1 Gene/ SİNEM UYKUN

ID 63 Investigation Of The Effects Of Melatonin On Brain Tissue In Eac Tumour Model By Immunostaining Via Tnf-A, Nf-Kb, Il-6/ SELDA KAHVECİ

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10:30-12:00

Session Chairs: *Ayça TAŞ - NEŞE KEKLİKÇİOĞLU ÇAKMAK*

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ID 81 Investigation of Theoretical Activities of Phenylmethamine Derivative Molecules Against Gastric Cancer Proteins/ İLAYDA BERSU B. KUL

ID 28 Preliminary Study: Optimization Of The Sample Preparation Process For Comparison Of Serum Copper, Zinc, And Manganese Levels Of Individuals With And Without Endometrium Cancer/ DİLARA ÜLGER ÖZBEK

ID 44 Effect Of Alogliptin On Dna Damage In Stomach Carcinoma By In-Vitro Method/ BEHZAD MOKHTARE

ID 67	Effects Of Lacosamide On Cell Viability In Various Cancer Cell Lines/ AYŞEGÜL ÖZTÜRK
ID 2	Investigation Of The Effect Of Sugammadex On Lung Cancer Cells In Terms Of Proliferation/ FATİH YULAK

TURQUOISE HALL

29.09.2023 Friday / 14:00-16:45

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ID 16	Antimicrobial Mouthwash Formulations For Dry Mouth And Removal Of Bad Odour/ EBRAR İNAL
ID 21	Investigation Of Anti-Tumor Activity Of Β - Glucan On Chronic Myeloid Leukemia Cell Line/ ZEKERİYA KESKİN
ID 82	Investigation Of The Antiproliferative Effect Of N-(P-Amylcinnamoyl) Anthranilic Acid On The Ags And Snu-1 Cell Lines/ ZIAD JOHA

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ID 88	Effect Of B-104 Compound Containing Azomethine Group On Prdx1gen In Saos-2 Cell Line/ GONCA KABAK
ID 54	The Most Common Causes Of Acute Kidney Injury In Oncological Patients Admitted To The Nephrology Clinic/ SARA YAVUZ İLERİ
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POSTER PRESENTATION PROGRAM

Poster presentations will be hung in the poster area on Thursday at 11:00 and will remain hanging throughout the congress.

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ID 58	Fibroepithelial Polyp Mimicking Sarcomabotryoid Carcinoma- A Rare Case Presentation/ ŞERİFE ÖZLEM GENÇ
ID 73	Protective Effects Of Thiamine Pyrophosphate And Cinnamon (Cinnamomum Verum) Against Oxidative Liver Damage Induced By Isoniazid And Rifampicin Combination In Rats/ ZEYNEP KOÇ
ID 96	Evaluation Of The Attitudes And Awareness Levels Of The Community Regarding Cervical Cancer And Human Papillomavirus Infection/ GÜLGÜN SEVİMLİGÜL
ID 95	Investigation Of Theoretical Activities Of Diflorobenzene Derivative Molecules Against Colon Cancer/ GAMZE TÜZÜN

PREFACE

We have organized the 4th International Cancer Days (4.ICD) this year, which is a multidisciplinary congress within the scope of the activities of the Sivas Cumhuriyet University Cancer Studies Application and Research Center (KANAM). This year's main theme of our congress, which included many kinds of research from Health Sciences such as Medicine, Pharmacy, and Nursing, as well as Physical and Life Sciences, Engineering, and Social Sciences, was "*Prostate Cancer*". Many scientists from inside and outside of Türkiye who conducted many studies in different disciplines shared the most current developments regarding cancer, especially prostate cancer, with the scientific community for three days.

We are honored as the increase in the number of participants since the 1st International Cancer Days (1.ICD) we held in 2019 reflects the care shown and the experiences gained in the organization of our congress. It is our greatest wish to make the International Cancer Days a tradition and to contribute to carrying scientific knowledge to the future. Of course, there is labor and support behind every organization. We would like to thank to Rector Prof. Dr. Alim Yildiz, and his team, as well as to Vice-Rector Prof. Dr. Hilmi Ataseven, and Cancer Studies Application and Research Center (KANAM), to Chairman of the Congress Prof. Dr. Esat Korğali, to Congress Scientific Committee and KANAM Advisory Committee members, to Congress Organizing Committee; Prof. Dr. Zekiye Hasbek, Asst. Prof. Dr. Mukaddes Yilmaz, Asst. Prof. Dr. Mahmut Uçar, Asst. Prof. Dr. Hüseyin Saygin, and Teach. Asst. Rukiye Aslan, to Congress Secretariat Assoc. Prof. Dr. Hayreddin Gezegen, and to the students who never spared their efforts in the execution of our congress, as well as to Sivas Cumhuriyet University Health, Culture and Sports Department, and to all sponsors for their financial support who participated in our congress for have supported us in our organizations and continuity of our congress since the first day we planned our first congress. See you at the 5th International Cancer Days (5.ICD) next year.

Prof. Dr. Zekiye Hasbek
Director of KANAM

Our congress provides the requirement which is included in the new associate professorship criteria "In the organizing committee of another international/national scientific meeting, there must be an academician representative of the university/institute/scientific institution/branch association officially appointed by the institution/legal entity/decision body" . You can scan the QR code on the side to access the relevant document.

PANEL PRESENTATIONS

JOURNEY OF NUCLEAR MEDICINE IMAGING IN PROSTATE CANCER

Abdullah Hanif Rosdi

Nuclear Medicine Department, Hospital Kuala Lumpur, Malaysia

ABSTRACT

Prostate cancer is the 6th leading cause of cancerous death in man in the world. The main hindrance in treating prostate cancer patients is the high percentage of biochemical recurrence incidents. To overcome this matter, a few nuclear medicine imaging methods have emerged from the last centuries.

For early detection of biochemical recurrence, several improvements have been made in nuclear medicine imaging by shifting from 2D to 3D imaging, gamma camera to PET imaging and improvement of radionuclides itself. With the latest high detection capability of Ga-68 and F-18 PSMA imaging with low PSA value, these modalities are the current gold standard imaging for prostate cancer biochemical failure.

Keywords: *Prostate cancer biochemical recurrence, Ga-68 PSMA, F-18 PSMA*

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ACTIVE MONITORING AND FOCAL TREATMENTS

M. Öner Şanlı

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ABSTRACT

Prostate cancer (PCa) is one of the most common cancers among men worldwide and represents a significant public health issue due to its high prevalence. This text provides a more in-depth look into prostate cancer, focusing on two key aspects: active surveillance and focal therapy for localized disease.

Prostate cancer is particularly prevalent among older men and occurs when cells in the prostate gland grow abnormally, potentially spreading to other organs over time. The significance of PCa lies in its high incidence and the quality-of-life issues it can cause. Statistics show that cases diagnosed with PCa are steadily increasing, primarily attributed to better screening methods and an aging population. Moreover, PCa carries a substantial burden, both for individuals and in terms of public health. Diagnosing and treating this disease can be costly and may negatively impact the quality of life of affected individuals. Additionally, those diagnosed with PCa and their families may face psychological and emotional challenges in coping with the diagnosis. Therefore, prostate cancer management should aim to improve patient's quality of life and optimize treatment outcomes.

One approach to managing PCa is active surveillance, especially for low- and low-risk patients. This strategy involves a monitoring approach rather than immediate aggressive treatments. Active surveillance allows patients to avoid direct surgical or radiation interventions, potentially sparing them from the side effects of these treatments.

Active surveillance includes regular monitoring of the cancer's progression through PSA (prostate-specific antigen) tests, digital rectal exams, and periodic biopsies. However, it's important to note that active surveillance can subject patients to ongoing uncertainty about the progression of their cancer, leading to psychological stress and anxiety. Furthermore, the strategy must be carefully managed, as there is a risk that the cancer may become more aggressive over time.

Localized PCa treatment through focal therapy has gained attention as an approach that aims to target only the affected regions within the prostate, minimizing damage to healthy tissue. While this approach may have fewer side effects than surgery or radiation therapy, it has potential downsides.

One major drawback is that focal therapy may focus solely on specific cancerous areas, potentially overlooking cancer cells in undetected regions. This can increase the risk of cancer recurrence. Additionally, there is limited long-term data on the effectiveness of focal therapy. In contrast, more traditional methods like surgery or radiation therapy have undergone more extensive long-term research and are better documented. Moreover, even during focal therapy, some patients may still experience unwanted side effects, including urinary incontinence and erectile dysfunction, which can significantly impact their quality of life.

In conclusion, PCa necessitates a comprehensive management approach due to its prevalence and significance. While active surveillance offers a conservative alternative, it can subject patients to prolonged uncertainty and psychological stress. Although focal therapy is promising in reducing side effects, it has disadvantages, such as the risk of undertreatment and limited long-term data. The management of PCa should be carefully tailored to individual patient needs and risk factors to achieve the best possible outcomes and improve overall quality of life.

RADIOTHERAPY AND COMPLICATIONS IN PROSTATE CANCER

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ABSTRACT

Definitive radiotherapy (RT) is one of the primary treatment options in localized prostate cancer and can be administered as external beam radiotherapy (EBRT) or brachytherapy (BRT). The lack of randomized studies comparing primary treatment models in prostate cancer, it difficult to compare the treatment options with each other. In the case of biochemical progression -free survival, the results of curative treatment options are equivalent. In low risk cases, the best biochemical progression -free survival is provided with BRT or EBRT. In medium risk cases, the EBRT+BRT combination alone did not give better results than EBRT and radical prostatectomy (RP). EBRT or BRT is administered in low -risk cases as monotherapy. However, brachytherapy and hormonotherapy (HT) are added to EBRT treatment in medium -risk cases. Biochemical -free survival is prolonged when high RT doses are applied in localized prostate cancer. Increasing RT dose increases biochemical control, but also increases the risk of toxicity. In the last twenty years; as a result of the development of three -dimensional conformal radiotherapy (3D-CRT), intensity modulated radiotherapy (IMRT), image guidance radiotherapy (IGRT), brachytherapy, stereotactic body radiotherapy (SBRT) and proton treatments ;treatment results improved and toxicity decreased. With modern RT techniques, it became possible to increase the tumor dose without a significant increase in acute and late toxicities. Brachytherapy is a radiotherapy method that provides high dose radiation to a limited area, and is applied by placing radioactive resources into or near the tumor. The most important difference from EBRT is that smaller treatment volumes are given higher doses and the rapid decrease in the dose except treatment volume. With this feature, BRT is the most conformal RT technique. Although a single treatment model (EBRT, BRT) is sufficient in low-risk cases, the positive effect of adding long-term HT to RT in high-risk cases has been clearly demonstrated in randomized studies. The use of combined HT and EBRT in intermediate-risk cases is one of the most controversial issues.. In these cases, it is predicted that treatment should be between the two, as the aggressiveness of the disease is low and high risk. However, the number of moderate cases in randomized studies is low and mature data for medium -risk cases are as well as being limited. However, in these cases, short -term HT is recommended with EBRT. Local control rates in prostate cancer increase due to dose, but complications that may occur due to adjacent neighboring organs limit the dose increase. Especially bladder, rectum and femur heads are basic dose limiting organs. Rectal bleeding, cystitis and avascular necrosis are side effects that may significantly disrupt the patient's quality of life.

Keywords: *Prostate cancer, external beam radiotherapy, brachitherapy*

RADIOLIGAND THERAPY IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

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ABSTRACT

Metastatic castration-resistant prostate cancer (mCRPC) presents a formidable challenge in oncology, demanding innovative therapeutic approaches to enhance patient outcomes. In recent years, radioligand therapy (RLT) has emerged as a groundbreaking option, revolutionizing the management of mCRPC. This talk explores the principles, benefits, and potential of RLT in mCRPC.

RLT is founded on the concept of precision medicine, tailoring treatment to target specific molecules expressed on cancer cells. Prostate-specific membrane antigen (PSMA) is a prime target in mCRPC due to its high expression on prostate cancer cells. Radioligands, such as Lutetium-177 (Lu-177) PSMA-617, bind specifically to PSMA receptors. They deliver a highly concentrated radiation dose to cancer cells, sparing healthy tissues. This targeted approach minimizes side effects and maximizes the therapeutic impact.

One of the primary advantages of RLT is its efficacy in patients who have exhausted conventional treatments. Clinical trials have shown that RLT significantly extends survival and enhances quality of life. Patients experience reduced pain, improved overall well-being, and better control over disease progression. RLT is particularly promising in cases where other therapies have failed.

Another critical aspect of RLT is its convenience and safety profile. Side effects are generally mild and transient, including fatigue and dry mouth. RLT is an attractive option for patients seeking therapies with manageable side effects.

Furthermore, ongoing trials preresults show that RLT demonstrates versat ility in combination therapy strategies. It can be seamlessly integrated with other treatments like hormonal therapy or chemotherapy, offering a multimodal approach to managing mCRPC.

ORTHOPAEDIC APPROACH TO BONE METASTASES

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ABSTRACT

Metastases are the main cause of destructive bone lesions in adult patients. In the diagnosis, a direct radiograph of the upper and lower joints is the main examination. In the presence of bone lesions in tumours of unknown primary, a biopsy should be obtained. The main principles of treatment are pain control, maintenance of patient mobility and fracture prevention.

Keywords: *Bone tumour, metastasis, orthopaedic approach*

Introduction

Bone is the third most common site of metastasis after lung and liver. Demographically, it is more common in patients over 50 years of age. In terms of anatomical location; vertebrae > proximal femur > humerus are the most commonly affected sites. Patients present with pathological fractures in the proximal femur and humerus respectively. In the follow-up of these fractures, 65% nonunion is encountered. In the proximal femur, the site of metasasis is: 50% femoral neck, 20% pertrochanteric, 30% subtrochanteric, respectively.

Acral (distal extremity) lesions are rare. If seen, it is usually: lung carcinoma. Occult metastasis: associated with lung cancer. Tumours that like to metastasise to bone are: breast, lung, thyroid, renal, prostate. The most common reason for presentation to the clinic is pain. There are two types of pain. The first one is movement pain due to bone destruction. The second is nocturnal pain due to tumour.

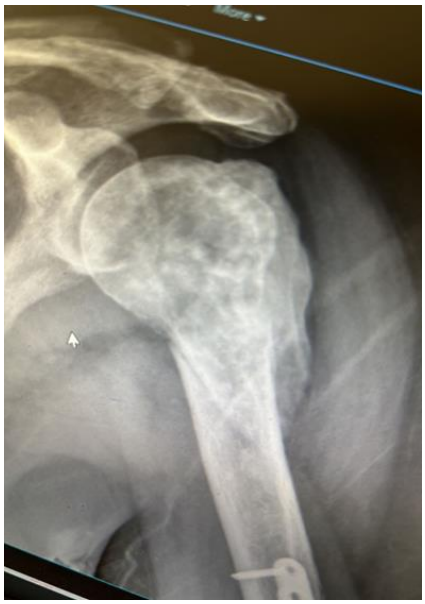

Figure 1. *AP view of the proximal humerus. Left shoulder. Blastic metastasis and pathological fracture of the proximal humerus are observed.*

Laboratory

A complete blood count should be requested from the patients at the first visit. In addition, hypercalcaemia, increased ALP, phosphorus and LDH may be observed in biochemistry. Serum immunoelectrophoresis and Bence-Jones proteinuria in urine may be investigated. Thyroid function tests should be requested. Specific tumour markers; PSA, CEA (colon, pancreas), CA125 (ovarian), CA19.9 (colon), CA 15.3 (breast) tests should be obtained in patients with metastasis.

In the presence of multiple bone lesions in the elderly patient; metastatic bone disease, myeloma, lymphoma, paget disease, hyperparathyroidism may be considered.

Non Operative Treatment

Bisphosphonate therapy can be used in lyticblastic and mixed lesions. It reduces lysis and associated hypercalcaemia. Denasumab is an agent that can be used in treatment. Indications for radiotherapy can be summarised as follows:

1 - Pain palliation and local tumour control

2 - Mirel score below 8

3 - Presence of radio-sensitive tumour

Operative Treatment

Fracture stabilisation and postoperative radiotherapy is a treatment approach used in metastases. The aim is to improve quality of life and pain control. Some tumours with high bleeding risk may require preoperative embolisation. These include thyroid and renal metastases (Figure 2).

5-year survival is 20% in the presence of multiple metastases and 40% in the presence of solitary metastases.

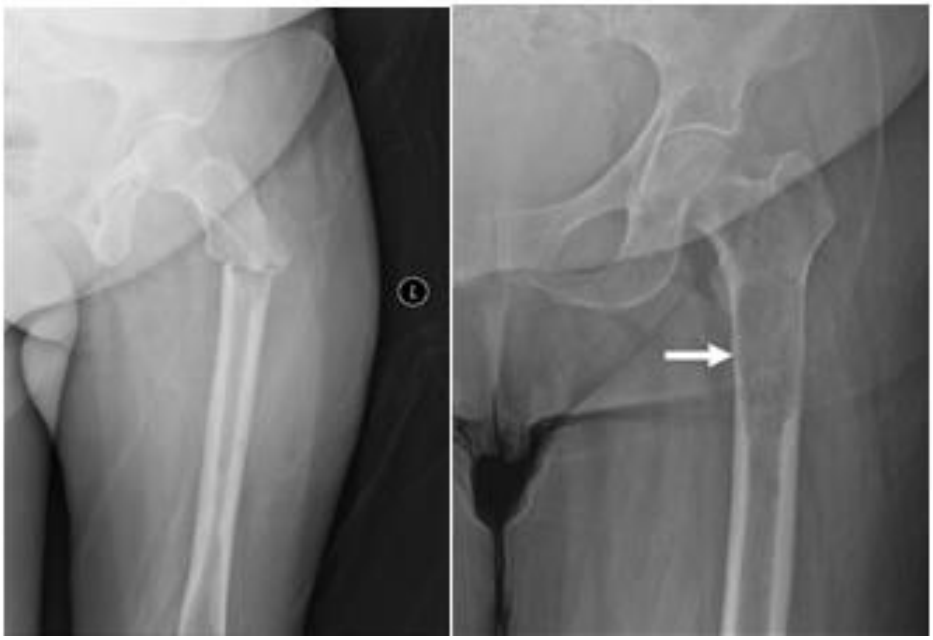

***Figure 2**. Fracture in the left proximal femur due to metastasis in the left figure and cortical thinning in the right figure.*

There are some scoring systems used before deciding on prophylactic fixation. Mirel scoring is the most important of these (Table 1).

Table 1. Mirel Criteria

Score	**1**	**2**	**3**
Location	Upper limb	Lower limb	Pertrochanteric
Pain	Mild	Moderate	Severe
Lesion	Blastic	Mix	Lithic
Size	<1/3	1/3-2/3	>2/3
If the score is > 8, prophylactic fixation is recommended.			

Treatment algorithm

If the primary lesion in the bone is not clear, surgical decision is not taken without biopsy. A fixation method that allows rapid mobilisation and load bearing of the patient should be preferred. Implant selection should be made considering the whole prognosis of the patient. These issues should be considered by evaluating the humerus and femur separately. Endoprosthesis may be preferred in proximal humerus lesions. In diaphyseal lesions, intramedullary nail, resection and intercalary spacer, and to a lesser extent plate screws may be preferred. In the distal humerus region, elbow prosthesis or flexible nails are among the treatment options. (Figure 3)

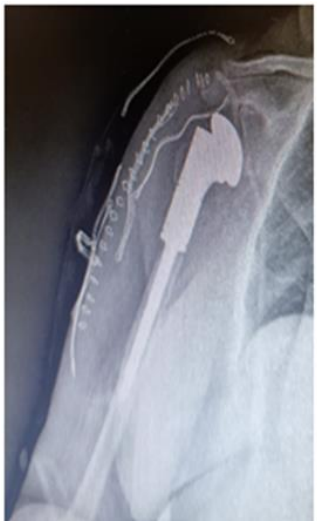
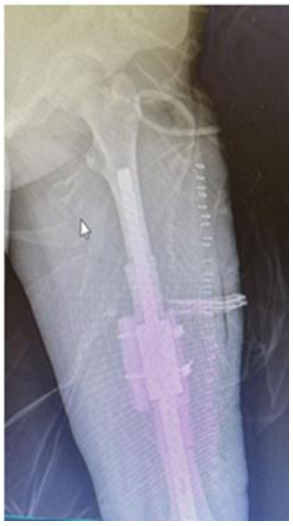

Figure 3. *Proximal humeral tumour prosthesis is seen on the left. On the right, an intercalary prosthesis application is observed.*

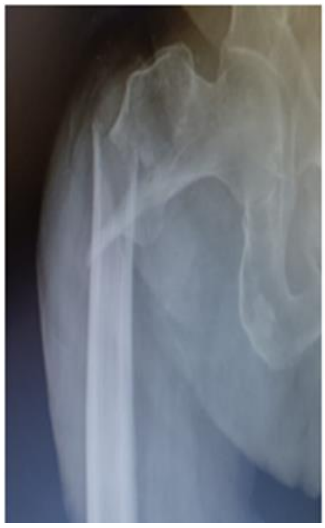
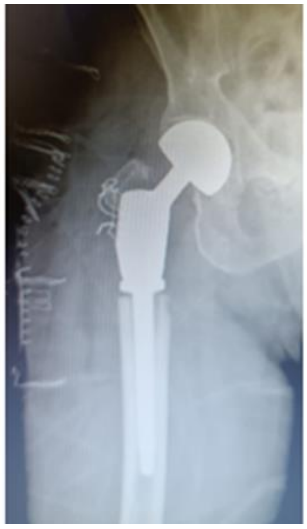

Figure 4. *Tumour prosthesis applied to the right hip of a patient with pathological fracture due to metastasis.*

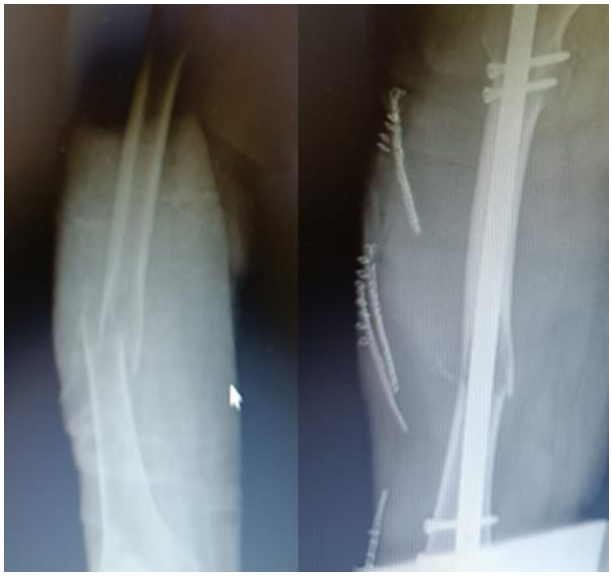

Figure 5. *Intramedullary nail application in a patient with pathological fracture of the femoral shaft.*

Intramedullary nails are preferred for pertrochanteric lesions of the femur. In patients with femoral neck and head involvement, hemiarthroplasty is preferred. If there is metastatic involvement of the acetabulum, total prosthesis should be considered (Figure 4).

Diaphyseal prostheses or intramedullary nails can be used for lesions in the diaphyseal region of the femur (Figure 5).

In Conclusion

The main cause of destructive bone lesions in adult patients is metastases. A direct radiograph showing one upper and one lower joint is the basis for diagnosis. In tumours of unknown primary, a biopsy should be taken from the bone lesion. The main principle of treatment is pain control, maintenance of patient mobility and prevention of fracture.

SURVIVAL FROM PROSTATE CANCER AND PSYCHOSOCIAL PROBLEMS

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ABSTRACT

Cancer is an important disease that threatens human health. Global cancer incidence and mortality rates have dramatically been increasing. However; thanks to technological advancements in health and cancer diagnosis and treatment in the last 30 years, quality of care has risen and thus the number of those who survive from cancer has increased. The people's post-cancer treatment status is described with the term of survivorship. The process of cancer survival includes the cancer diagnosis, the process of therapy and the transition period from the termination of therapy to normal living period. Cancer survival rate is affected by many factors such as type of cancer, stage of cancer, age of patients, presence of comorbid diseases and the therapy administered. Significant differences exist among the countries in terms of cancer survival rates.

Since cancer diagnosis is a serious crisis experience, it is stated that patient problems are taken into consideration much more in the acute treatment period but problems of those who have recovered are not listened to enough. Patients can suffer from treatment-induced effects in cancer survival period long after they return to healthy life after the therapy and can undergo many physical, psychological and social problems. These problems influence their lives negatively and weaken their quality of life. Prostate cancer is one of the cancers whose survival rate is high. It is suggested that among the prostate cancer survivors, risk of occurrence of psychological disorders is high and such psychological disorders as anxiety, depression are often seen. Cancer survivors need to get health services in survival period as in treatment period. Therefore; it is necessary that cancer survivors should be monitored and measures that include improving physical functioning, preventing complications and offering supports to patients and families should be taken in health facilities.

Introduction

Today, cancer is still considered as a crucial disease that threatens human health. Over the world, cancer incidence and mortality rates have fast been increasing. According to global health statistics 2018, the number of patients with cancer is 18 million and it is projected that the number of new cancer cases will have risen to 27 million by 2030 and if necessary measures are not taken, the number will have reached 40 million by 2040 [1]. The Global Cancer Observatory (GCO) has reported that the number of patients with cancer diagnosis was 19.3 million in 2020 and nearly 10 million people die of cancer each year [2]. As new diagnosis tests and screening programs are performed depending on technological developments in health, cancer diagnosis can be made earlier. The number of those surviving from cancer has grown thanks to the advancements in cancer treatment and thus improvements in cancer care. With prolonged cancer survival period, cancer has now been considered as a chronic disease and new terms such as survival and five year survival are now in literature [3].

Cancer survival in literature is linked to "survivors" meaning "cancer survivors/ cancer survival" after cancer diagnosis. The term has been coined and published in the literature for the first time by Fitzhugh Mullan, a medical doctor, in 1985 with his article "Seasons of survival: reflections of a physician with cancer". Mullan identified his survival period as "acute survivorship" -which starts with cancer diagnosis and initial treatment-, "extended survivorship" -which includes the termination of treatment and remission period- and "permanent survivorship" -in which disease is inactive [4]. In 2019, American Cancer Society identified cancer survival

phases as the initial period in which cancer diagnosis is made and the therapy is terminated, the transition period that continues from the end of therapy to returning to normal life and the long term period without cancer [5]. The dictionary of Turkish Language Association describes survival as "continuing to live or exist".

Another term, used together with cancer survival, is "five year survival rate". This term is a popular and frequently referred for life time statistics. This term means the percentage of people who are alive at least five years after following diagnosis [5]. Globally speaking, there are significant differences among the countries in terms of cancer survival rates. In a study done in relation to five year cancer survival, records of 37 million 513 thousand and 25 patients diagnosed with cancer were reviewed between 2000-2004 in 71 countries and it was found that five year cancer survival rate in America, Canada, Australia, New Zeeland, Finland, Iceland, Norway and Sweden were high among the patients diagnosed with cancer [6]. It is reported that targeted treatments and new treatment protocols have positively affected survival rates in hematopoietic and lymphoid malignancies and five year cancer survival rate among the patients diagnosed with chronic myeloid leukemia was 22% in 1970s whereas it rose to 70% between 2009 and 2015 [7].

Cancer survival rate is affected by numerous factors like age of patients, type of cancer, phase of cancer, presence of comorbid disorders, therapy administered (American Cancer Society 2019).

It is reported that survival rates in America are 98% for prostate cancer, 92% for skin melanoma, 90% for breast cancer, 20% for esophagus cancer, 19% for lung cancer, 18% for liver cancer and 9% for pancreas cancer (American Cancer Society 2019; Siegel 2020). In a study in which cancer records in our country were reviewed by Ege University Cancer Research Center between 1992 and 2017; survival rates were reported to be 96% for thyroid cancer, 85.3% for breast cancer, 74.2% for prostate cancer, 53.1% for colorectal cancer, 27.3% for stomach cancer and 15.2% for lung cancer [8]. The term of survival means differently for patients with cancer diagnosis, treatment providers and those in society. Survival means "living the moment/seizing the day" for patients, "the period that begins with diagnosis and continues without disease or relapse" for oncologists and "continuing their own lives after the death of a bellowed one or a family member" for society [9].

Because cancer diagnosis is a serious crisis experience, health personnel and family pay more attention to patients' problems during acute treatment period and all energy and resources are spent for recovery but problems of those recovering are not dealt with enough [10]. In this sense, cancer survivors have written many books on enhancing the term of survival. These books draw attention to how they have defeated cancer by controlling their own lives, thinking positively and changing their values. Although these stories of survivors inspire those with cancer diagnosis, dark side of cancer still manifests itself. Cancer survivors experience ambiguity about their roles in life and generally have difficulty resuming pre-cancer roles. Their friendship relations change and close relations weaken. They feel concerns and ambiguity about future but these are not signs of depression. Such symptoms as recurrent nightmares, inappropriate emotions and difficulty with concentration may be seen among these individuals but they are not post traumatic stress disorders. Suicide is rare among cancer survivors [9].

Cancer survivors are aware of the change that they experience. There are three common realizations among these surviving individuals. First; cancer patients are always cancer patients; that is, they are aware of cancer stigma. Second; cancer patients are aware of the delusion of his body and disease itself. They have the thought and fear that the body is no more transparent and disease may recur. Third; cancer patients are aware that they undergo an intense and different experience and this experience is specific only to them. Since cancer is a serious threat to existence, survivors do not give meaning to life as they do in pre-diagnosis period and try to lead a life in which they do things that make them feel good [11].

During cancer survival, individuals can have long term aftereffects due to cancer therapies, even long after they have resumed healthy life; like physical problems (neuro-sensory changes, low saliva production, low taste perception, periodontal diseases, cardiac disorders, skin problems, secondary cancers) and psychological problems (anxiety, depression) and social problems (difficulties at work, role changes); which may influence negatively their lives and result in poor quality of life (Kıyak and Özkahraman 2021). Besides, survivors' anxiety levels go up due to new post-treatment confusions relating who will give them health services, how often they

will receive these services, disease recurrence, management of late side effects, role and responsibility changes, secondary malignancies, reproduction disorders, body image changes [12,13].

In cancer survival; individuals think of death even if they do not want to, when they meet someone diagnosed with cancer, visit health facilities for medical checks or anniversaries of hard times during disease process (for example, the time diagnosis is made). Moreover, psychological problems like anxiety, depression may be experienced owing to communicational problems, difficulties at work, fear of disease relapse [14,15].

One of the cancers survival rate of which is high is prostate cancer. It is the second most commonly seen cancer among men and is ranked as the fifth cancer-caused death [16]. Prostate cancer has the second highest five year survival rate (98%) following thyroid cancer [17]. In a study done by [18] survival period of 66% of the prostate cancer patients was reported to be 6 years.

Over the last 20 years, prostate cancer mortality rate has reduced in high income countries while its global incidence and disease burden has increased [19]. Therefore, quality of daily life of patients living with prostate cancer is negatively affected in the long journey of cancer survival due to prolonged survival period and increased disease burden. Additionally; it is underlined that patients with prostate cancer diagnosis and those who have survived from the disease are likely to develop psychological disorders, this risk is 1.5 times greater than other cancer patients and twice higher than those men who have never received cancer [20,22]. In the studies done, it is identified that anxiety prevalence in prostate cancer survivors ranges between 15% and 27% whereas anxiety prevalence in those men at similar ages in the general population is smaller than 6% [21]; rate of depressive symptoms varies between 16% and 30% while it is lower than 9% in men at similar ages in the general population [23]. On the other hand; it is argued that patients' psychological and physical needs are more common during the early phases of prostate cancer survival period while in later periods physical, social and spiritual needs are more dominant [27]. In a study done by Zhou et al. [24] with prostate cancer survivors, it was reported that 27% of the individuals needed information and support to cope with emotional problems, 52% of them were unable to overcome late side effects of therapy and 64% of them suffered from sexual dysfunctions. Marziliano et al. [25] found both physical (urinary, bowel problems, sexual dysfunctioning) and psycho-social (high anxiety, low quality of life, depression, adaptation difficulties, fears about cancer recurrence) problems among prostate cancer survivors due to the disease and treatment.

No matter what type, surviving cancer patients meet oncology team less after cancer treatment and their follow-up are mostly performed by primary health care services. Yet, it is reported that surviving cancer patients have difficulties achieving comprehensive care and follow-ups at primary health care facilities due to poor capacity of these systems. As a result, it is necessary to provide basic arrangements in health services for monitoring cancer survivors and to design required strategies and policies (26,3). Likewise, using rehabilitative and supportive approaches, cancer survivors' physical functioning can be improved, complications can be prevented and high quality of life can be achieved [29].

It is important for patients surviving cancer to go on daily life and to go back to professional life; which will help them attain high productivity, high self-worth and high socialization [30]. Besides, cancer survivors should be backed to learn and to use successful coping methods against physical and emotional changes and be encouraged to reorganize new life styles. It will help them enjoy life when they join support groups and maximize interaction with family and other social support resources [31].

In America and Europe, follow-up programs that assess cancer survivors in a multidisciplinary approach, detect and treat recurrence signs and late signs earlier, create awareness against disease stigma, teach patients how to adopt health promoting attitudes and behaviors and offer the patients and their families support and counseling have been designed [32].

Understandings about the experiences of cancer survival are new both for health system, members of health team, cancer survivors and families. Therefore; it is crucial to understand that "surviving from cancer is not just the end of a story but the start of another story, which is generally a rather overwhelming story" and to provide basic plans and arrangements. Cancer surviving individuals need to get health services in survival period as in treatment period. In sum; measures that include monitoring cancer survivors, improving physical functioning, preventing complications and offering supports to patients and families should be taken in health facilities.

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NURSING CARE IN PROSTATE CANCER

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Prostate cancer

It is the second most common type of cancer in men in the world, after lung cancer. It is the fifth type of cancer that causes death in men, with a mortality rate of 7.6 per 100,000 people worldwide. It is the second most common cancer type among men in Türkiye, with a prevalence of 13%. Although it is a serious public health problem in the world, treatment and care require a professional approach. With advances in diagnostic methods, prostate cancer can be diagnosed in the early stages. The incidence of prostate cancer increases with age, and when diagnosed early, the survival rate is quite high with the right treatment and care. Patients diagnosed with prostate cancer often experience many problems such as psychosocial problems, fear, pain, inability to eat, weight loss, sleep problems, getting tired easily, and weakness due to treatment. In this sense, nursing care in prostate cancer is complex and very important. Individuals diagnosed with prostate cancer may experience both psychological and physical problems.

O'Shaughnessy et al., in their study where they determined the supportive care needs of patients diagnosed with prostate cancer; Fear, Anxiety, Depression, low self-esteem, sexual problems, Pain, urinary incontinence, Decrease in quality of life, They determined that they experienced lifestyle changes. Especially in Individuals Diagnosed with Prostate Cancer Who Are Undergoing Chemotherapy Treatment; Feeling of discomfort while urinating, frequent urination, Nausea, Loss of appetite and weight loss. These symptoms affect individuals physiologically, psychologically and socially: Weakness, fatigue, Problems in sexual life, Pain, Deterioration in social relationships, Stress, anxiety, depression, Sleep problems may occur.

Nursing care in prostate cancer

Pre-Operatıve Care In Prostate Cancer

1. Preparation until the night of surgery, 2. Preparation the night before surgery, 3. Preparation for the day of surgery

Nurses should aim to increase the quality of life of the patient by considering the patient's physical, social, cultural and spiritual whole with the care interventions they provide before, during and after prostate cancer surgery, and nursing care should be planned individually, sensitively and holistically.

pain control, Urinary catheter care, Ensuring proper nutrition and hydration, Continuing activity-exercise, Pelvic muscle exercise training, Informing the patient. It has been determined that it is aimed at providing education and psychosocial counseling regarding the signs and symptoms of postoperative complications.

1-Preparation until the night of surgery

Preoperative preparation and care, which begins with the patient's admission to the surgical clinic: Psychological preparation, physiological readiness, legal preparation, Preoperative education, Psychological Preparation. Surgery is not only a source of physiological stress for the patient, but also a strong source of psychological stress. Therefore, the patient's psychological preparation before surgery is as important as his physiological preparation. A good evaluation of the patient's condition during this period depends on collecting data regarding problems that may arise in the pre- and postoperative period.

Psychological Preparation

Although patients accept that surgery is beneficial for them, they are afraid of the risks of surgery.

One of the most important causes of anxiety before surgery is the fear of the unknown. Therefore, patients need information about postoperative pain, activity level, exercises, possible complications, care of the surgical area, surgical method to be applied, hospital stay, discharge and post-operative education. Nurses should reduce the anxiety of the patient and his family by providing information about the period before, during and after surgery. Preoperative patient education reduces the patient's anxiety and helps control pain. Complementary therapies can also be used as nursing interventions to reduce preoperative anxiety. In the study examining the effect of music in reducing patients' anxiety; It was determined that the anxiety levels of the patients in the experimental group decreased significantly.

Before surgery, the patient's health status can be determined by a good physiological evaluation; Age, Pain, nutritional status, Infection, Fluid-electrolyte balance, cardiovascular function, Pulmonary function, GIS functions, liver function, endocrine function, neurological function, Hematological function, renal function, Medicines, Preoperative education, Deep breathing exercises, Cough exercises, Rotation and limb exercises.

2-Preparation for the Night Before Surgery

Determining the day of surgery increases the patient's anxiety and fear, and may cause inadequacies in his/her participation in care and in perceiving and implementing what is said. Therefore, it is important to determine whether patients understand what is said correctly and completely. Preparation the night before surgery; Skin preparation, Gastrointestinal system preparation, Anesthesia preparation, Providing rest and sleep

3-Surgery Day Preparation

The patient and his/her relatives are informed. It is checked whether the patient is hungry or not. It is checked whether the patient's bowel has been cleaned or not. Medicines that need to be given orally and are important are given with a very small amount of water. The patient's vital signs are taken and recorded, and if there is an abnormal situation, it is shared with the team. If there is a special situation such as IV fluid administration, these are applied. The patient's bladder is emptied. It is ensured that the bladder of the patient with a urinary catheter is empty. If the patient has requested blood, it is checked whether the blood is ready or not. The patient is told to brush his teeth and remove any dentures. The patient is sent to the operating room on a stretcher with his file, medications, supplies and fluids.

Post-Operative Care In Prostate Cancer

Mata et al., in their study in Brazil, found that nursing care after prostate surgery; Drug administration (analgesics, antiemetics, antibiotics and histamine antagonists), Monitoring vital signs, The impression he gets, Permanent vesical catheter management, They determined that it focused on infection prevention and wound care.

Pain Control: It is reported in the literature that the pain level after laparoscopic/robotic prostatectomy is mild to moderate. Prospective cohort studies by Lukasewycz et al. emphasized that pain after robotic radical prostatectomy is adequately controlled primarily with NSAIDs (non-steroidal anti-inflammatory drugs) and opioids. Although postoperative pain is perceived as normal due to a concrete reason such as surgical trauma, it must be controlled with a multimodal approach, as it negatively affects the activity of many organs/systems, especially the respiratory and circulatory systems, disrupts their functions and prolongs the healing process.

Urinary Catheter Care: Maintenance of the catheter is as important as its application. Providing information about the importance of postoperative fluid intake and catheter care is an indispensable practice in preventing urinary infections. Hands should be washed before and after contact with the catheter. Sterile gloves should be used for each patient. The area around the urethra should not be wiped with antiseptic solutions while the patient has a catheter. It is stated that regular washing or wiping with antiseptics is not beneficial in preventing infection. Procedures regarding the care, application and removal of the catheter should be

recorded, and healthcare professionals should be constantly trained about the application and complications of the catheter.

A guide for the prevention of catheter-associated urinary infections (CI-UTIs) was published by the Centers for Disease Control and Prevention (CDC) Health Care Infection committee in 2009 and was updated in 2017; The catheter should be inserted by healthcare professionals, The catheter should only be used when indicated, The catheter should be inserted using aseptic technique, Before inserting the catheter, the perineal area should be cleaned with antiseptic sterile solutions, Protection of the closed drainage system must be ensured, The catheter should be removed as soon as possible.

Teaching the patient and their family how to empty the bladder bag, and informing them that the bladder bag should be placed next to the bed to ensure the patient's comfort while sleeping at night,

Securing the catheter to the upper inner thigh or abdomen with water-resistant tape to prevent it from dislodging. Reporting when, where and by whom the catheter was removed are also recommended practices. Pelvic Muscle Exercise Training Pelvic floor exercises are recommended for patients to ensure early continence in the postoperative period. The patient should be instructed to perform pelvic exercises daily after the catheter is removed to help with urinary incontinence.

Activity-Exercise: After prostatectomy, the patient should be mobilized as soon as possible. Inactivity; It causes problems such as venous thromboembolism, loss of muscle strength, respiratory problems, ileus, decrease in tissue oxygenation and increase in insulin resistance. Exercise is recommended for men with prostate cancer because it increases muscle strength and quality of life and reduces the effect of fatigue on daily life. The patient should be informed about restricting activities such as heavy lifting, driving and sexual intercourse after discharge, and about returning to work.

Nutrition-Hydration: The risk of developing complications should be reduced by ensuring good nutrition after prostatectomy. It is recommended to evaluate the nutritional status of patients using valid tools such as postoperative malnutrition universal screening tool (MUST) and nutritional risk screening (NSI). Recommendations regarding postoperative nutrition from the European Society for Clinical Nutrition and Metabolism (ESPEN): Informing the Patient and Maintaining Communication, Communication problems between nurses and patients after prostatectomy should be identified and appropriate interventions should be planned. However, it is important to inform patients verbally and in writing to improve their self-care skills.

Psychosocial Problems And Nursing Approaches İn Prostate Cancer

Stress In Prostate Cancer: Causes of stress; After treatment, men lack information about whether erectile dysfunction is long-lasting and when they will return to their previous state.Possibility of cancer recurrence in patients diagnosed with prostate cancer and recovered, Patients re-diagnosed with cancer, They may re-experience the feelings of shock, disbelief, anxiety, fear, grief, loss of control and stress that they previously experienced when they were first diagnosed. Patients who re-experienced these feelings stated that they could not find the strength to relive the treatment process. Nursing care to be given to patients experiencing stress

Anxiety In Prostate Cancer: Studies have shown that the anxiety levels of prostate cancer patients are proportional to the stage of the disease. High anxiety levels may affect the patient's decision-making in determining the preferred treatment. In the study of Johannes et al., it was observed that the pain score in patients with advanced prostate cancer was significantly higher than in those with early stage prostate cancer, and cancer pain had a significant effect on the anxiety level in prostate cancer patients. High anxiety level negatively affects the quality of life of patients with prostate cancer. Therefore, it is important to determine the anxiety levels of patients in the early period. Nurses; It is important to determine the anxiety level of all patients, especially considering that patients who are young, have had a biopsy or PSA test, and have a family member with prostate cancer may have high anxiety levels.As a result of the study conducted by Albaugh et al., group-based cognitive behavior interventions, education given by nurses, peer support and group discussion, etc., are used to increase treatment compliance and reduce anxiety levels of prostate cancer patients. It is recommended to implement psychosocial interventions.

Depression In Prostate Cancer: Since depression negatively affects the patient's quality of life and the prognosis of the disease, routine monitoring is recommended. It is important for nurses to evaluate prostate cancer patients with depression appropriately and at regular intervals. It should be determined whether patients diagnosed with depression have suicidal thoughts and necessary precautions should be taken. If necessary, the patient should be referred to a psychiatrist. In addition to their roles in the medical treatment of depression, nurses have a significant impact on the patient's compliance with his treatment by collaborating with the patient and his family.

Social Isolatıon In Prostate Cancer: Psychosocial Problems and Nursing Care Psychosocial care in prostate cancer patients requires a multidisciplinary approach. In this approach, nurses have important duties. The nurse has an important position in detecting and managing the patient's existing psychosocial problem, helping the patient and his family cope with the problems, and eliminating the problems. The key to detecting and solving psychosocial problems is effective communication. Nurses should care about the patient's privacy and encourage patients to talk about this issue when providing an appropriate conversation environment.

The nurse should approach the patient sensitively and display a non-judgmental and accepting attitude.

Body image may be negatively affected as a result of changes in the body caused by cancer treatment methods. The patient should be given the opportunity to express his/her feelings, thoughts and self-perception. In order to develop a positive body image, possible coping methods (pleasant smells, etc.) should be discussed with the patient.

The nurse should observe patients for possible psychiatric disorders such as depression, anxiety, and delirium, and investigate patients' suicidal thoughts. Cancer causes patients to confront the reality of death and experience fear of death. Nurses; Patients should not hesitate to talk about the meaning they attach to the disease, their expectations from treatment, and their feelings about death. Group-based cognitive behavior interventions, education provided by nurses, peer support and group discussion, etc. to increase patient compliance and reduce anxiety and depression levels in patients with prostate cancer. It is recommended to implement psychosocial interventions. In the qualitative study of Albough, Sufrin, Lapin, Petkewicz and Tenfelde with 27 patients with prostate cancer, 92.6% of whom underwent surgical intervention, it was determined that patients needed accurate information before, during and after prostate cancer treatment.

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PROSTATE CANCER AND EXERCISE TREATMENT

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ABSTRACT

Cancer is the uncontrolled growth of cells. Prostate cancer is a type of cancer that affects the prostate gland, which produces seminal fluid. Although there have been publications about the relationship between physical activity and cancer recently, there are very few publications in the literature about prostate cancer and exercise. This study aims to explain both the protective effect of exercise in prostate cancer and its use as a medicine, based on the literature.

Exercise prescription should be created with a targeted program according to the patient's stage. If the patient is in good condition, a program consisting of 75 to 150 minutes of moderate intensity aerobic exercise and two or more resistive exercises can be applied. Resistant exercise should include all main muscles and can be performed in 4 sets of 6-12 repetitions. This program can be applied 5-6 days a week or every day.

In conclusion, physical activity reduces mortality and morbidity in men with prostate cancer. Exercise therapy can be given to reduce the side effects of other treatments or to increase their effectiveness.

Keywords: *Prostate cancer, exercise, physical activity, exercise prescription*

Introduction

Cancer is the uncontrolled growth of a group of cells. The main function of the prostate is to produce seminal fluid. Prostate cancer is the second leading cause of cancer related deaths in men [1]. According to TÜİK 2018 data the incidence of prostate cancer in men in all age groups in Türkiye is 15% [2]. The incidence of all cancer types is lower in both men and women than in Europe, Canada, America and Australia [3]. There are two main topics studied regarding cancer and physical activity. These are the protective effect and the healing effect of physical activity [3-7]. In this study, it is aimed to explain both the protective effect of exercise in prostate cancer and its use as a medicine, based on the literature.

With the use of exercise in cancer patients, the number of publications in the literature has begun to increase [3–7]. However, the number of publications about prostate cancer is very low.

Exercise is now accepted as a medicine all over the world and its use is called exercise medicine. Prescribing exercise is regulated and implemented within the protocol. The field of use in cancer patients is called exercise oncology [6,7]. Cancer cells affect both the anatomical and systemic structure of the body. Treatment methods used in cancer also produce different effects. Androgen deprivation therapy (ADT), the primary treatment for prostate cancer, affects quality of life. ADT inhibits testosterone production, suppresses androgen receptors and delays the progression of prostate cancer. Loss of muscle mass, fatigue, psychological problems, cardiovascular diseases and bone fractures may occur in patients. Studies have shown that men with low muscle mass have a higher mortality rate than those with high muscle mass. Again, men with high fat mass have a high mortality rate. The prognosis is also poor. Exercise both increases muscle mass and decreases fat tissue [6–8].

Protective Effect of Exercise Against Cancer

Exercise is a physical activity that requires energy expenditure and contributes significantly to human health [6]. The American Sports Medicine and the American Heart Association defined exercise as a drug in the

prevention and treatment of chronic diseases [3]. According to the World Health Organization Physical Activity 2022 Global Status Report, exercise; Its importance is emphasized in terms of all cause mortality rate, cardiovascular disease mortality, hypertension rate, type 2 diabetes rate, region-specific cancer frequency, mental health (reduction of anxiety and depression symptoms), cognitive health, sleep and obesity reduction [9]. Regular aerobic exercise reduces serum insulin-like growth factor (IGF-1) and insulin levels. However, the IGF-1 rate increases in high-intensity and resistant exercises [10]. They are found in circulation bound to IGF-bp. Since regular physical activity increases IGF-bp, the IGF-1 level in the blood decreases [3,6,10]. IGF-1 reduces the level of cancerous cells.

In recent years, telomeres have been investigated about the protection of exercise in cancer. Telomeres are specialized heterochromatin structures at the ends of eukaryotic linear chromosomes that do not encode any genes. Telomere shortness; It is seen in cancer, psychological disorders, low socioeconomic status, diabetes and cardiovascular diseases [3 11].

Exercise or physical activity (PA) is known to increase oxidative stress. However, continuous application may improve antioxidant activity and benefit REDOX balance [3].

Exercise reduces the amount of fat in the body, which reduces cytokines such as tumor necrosis factor-α (TNF-α), which is released from brown fat tissue and triggers cancer cells, and also increases the level of IL-10, an anti-inflammatory cytokine [12]. When adipose tissue increases, testosterone and estrogen hormone levels increase and cancer types such as prostate and breast cancer are triggered. The reduction of fat tissue with exercise is also protective against cancer in this respect [3,6,13].

Exercise Prescription

First of all, the patient should be evaluated according to the rules of ICF: International Classification of Functioning, Disability and Health (WHO; 2001). ICF guidelines should be taken as a basis for creating exercise prescriptions for cancer patients.

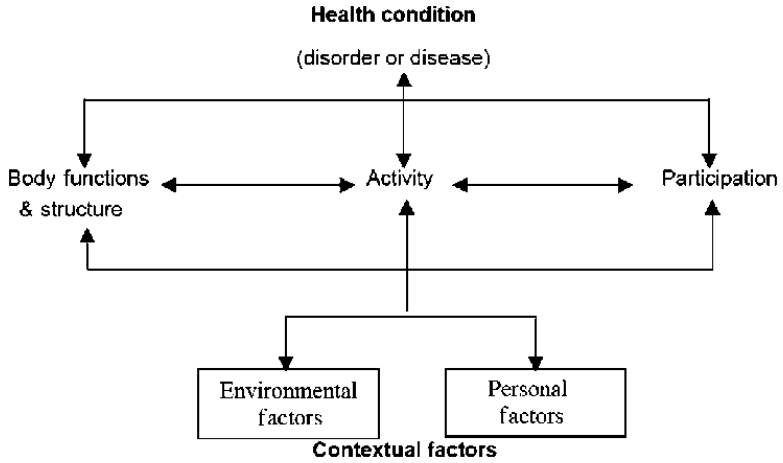

Figure 1. ICF: *International Classification of Functioning, Disability and Health (WHO; 2001)*

Exercise prescription should be created with a targeted program according to the patient's stage. If the patient is in good condition, a program that includes 75 to 150 minutes of moderate-intensity aerobic exercise and two or more resistive exercises can be applied. Resistant exercise should include all main muscles and can be performed in 4 sets of 6-12 repetitions. This program can be applied 5-6 days a week or every day [3, 6].

In patients with high fatigue, a short-term 5-10 minute multiple exercise program can be applied [3, 6]. It is stated that aerobic exercises and resistance exercises are not effective in bone mass loss in patients on ADT treatment. It is suggested that plyometric exercises should be added to the program. In these patients, aerobic exercise should be avoided and resistance exercises should be performed for muscle hypertrophy [3, 6].

The important thing for men with ADT is to prevent bone mass loss. Medium-high intensity, 3-5 sets of 10 to 20 repetitions of jumping exercises (rope jumping, trampoline, etc.) can be applied [3, 6].

Conclusion

Physical activity reduces mortality and morbidity in men with prostate cancer. Exercise therapy can be given to reduce the side effects of other treatments or to increase their effectiveness. Perfusion increases with exercise. It has been observed that 10-20 minutes of exercise in patients receiving radiation makes radiation therapy more effective. Immunity and signaling molecules increase with exercise. It eliminates negativities such as fatigue and loss of bone mass in the patient [4, 7], [14–19].

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SYNTHESIS AND IN VITRO STUDIES OF NEW PEPTIDES THAT CAN BE USED IN THE DIAGNOSIS AND TREATMENT OF PROSTATE CANCER

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Introduction

Prostate cancer is the second most common type of cancer in men and the fifth cause of cancer death worldwide [1]. PSMA, a type II transmembrane protein, is is overexpressed at a high rate and therefore has become an important target for imaging and treating of metastatic PCa. Magistral use of these drugs will not be possible after large pharmaceutical companies complete their licenses. Therefore, starting to develop original PSMA inhibitors is important for our country and for the pharmaceutical industry. In this direction, we aimed to synthesize new patentable peptides for PCa imaging and treatment, based on PSMA-617 and PSMA-11 structures.

Materials and Methods: Receptor-ligand compatibility of peptides was calculated by molecular docking method. Synthesis of peptides was carried out using the solid phase peptide synthesis method. Inhibition studies were performed using the Glutamate Carboxypeptidase II Inhibitor Screening Kit. Total uptake, membrane bound and internalization studies were performed in in-vitro studies.

Results and Discussion: As a result of docking studies, it is shown that the unique molecules we proposed in the project bind to the receptor better than the reference drug currently used. Our aromatic diversified drug candidates are to replace or enhance the aromatic/hydrophobic interactions introduced by the hydrophobic linker. In vitro results showed that the total uptake results of the patentable peptide, which is named as PSMA-dpe and PSMA-bp were closest to the reference peptide (Figure-1). In the future, new modifications will be made and first in vitro and then in vivo studies will continue.

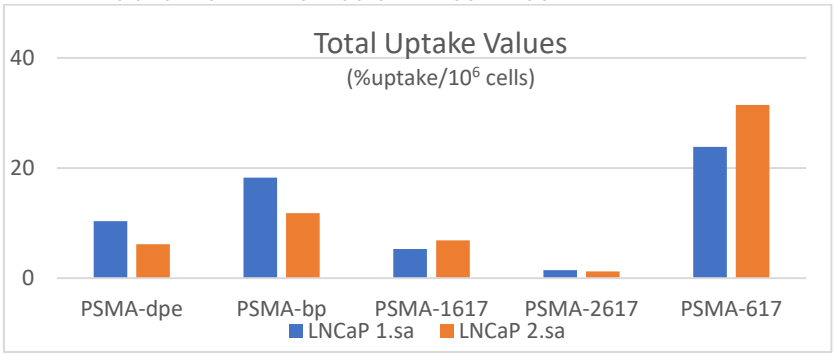

Figure 1. *Total uptake values of LNCaP (PSMA positive) cells*

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NEW BIOMARKERS IN PROSTATE CANCER

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ABSTRACT

The National Cancer Institute (NCI) in the USA defines the concept of biomarker as a molecular structure found in blood, other body fluids or tissues that can be objectively measured and evaluated as a sign of a normal or abnormal biological process and a pathogenic condition or disease.

A biomarker can be used for screening purposes, for assessing disease diagnosis and prognosis, for assessing disease propensity, and for monitoring treatment responses to various therapeutic interventions.

PSA is a serine protease molecule associated with kallikrein produced by the epithelial cells of the prostate gland. It is found in normal prostate secretions and is known to be increased in prostate cancer. Since the 1980s, PSA screening has significantly improved the management of prostate cancer.

There is no biomarker more valuable than PSA for prostate cancer yet, and only a few prostate cancer biomarkers have been approved by the US FDA. Current support biomarkers used can be listed in terms of valuations and molecules as follows: Prostate health index, Prostate cancer antigen 3, Prostate specific acid phosphatase, TMPRSS2-ERG gene fusion test, Mi-Prostate score test, Prostarix test, ConfirmMDx test, Prostate secretory protein of 94 amino acids (PSP94), Prostein etc..

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GENE THERAPY STRATEGIES: GENE SILENCING

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ABSTRACT

Gene silencing is a promising therapeutic strategy with various applications in cancer treatment and other diseases. It involves the downregulation or suppression of specific genes responsible for disease development or progression. There are several approaches to gene silencing, including RNA interference (RNAi), antisense oligonucleotides (ASOs), and CRISPR/Cas9-based methods. Gene silencing for therapeutic applications can be used to selectively target and inhibit the expression of genes that are critical for cancer cell growth, survival, and metastasis. This can be achieved through the delivery of siRNA or ASOs that specifically target oncogenes or genes associated with drug resistance. Gene silencing can also be used to modulate the immune system's response to cancer. For example, by inhibiting certain immune checkpoint genes (e.g., PD-1 or CTLA-4), it is possible to enhance the immune system's ability to recognize and attack cancer cells, leading to immunotherapy approaches. Here we will give some examples from our studies about how gene silencing can be used to overcome drug resistance, enhance immune responses, and effect cell survival in combination with other cancer treatment modalities, such as chemotherapy and radiation treatment. It's important to note that while gene silencing therapies hold great promise, they also face challenges, including delivery methods, off-target effects, and the need for precise target identification. Nevertheless, ongoing research and advancements in gene-silencing technologies continue to expand their potential in cancer treatment, and they may play a significant role in the future of personalized cancer therapy.

ORAL PRESENTATIONS

CERVICAL CANCER SCREENINGS IN SIVAS: COVID-19 PANDEMIC PERIOD, BEFORE AND AFTER

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ABSTRACT

Objective: This study aimed to evaluate cervical cancer screening results before, during and after the COVID-19 pandemic in Sivas.

Method: In this retrospective cohort study, Human Papilloma Virus (HPV) test and cervical smear results performed on women aged 30-65 years in the Cancer Early Diagnosis and Screening Centre (CEDSC) in Sivas between the years 2019-2022 were evaluated considering the COVID-19 pandemic. The data between 1.01.2019, and 10.03.2020, was grouped as the pre-pandemic period, the data between 11.03.2020, and 28.01.2022, was grouped as the pandemic period, and the data between 29.01.2022, and 31.12.2022, were grouped as the post-pandemic period.

Results: In total, the screening results of 27309 women were analysed. The screening rate decreased by 52.7% during the pandemic period compared to the previous year. The rate of 70% in the target population screening was exceeded in the post-pandemic period. The mean age of women was higher in the post-pandemic period ($p<0.001$). The rate of screening in the city centre was higher during the pandemic period ($p<0.001$). The HPV test positivity rate was 3.9% and there was no difference according to the pandemic periods ($p=0.178$). The most common serotype detected in the screening was HPV16 (1.1%). HPV56 in the pandemic and post-pandemic period ($p<0.001$), HPV45 in the post-pandemic period ($p=0.004$), HPV53-70-6-61-81-11-54-84 and other serotypes in the pre-pandemic period, were the serotypes detected more frequently. The most common cervical cytology results in women were normal cytology and infection. There was no difference between cytology types according to the pandemic periods ($p>0.05$).

Conclusion: Although the cervical cancer screening rates decreased during the pandemic period, it is pleasing that it increased in the post-pandemic period. The increased rate of high-risk HPVs during and post-pandemic suggested that cervical cancer screening was delayed by women.

Keywords: *COVID-19, cancer of cervix, screening*

Introduction

Cancer is one of the most important health problems worldwide and in Türkiye [1]. Among cancers, cervical cancer is the fourth most common cancer in women in the world, while it is the ninth in Türkiye [2,3]. The cervical cancer incidence in Türkiye was determined as 4.3 per 100 thousand according to 2017 data [3].

Cervical cancer is the only cancer whose cause has been fully elucidated and 100% curable if detected early [4]. For this reason, the World Health Organization (WHO) recommends that cervical cancer be screened nationwide in all countries [5]. Scanning method and interval may change according to country settings [6]. Currently, there is no common cervical screening strategy that can be applied in every country. For most countries, screening with a smear every two years, cytology/Human Papilloma Virus (HPV) co-testing every three years, or a HPV test every five years, if it does not start before the age of 30, is recommended [7,8].

While cervical cancer screening in Türkiye has been performed with cervical smear since 1992, the Cancer Department of the General Directorate of Public Health in Türkiye has decided to primarily screen with the HPV test since 2012 [1]. Accordingly, 30-65 years old women are given a free HPV test every five years, and positives

are re-examined with a smear. The highest important measure for cancer screening to be community-based is to reach 70% of the target population. But the scope of cervical cancer screening in Türkiye is at the level of 20% due to the dependency on the specialist, the indifference of the specialists to the subject, and the lack of public interest [1].

The consequences of the COVID-19 pandemic have affected all areas of daily life, including admission to healthcare. Routine or elective healthcare services have been suspended due to curfews, delays of any non-critical health issues by individuals, and the allocation of the available workforce to COVID-19 cases in healthcare facilities [9,10]. A study from the Centres for Disease Control and Prevention (CDC) reported a dramatic decline in cervical cancer screenings, reaching roughly 80% [11]. A survey conducted among 1520 family physicians working in primary care in 75 provinces in Türkiye in December 2020 revealed that screenings decreased by over 90% during the pandemic [12]. These decreases in screening and hospital admissions theoretically constitute the expectation of increased diagnosis of advanced disease or lesions in the later period.

This study aimed to evaluate cervical cancer screening results before, during and after the COVID-19 pandemic in Sivas. Thus, it was aimed to determine the effect of the pandemic on cervical cancer screening.

Method

In this retrospective cohort study, HPV test and cervical smear outcomes of 30-65 years old women who applied to Family Health Centres (FHC) and Cancer Early Diagnosis and Screening Centre (CEDSC) in Sivas between 2019-2022 were evaluated considering the COVID-19 pandemic. To determine the screening rates by years, annual target population, CEDSC and non- CEDSC screening numbers were obtained from the Provincial Health Directorate. HPV test and cervical smear results were obtained retrospectively from the National HPV Laboratory software between April 15, 2023, and June 15, 2023. Sivas Cumhuriyet University Non-Interventional Clinical Research Ethics Committee approval was obtained (Decision no: 2023-03/01, Date: 22.03.2023).

The data between January 1, 2019, and March 10, 2020, was grouped as the pre-pandemic period, the data between March 11, 2020, and January 28, 2022, was grouped as the pandemic period, and the data between January 29, 2022, and December 31, 2022, were grouped as the post-pandemic period [13,14]. The women age, the place where the screening was performed (district or provincial centre), HPV test results and serotypes, and cervical cytology outcomes were evaluated according to the pandemic periods.

The association of HPV DNA with cervical cancer has been proven, and the presence of HPV DNA has been shown in 99.9% of patients with cervical cancer [15]. According to the 10-year results of the studies conducted to show that cervical screening can be performed primarily with HPV testing, the preinvasive and invasive cervical cancer risk in the following 10 years in a case with a negative HPV test is quite low [16–18].

Cervical smear test is the staining of cells collected from the cervix by spreading on a slide and examining them under a microscope [1]. This test is a cytological screening test and can detect cervical lesions that have not yet become symptomatic. The better the standards for smear testing and the greater the participation of the community, the better the screening. Indispensable for quality is the contribution of minimum 70% of the target population [1]. In addition, it does not allow the scanning period to be longer than 2 years, with a sensitivity ratio of up to 50% [19]. Due to these and similar limitations of the test, HPV tests have started to take place more in cervical screening today [1].

Data were evaluated in SPSS (ver 22) program. Descriptive statistical methods (number, percentage, mean, standard deviation), F test (ANOVA) (post hoc Tamhane's T2) and chi-square test were used in the analysis.

Results and Discussion

Table 1 presents target population CEDSC and non- CEDSC screening rates by year. The lowest screening rate was in 2020 (CEDSC 10.7%, non-CEDSC 20.1%, total 30.8%), while the highest was in 2022 (CEDSC 41.8%, non-CEDSC 35.1%, total 76.9%). The screening rate decreased 52.7% in 2020 contrasted to the previous year, from 58.5% to 30.8%. Non-CEDSC screening rates were higher in all other years except 2022.

Delays in screening and early diagnosis are thought to initiate a raise in the diagnosis of advanced diseases and cancer-related deaths [20]. In the results of a comprehensive cross-sectional survey by the International Agency for Research on Cancer (IARC), it has been determined that screening, diagnosis, and treatment services have been reduced by more than half of the country's capacities compared to the pre-pandemic period. These decreases have also been observed in other studies conducted in developed countries. In fact, it has been stated that participation in cancer screening programs decreased by 62% in the USA [21]. Kurtgöz et al. evaluated the CEDSC cancer screening results in Balıkesir and reported that the number of HPV-Pap smear screenings decreased by 70% in the pandemic period compared to the pre-pandemic period [22]. Similar conclusions were found in the study conducted in Niğde [23]. In consequence, in the current study, in 2020, when COVID-19 was announced as a pandemic, it was detected that the cervical cancer screening rate decreased by more than half compared to the previous year. However, instead, it was examined that the screening rate in 2022, which includes the post-pandemic period, was much higher than the years that included the pandemic and pre-pandemic period. In fact, it was concluded that the 70% rate in the target population screening, which is important for cancer screenings, was exceeded. This finding is important as it shows that more strict attention is given to the screening program in the post-pandemic period to compensate for the decreased screening rates during the pandemic period.

Table 1. *Target population Cancer Early Diagnosis and Screening Centre (CEDSC) and non-CEDSC screening rates by year*

Years	**Annual target population**	**CEDSC screening**		**Non- CEDSC screening**		**Total screening**	
		n	**%**	**n**	**%**	**n**	**%**
2019	26594	6868	25.8	8683	32.7	15551	58.5
2020	26532	2842	10.7	5321	20.1	8163	30.8
2021	26644	6637	25.9	8070	30.3	14707	56.2
2022	26644	11128	41.8	9352	35.1	10950	76.9

The distribution of the patients' age and the screening place according to the study periods is given in Table 2. The women mean age was 44.6±9.5. The women mean age was higher in the post-pandemic period than in other periods (p<0.001). Similarly, Erdoğan et al. evaluated the CEDSC screening results in Niğde and reported that there was a reduce in the applications for cervical cancer screening of over the 60 years old women in the pandemic period contrasted to the pre-pandemic period [23]. This may be owed to the delay of the application for screening due to restrictions, especially in the elderly, in the pandemic period. Also, in the current study, we examined that the screening rate in the city centre was higher in the pandemic (p<0.001). This may be because the health manpower, which is already limited in the districts, has been shifted mainly to the areas related to the pandemic in the pandemic period.

Table 2. *The distribution of the patients' age and the screening place according to the study periods*

	Total (n= 27309)	**Pre-pandemic (n= 8014)**	**Pandemic (n= 8362)**	**Post-pandemic (n= 10933)**	
	Mean±SD/ n(%)	**Mean±SD/ n(%)**	**Mean±SD/ n(%)**	**Mean±SD/ n(%)**	
Age (years)	44.6±9.5	43.5±9.5	44.0±9.3	45.9±9.4	F=181.841, p**<0.001**
Post hoc test results		Post-pandemic> Pre-pandemic			p**<0.001**
		Post-pandemic> Pandemic			p**<0.001**
Screening place					
County	5469 (20.0)	1845 (23.0)	1323 (15.8)	2301 (21.0)	x^2=144.322, p**<0.001**
City centre	21840 (80.0)	6169 (77.0)	7039 (84.2)	8632 (79.0)	
SD Standard deviation					

Table 3 shows the distribution of the patients' HPV characterization from cervical samples according to the study periods. The HPV test positivity rate was 3.9% and did not vary according to the pandemic periods (p=0.178). HPV56 in the pandemic and post-pandemic period (p<0.001), HPV45 in the post-pandemic period (p=0.004), HPV53-70-6-61-81-11-54-84 and other serotypes in the pre-pandemic period, were the serotypes detected more frequently. HPV types are clinically divided into 3 categories: low-risk (LR-HPV), possible high-risk and high-risk HPVs [(HR-HPV) 16, 18, 31, 33, 35, 39, 45, 51, 56, 58, 59, 68, 73, 82] [24].

Twelve of the HPV types detected in the current study were in the HR-HPV category, and these twelve HPV types were among the top fifteen HPV types in the study, in order of frequency. In the current study, we determined that HPV types that were detected significantly more in the pre-pandemic period were in the LR-HPV category, while HPV56 and 45, which were in the HR-HPV category, increased significantly in the pandemic and post-pandemic periods. Also, it has been stated that the rates of serotypes defined as high-risk in HPV DNA analyses increased significantly in the pandemic, according to the cervical cancer screening results of women who applied to the Obstetrics and Gynaecology Department of a university hospital in Samsun [25]. These results may be due to delayed application due to the pandemic.

Table 3. *The distribution of the patients' HPV characterization from cervical samples according to the study periods*

	Total (n= 27309)	**Pre-pandemic (n= 8014)**	**Pandemic (n= 8362)**	**Post-pandemic (n= 10933)**	**p****
HPV serotypes*	**n(%)**	**n(%)**	**n(%)**	**n(%)**	
HPV test	1070 (3.9)	317 (4.0)	351 (4.2)	402 (3.7)	0.178
HPV16	290 (1.1)	84 (1.0)	97 (1.2)	109 (1.0)	0.544
HPV51	169 (0.6)	44 (0.5)	56 (0.7)	69 (0.6)	0.603
HPV56	135 (0.5)	17 (0.2)	53 (0.6)	65 (0.6)	**<0.001**
HPV31	127 (0.5)	26 (0.3)	43 (0.5)	58 (0.5)	0.087
HPV52	126 (0.5)	43 (0.5)	43 (0.5)	40 (0.4)	0.160
HPV39	113 (0.4)	24 (0.3)	33 (0.4)	56 (0.5)	0.075
HPV68	87 (0.3)	23 (0.3)	19 (0.2)	45 (0.4)	0.066
HPV35	82 (0.3)	22 (0.3)	22 (0.3)	38 (0.3)	0.501
HPV59	76 (0.3)	17 (0.2)	26 (0.3)	33 (0.3)	0.406
HPV18	68 (0.2)	20 (0.2)	20 (0.2)	28 (0.3)	0.973
HPV45	68 (0.2)	17 (0.2)	11 (0.1)	40 (0.4)	**0.004**
HPV66	68 (0.2)	19 (0.2)	22 (0.3)	27 (0.2)	0.944
HPV58	62 (0.2)	14 (0.2)	21 (0.3)	27 (0.2)	0.503
HPV53	29 (0.1)	29 (0.4)	0 (0.0)	0 (0.0)	**<0.001**
HPV33	27 (0.1)	7 (0.1)	9 (0.1)	11 (0.1)	0.916
HPV70	14 (0.1)	14 (0.2)	0 (0.0)	0 (0.0)	**<0.001**
HPV6	5 (0.0)	5 (0.1)	0 (0.0)	0 (0.0)	**0.002**
HPV61	5 (0.0)	5 (0.1)	0 (0.0)	0 (0.0)	**0.002**
HPV81	5 (0.0)	5 (0.1)	0 (0.0)	0 (0.0)	**0.002**
HPV11	4 (0.0)	4 (0.0)	0 (0.0)	0 (0.0)	**0.007**
HPV54	4 (0.0)	4 (0.0)	0 (0.0)	0 (0.0)	**0.007**
HPV84	3 (0.0)	3 (0.0)	0 (0.0)	0 (0.0)	**0.025**
HPV62	2 (0.0)	2 (0.0)	0 (0.0)	0 (0.0)	0.086
HPV42	1 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	0.293
HPV72	1 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	0.293
HPV83	1 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	0.293
Others	164 (0.6)	92 (1.1)	12 (0.1)	60 (0.5)	**<0.001**
**Positive **Chi-square test*					

Table 4. *The distribution of the patients' cervical cytology assessments according to the study periods*

	Total (n= 27309)	**Pre-pandemic (n= 8014)**	**Pandemic (n= 8362)**	**Post-pandemic (n= 10933)**	**p****
Cervical cytology*	**n(%)**	**n(%)**	**n(%)**	**n(%)**	
Normal	539 (2.0)	152 (1.9)	176 (2.1)	211 (1.9)	0.578
Infection	319 (1.2)	91 (1.1)	105 (1.3)	123 (1.1)	0.669
ASC-US	54 (0.2)	15 (0.2)	20 (0.2)	19 (0.2)	0.580
LGSIL	16 (0.1)	6 (0.1)	7 (0.1)	3 (0.0)	0.222
ASC-H	4 (0.0)	1 (0.0)	2 (0.0)	1 (0.0)	0.827
HGSIL	2 (0.0)	0 (0.0)	1 (0.0)	1 (0.0)	1.000
Inadequate sample	136 (0.5)	62 (0.6)	40 (0.5)	44 (0.4)	0.056
**Yes **Chi-square test*					

The distribution of the patients' cervical cytology assessments according to the study periods is presented in Table 4. The most common cervical cytology results were normal cytology and infection. There was no difference concerning cytology types according to the pandemic periods (p>0.05). In the study conducted by Önal et al. on women who applied to the Department of Obstetrics and Gynaecology, it was observed that the percentage of normal cytology results decreased, and the percentage of ASC-US diagnosis increased in the pandemic contrasted to the pre-pandemic. The reason for this difference in study results may be that the current study presented screening results in a healthy population who did not show any symptoms yet.

The present study is important in expressions of evaluating cervical cancer screening results in a large population according to pandemic periods. However, the fact that it did not include the results of follow-up, examination, and diagnosis of women with high cervical cancer risk because of screening constituted the limited aspect of the study. The explanation for this is that the women referred to the Obstetrics and Gynecology outpatient clinic by the provincial health directorate are not followed up.

Conclusion

It was observed that in 2020, when COVID-19 was declared a pandemic, the cervical cancer screening rate decreased by more than half compared to the previous year, but in 2022, which includes the post-pandemic period, the screening rate was much higher than in the years including the pandemic and pre-pandemic period. The average age of women in the post-pandemic period was higher. The rate of screening in the city centre was higher in the pandemic. Twelve detected HR-HPV types were among the first fifteen HPV types in frequency order in the study. HPV test positivity rates did not differ significantly according to pandemic periods. However, it was determined that HPV types detected more frequently in the pre-pandemic were in the LR-HPV category, and the types in the HR-HPV category increased in the pandemic and post-pandemic periods. There was no difference concerning cytology types according to the pandemic periods. Although it was observed that cervical cancer screening rates decreased during the pandemic period, it is pleasing that it increased in the post-pandemic period. The increased rate of HR-HPV during and after the pandemic suggested that cervical cancer screening was delayed by women.

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INVESTIGATION OF THE EFFECT OF SUGAMMADEX ON LUNG CANCER CELLS IN TERMS OF PROLIFERATION

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Background

Lung cancer remains the leading cause of cancer-related death worldwide. It is considered a highly heterogeneous, aggressive, and relentlessly progressive disease with few treatment options and poor survival, largely because most (~ 70%) cases are diagnosed at an advanced stage. Surgery has the best prognosis for early stage patients. Sugammadex is a chemical chelator commonly used by anesthesia in lung cancer operations to reverse the effect of neuromuscular blocker drugs. It is not yet known how it affects the proliferation of lung cancer cells. The aim of this study is to investigate how sugammadex affects the proliferation of lung cancer cells.

Methods

Using XTT test, the effect of sugammadex on the survival of A549 cells was investigated. These cells were cultivated at a concentration of 1×10^4 cells per well and incubated overnight before the addition of sugammadex. After that the different concentrations (1, 5, 10, 25, 50 and 100 µg/ml) of sugammadex were applied to cells for 24 h. Cells that had not been treated were used as a control. After incubation, 50 µL of XTT mixture was supplemented to each well. Following 4-hour incubation, the cells were shaken and the absorbance was measured using a microplate reader (Thermo Fisher Scientific, Altrincham, United Kingdom) at 450 nm. After performing each experiment three times, cell viability was assessed and expressed as the percentage of viable cells relative to the control. Statistical evaluation of the data was performed by One Way ANOVA, statistical significance was defined at $p<0.05$.

Results

There was no significant change in the viability of A549 cells in the treated groups compared to the control. ($p >0.05$).

Conclusions

Sugammadex had no effect on the proliferation of lung cancer cells.

Keywords: *Sugammadex, lung cancer, A549 cell line*

EVALUATION OF THE RELATIONSHIP BETWEEN MAGNETIC RESONANCE IMAGING AND PATHOLOGICAL SUBTYPE IN RENAL CELL CANCERS

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ABSTRACT

Renal Cell Cancers (RCC) are usually detected incidentally by radiological imaging methods [1]. There are studies showing that the Apparent diffusion coefficient (ADC) obtained from Magnetic Resonance (MR) Diffusion-weighted images (DWI) is useful in distinguishing RCC subtypes [2]. Our study aims to evaluate RCCs with DWI and investigate the contribution of cellular subtypes to diagnosis.

In our study, 35 patients over the age of 18 who were diagnosed with RCC and whose MRIs were available in the system were evaluated. The age, gender, mass size, and ADC values obtained from MRI were examined in these patients. The relationship between ADC and RCC pathological subtype was investigated.

Of the RCC patients, 23 had clear cell RCC, 9 had papillary type RCC, and 3 had chromophobe type RCC. The mean ADC value of clear cell RCC is 1.301x10-3 mm2/sec, the mean ADC value of papillary type RCC is 0.792x10-3 mm2/sec, and the mean ADC value of chromophobe type RCC is 0.980x10-3 mm2/sec. Correlation analysis was performed between mass size and ADC value and it was not found to be statistically significant ($p>0.05$). A statistically significant difference was detected between the ADC values of clear cell RCC and Papillary type RCC ($p<0.05$). There was no statistically significant difference between clear cell and Chromophobe cell RCC and between Papillary type RCC and Chromophobe cell RCC ($p>0.05$). ADC values obtained from DWI imaging appear to be useful in distinguishing RCC cellular subtypes in the preoperative period.

Keywords: *Renal cell carcinoma, diffusion-weighted imaging, apparent diffusion coefficient*

Introduction

Renal Cell Cancers (RCC) are usually detected incidentally by radiological imaging methods[1]. Renal masses are recognized by radiological imaging such as ultrasonography (US), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI), often helping to differentiate benign and malignant [2]. MRI does not contain ionizing radiation and has high contrast resolution. Additionally, gadolinium-based contrast media is less toxic than iodinated contrast media [1,2]. Diffusion-weighted imaging (DWI) is a method that characterizes water molecules based on their movement within the tissue. These images are expressed numerically with ADC maps [3]. There are studies showing that ADC values are useful in distinguishing different subtypes in RCC [4].

Our study aims to evaluate renal cell carcinomas with diffusion-weighted imaging (DWI) and investigate the contribution of cellular subtypes to the diagnosis.

Method

In our study, 35 patients over the age of 18, diagnosed with RCC, whose MRIs were in the system for various reasons, were evaluated between January 2015 and July 2023. The age, gender, long size of the mass, ADC values obtained from MRI, and pathology results of these patients were examined. The long dimension of the mass was evaluated on T2 images in three different axes and the longest one was taken into account. Measurements were made by placing three different ROIs on the mass in axial images from ADC maps. The patient's pathological outcome is unknown when the measurement is made. The average ADC value was found by taking the average of these three values (Figure 1).

Statistical analysis

The data obtained from our study were evaluated with the SPSS 22.0 program. The normality of the data was checked with the Kolmogorov-Smirnov test. If the data met parametric conditions, the independent sample t-test was used for two independent groups, and if the assumptions were not met, Mann Whitney U test was used for two independent groups. The Pearson correlation coefficient was used for the relationship. The error level was taken as 0.05.

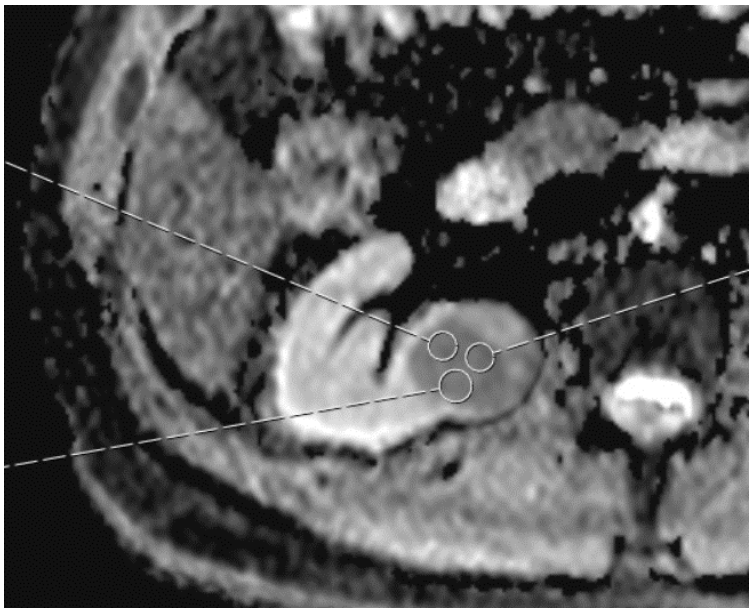

***Figure 1**: ADC measurement from the right kidney mass*

Results and Discussion

The mean age of 35 patients included in our study was 58.17±11.24 years. Of the cases, 10 (29%) were female and 25 (71%) were male. The mass's long dimensions are 46.65±30.0 cm on average. Clear cell RCC was found in 23 (65.7%) RCC patients, Papillary type RCC was found in 9 (25.7%) and Chromophobic RCC was found in 3 (8.6%) RCC patients.

The mean ADC value of clear cell RCC is 1.301x10-3 mm2/sec, the mean ADC value of papillary type RCC is 0.792x10-3 mm2/sec, and the mean ADC value of chromophobe type RCC is 0.980x10-3 mm2/sec.

Correlation analysis was performed between mass size and ADC value and it was not found to be statistically significant ($p>0.05$). A statistically significant difference was found between the ADC values of clear cell RCC and papillary cell RCC ($p<0.05$). There was no statistically significant difference between RCC with clear cell and chromophobe cell, and between RCC with papillary cell and chromophobe cell ($p>0.05$)(Table 1).

***Table 1:** Correlation analysis between RCC pathological subtypes*

Pathology	Mean Difference	Std. Error	P
Clear cell RCC-Papillary RCC	507,64251	106,74623	**0,0001***
Papillary RCC-Chromophobe RCC	-187,88889	180,99703	0,559
Chromophobe RCC-Clear cell RCC	-319,75362	166,65749	0,150

RCC: Renal Cell Cancer

*p<0,05 statistically significant

Conclusion

In some studies, DWI and contrast-enhanced MRI have been compared in detecting renal lesions[5]. In our study, ADC is clear, chromophobe, and papillary, in order from high to low. Similar to our study, Hassanen et al.[6] found clear cell RCC ADC values higher than the others.

Our study found the average ADC value of papillary RCC was significantly lower than clear cell RCC ($p<0.05$). Similarly, in the study of Er et al., the papillary RCC ADC value was found to be statistically significantly lower than the clear cell RCC ADC value [7].

There are some limitations in our study. First of all, it is a retrospective study. Our study population is small. It seems that studies on a larger population are needed.

As a result, ADC values obtained from DWIs appear useful in differentiating RCC cellular subtypes in the preoperative period.

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TUMOR SUPPRESSOR GENE AND PROTO-ONCOGENE MUTATIONS IN LUNG CANCER

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Background: The most common form of primary lung cancer is non-small cell lung cancer (NSCLC) and can be subdivided into adenocarcinoma, squamous cell carcinoma and large cell carcinoma [1]. A less common form, small cell lung cancer is a high-grade neuroendocrine tumor that commonly occurs in heavy smokers and has a poor differentiation and prognosis [2]. The investigation on the genetic basis of lung cancer is important in terms of the formation, course and treatment options of this disease. We evaluated possible tumor suppressor gene and proto-oncogene mutations in lung cancer patients.

Material and Method: Molecular analysis was performed from paraffin-embedded lung tissue of 36 lung cancer patients. In these patients (27 adenocarcinoma, 9 other non-small cell lung cancer, NSCLC), 42 genes were screened by Next Generation Sequencing (NGS, Qiagen Targeted Panel DHS-005Z-12). The obtained data were analyzed with Qiagen Clinical Insight (QCI) and Franklin variant analysis program.

Results: Twenty-eight of the patients were male and eight were female. The mean age of the patients was 62.4±8.04 years. One or more mutations were detected in 14 of 36 patients (38.9). Possible tumor suppressor gene and proto-oncogene screening with Next Generation Sequence analysis (NGS) for those patients revealed 29 mutations. These included 7 TP53, 4 STK11, 3 CDKN2A, 2 SMARCA4, 1 RB1, 1 PTEN, 1 APC, 1 ATM mutation as tumor suppressor and 5 KRAS, 1 BRAF, 1 EGFR, 1 ROS1, 1 KIT mutation as proto-oncogene. Mutations other than ROS1 were pathogenic or likely pathogenic. The ROS1 mutation was a variant of uncertain significance (VUS).

Conclusions: The detected mutations were compatible with the clinical findings of the patients. Loss of function of tumor suppressor genes and gain of function of proto-oncogenes may have contributed to the formation and progression of this disease. Inactivation of STK11 leads to lung cancer progression with the activation of metastatic process [3]. Patients with KRAS-mutant NSCLC generally have a poor response to chemotherapy, and a number of new therapeutic strategies (KRAS inhibition, immunotherapy, etc.) have been developed in this context [4]. The most frequent alterations among tumor suppressor genes in lung cancer are TP53 and CDKN2A mutations [5].

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A NOVEL BLOCK IN BREAST CANCER SURGERY FOR ANALGESIA

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ABSTRACT

Female breast cancer is the most common type of cancer worldwide (12.5%)[1]. The primary treatment for breast cancer is surgery[2]. Modified Radical Mastectomy (MRM) is the prevailing surgical method. Patients experience severe acute pain after surgery, which may become chronic [3]. Various body blocks are utilized for postoperative analgesia in breast surgery [4], [5]. The Serratus Posterior Superior Intercostal Plane Block (SPSIPB), as described by Tulgar et al. in 2023, has been reported to be applicable for postoperative analgesia in thoracic surgeries [6]. We applied this recently introduced block to seven patients who underwent MRM for analgesia. The mean age, body mass index, surgical time, and total tramadol consumption of the patients were 59.4 years, 28.3 kg/m2, 98.5 minutes, and 35.7 milligrams, respectively. We observed low Numeric Rating Scale scores and reduced tramadol consumption in patients. We believe that SPSIPB could be an effective analgesic method in these surgeries and might be utilized as a new indication.

Table 1. *Static and dynamic NRS scores of patients*

	1st hour		6th hour		12th hour		18th hour		24th hour		Tramadol
	Stat.	Dyn.	Stat.	Dyn.	Stat.	Dyn.	Stat.	Dyn.	Stat.	Dyn.	Consumption(mg)
Case 1	2	3	1	2	1	1	1	1	1	1	0
Case 2	3	4	2	3	2	3	1	2	1	2	50
Case 3	3	4	2	3	2	3	1	2	1	2	50
Case 4	4	5	2	3	2	3	1	2	1	2	50
Case 5	5	6	3	4	4	5	2	3	2	3	100
Case 6	3	4	2	3	2	3	1	2	1	2	0
Case 7	2	3	2	3	1	2	1	2	0	1	0

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FDG PET-CT IN METASTATIC CASTRATE RESISTANT PROSTATE CANCER DURING CURRENT ERA OF TARGETED THERAPY, PERSONALISED CARE AND THERANOSTICS

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ABSTRACT

Introduction

Although less commonly done for staging of newly-diagnosed prostate cancer, FDG PET-CT can provide important information needed in managing advanced cases and may influence targeted therapy, personalised care and theranostics. We present case series and scan images pictorial review of metastatic castrate resistant prostate cancer (mCRPC) patients who underwent FDG PET-CT in our institution between October 2020 and May 2023 with total of 6 examinations.

Report

Four males aged between 65 and 78 years old. None had prostatectomy. Prior imaging studies included PSMA and FDG PET-CT, bone scan and MRI whole spine. One patient had 3 PET-CT examinations during the study period. Indications for current FDG PET-CT were treatment response, restaging and pre-radionuclide therapy assessment. Recent PSA level at the time of scan request noted between 9.26 and 437 ng/ml. All examinations were positive and FDG-avid bone metastases detected in all cases corresponding to predominantly sclerotic changes (n=3) and lytic lesions (n=1). These bone lesions showed high FDG avidity up to SUVmax 13.8. Other significant FDG-avid involvement included right seminal vesicle (n=1), left supraclavicular and abdominopelvic nodes (n=1), liver (n=1) and lungs (n=2). Two patients had mildly avid indeterminate but strictly suspicious FDG uptake in the prostate. Latest FDG PET-CT in the only patient who had follow-up examinations showed disease progression. FDG PET-CT appears to be useful for metastasis detection in some patients with biochemical failure whereby its sensitivity increases with higher PSA level; prognostication; and extent of metabolically active lesions and response assessment in mCRPC [1-3]. In assessing treatment and prognosis, combination of FDG and PSMA PET-CT can be more beneficial [4].

Conclusion

We discussed current application and scan findings of FDG PET/CT for mCRPC patients. Positive FDG PET-CT with widespread disease may indicate more aggressive malignancy.

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ABDOMINAL ULTRASONOGRAPHY AND COLONOSCOPY SHOULD BE PERFORMED BEFORE INGUINAL HERNIA SURGERY TO IDENTIFY FACTORS THAT WOULD INCREASE INTRAABDOMINAL PRESSURE

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ABSTRACT

Introduction

Spermatic cord lipoma, sarcoma, inguinal lipoma, and lymphadenopathy may mimic inguinal hernia. Therefore, ultrasound imaging should be performed routinely to confirm hernias before surgical intervention. Moreover, other intraabdominal pathologies that would increase intraabdominal pressure to cause inguinal hernia should be examined prior to surgery. Thus, we propose a novel approach involving routine abdominal ultrasonography and colonoscopy to evaluate intraabdominal pathologies in patients complaining of inguinal hernia over the age of 50.

Method

Routine abdominal ultrasonography and colonoscopy were included as parts of our diagnostic process for individuals presenting with suspected inguinal hernias. The primary goal of this comprehensive evaluation was to uncover hidden concomitant illnesses causing elevated intraabdominal pressure. This procedure was followed not only in the Department of General Surgery at Ankara Gazi University School of Medicine but also at Zonguldak Devrek State Hospital and Aksaray University School of Medicine.

Result

A significant case emerged among the patients subjected to the proposed comprehensive assessment. A 55-year-old Caucasian male patient with a right inguinal hernia was diagnosed with pancreatic head carcinoma via preoperative abdominal ultrasonography. This finding highlighted the diagnostic power of incorporating routine abdominal imaging into inguinal hernia evaluation.

Conclusion

Our findings support a more nuanced preoperative assessment approach for inguinal hernia patients. Latent intraabdominal pathologies can be revealed by routine abdominal ultrasonography and colonoscopy, particularly in patients with inguinal hernia over the age of 50.

Keywords: *Abdominal ultrasonography, colonoscopy, inguinal hernia, intraabdominal pressure, preoperative evaluation*

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FRESH FROZEN PLASMA PLUS FUROSEMIDE AS A POTENTIAL HUMAN ALBUMIN SUBSTITUTE IN CANCER PATIENTS IN RESOURCE-LIMITED SETTINGS

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ABSTRACT

Introduction

Human albumin's high cost and scarcity pose significant challenges in resource-constrained healthcare settings. Though concerns about bloodborne diseases, clotting factors, and adverse reactions remain, fresh frozen plasma (FFP) is emerging as a cost-effective alternative. This study looks into the feasibility of combining FFP and furosemide to address these concerns and provide a practical solution.

Methods

From 2000 to 2023, a comprehensive review of PubMed and Google Scholar was conducted to identify studies that used FFP as an alternative to human albumin. Data on clotting, transfusion reactions, and cost-effectiveness were extracted and analyzed.

Results

Despite the widespread preference for human albumin, the treatment with FFP and furosemide remains promising, particularly in resource-constrained settings. It is critical to administer FFP with caution, address transfusion reactions, and ensure ABO compatibility. The importance of safe transfusion practices and vigilant infectious disease risk management cannot be overstated. Choosing FFP wisely while avoiding unnecessary administration has clinical and economic benefits.

Conclusion

Given the general preference for human albumin in the medical literature, the combination of FFP and furosemide is promising in resource-limited healthcare. While more research is needed, careful examination of this strategy may solve problems associated with cost and availability of human albumin in low-income countries.

Keywords: *Fresh frozen plasma, furosemide, human albumin, transfusion*

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CAN WE DEFINE A MEASURABLE LABORATORY PARAMETER THRESHOLD TO INITIATE CYTOKINE ADSORPTION THERAPY FOR CANCER PATIENTS IN THE INTENSIVE CARE UNIT?

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ABSTRACT

Introduction

Cytokine Adsorption Therapy (CAT) may provide relief from cytokine storms in critically ill cancer patients in the intensive care unit. These storms aggravate acute respiratory distress syndrome (ARDS) and cause multi-organ failure, increasing morbidity and mortality. The lack of universally accepted initiation criteria for CAT poses a significant challenge for the standardization of cytokine adsorption therapy. The purpose of this study is to elucidate the optimal initiation criteria for CAT by assessing changes in cytokine levels, complete blood count (CBC), and biochemistry panels.

Methods

This study included data from PubMed and Google Scholar between the years 2000 and 2023. The analysis of studies elucidating the relationship between various biomarkers and CAT initiation was conducted.

Results

Among the parameters studied, which included white blood cell (WBC) count, ferritin, interleukin-6 (IL-6), procalcitonin, and C-reactive protein (CRP), there is evidence that IL-6 levels may serve as a reliable indicator for initiating CAT. In critically ill cancer patients, elevated IL-6 levels correlate with the severity of cytokine storms and poor clinical outcomes.

Conclusion

The lack of universally accepted cut-off or threshold values for initiation criteria highlights the critical need for additional research. CAT may improve patient outcomes, reduces ARDS and multi-organ failure in the context of severe malignant diseases by addressing complex cytokine storms. This study not only emphasizes the importance of CAT in critical care, but it also emphasizes the need for standardized criteria to optimize its application for improved patient prognosis and survival rates.

Keywords: *Cancer, cytokine adsorption therapy, intensive care unit, threshold*

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ANTIMICROBIAL MOUTHWASH FORMULATIONS FOR DRY MOUTH AND REMOVAL OF BAD ODOUR

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ABSTRACT

Introduction

Xerostomia also known as dry mouth is often seen in cancer patients either during radiation therapy to the neck/head region or as a side effect of some chemotherapeutics [1,2]. Dryness in the mouth is sometimes accompanied by bacterial malodour and oral-dental disorders [2], thus a successful formulation for the treatment must provide hygiene in addition to wetness in the mouth. In this study, it was aimed to prepare herbal ingredients including mouthwash that can meet both requirements.

Methods

Two group formulations including *Citrus bergamia* L. fruit peel oil with *Vitis vinifera* L. seed oil, and *Cinnamomum zeylanicum* Blume leaf oil with *Corylus avellana* L. seed oil both in combination with carboxymethyl cellulose as polymer were prepared (essential oil amount varied 1-6%) and were evaluated by organoleptic, pH, density, viscosity and antimicrobial activity controls. The chemical components of the essential oils were analysed by using GC-FD/MS.

Results

All the formulations were presented palatable and acceptable physical properties and compatible with mouth pH, while 2% or more cinnamon oil included ones showed antimicrobial activity against all investigated mouth pathogens (*S. pyogenes, S. mutans, S. mitis, S. aureus, C. albicans*), 1-6% bergamot oil included ones had limited activity and they were not effective on *S. mitis*.

Conclusion

As a conclusion, cinnamon oil included formulations, which were successful in terms of researched parameters were found to be encouraging for further studies including clinical trials.

Keywords: *Xerostomia, mouth malodour, mouthwash, carboxymethyl cellulose, essential oils*

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PUNCH BIOPSY RESULTS IN NASOPHARYNGEAL PATHOLOGIES

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ABSTRACT

Aim

In our study; the aim was to analyze the age, gender, and clinical findings of patients who underwent biopsy due to suspicious lesions/masses in the nasopharynx, retrospectively evaluate their histopathological data, determine the benign/malignant ratio of these lesions, and present the distribution of histopathological diagnoses.

Method

A retrospective study included 126 cases (47 females, 79 males) who underwent nasopharyngeal endoscopic punch biopsy at our hospital's Ear, Nose, and Throat clinic between 2018 and 2023. The age, gender, reason for biopsy and biopsy results were evaluated for all cases. The pathological diagnoses were evaluated and classified into malignant and benign categories.

Results

Out of 126 patients, 106 (84.10%) had benign pathologies, including lymphoid hyperplasia, chronic lymphoid process, and Tornwald cyst. In 20 cases (15.90%), nasal pharyngeal carcinoma was diagnosed due to suspicion of malignancy and further investigation. Among these 20 cases, two were diagnosed as keratinizing squamous cell carcinoma (WHO Type 1), 12 were diagnosed as non-keratinizing squamous cell carcinoma (WHO Type 2), and the remaining 6 cases were classified as other categories, including five lymphomas and one adenocarcinoma.

Conclusion

Histopathological correlation is required for the differential diagnosis of patients with a suspicious mass/lesion in the nasopharynx. In our study, the malignancy rate was determined as 15.9%. According to the literature, this high rate emphasizes the need to rule out malignancies. Even in the absence of an occupying mass during the nasopharyngeal endoscopic examination, obtaining a punch biopsy that includes the mucosa and submucosa will enable early diagnosis and treatment of nasopharyngeal cancer.

Keywords: *Nasopharyngeal cancers, symptom, histopathology*

Introduction

Nasopharyngeal cancers (NPC) are among the most common head and neck cancers, exhibiting a distinct geographic distribution. While they account for approximately 2% of head and neck cancers, their prevalence among all cancers is around 0.25% [1].

Genetic factors, male gender, high alcohol consumption, Epstein-Barr virus, nasopharyngeal cancer in first-degree relatives, and environmental and occupational factors are implicated in the aetiology of nasopharyngeal cancers [2, 3].

While almost all cases of nasopharyngeal cancers are symptomatic, the number of cases diagnosed during the asymptomatic period is less than 1%. Most patients seek medical attention due to symptoms such as a mass

in the posterior cervical triangle, nasal obstruction, recurrent epistaxis, unilateral serous otitis media, conductive hearing loss, otalgia, and headaches [4, 5].

Wei and Sham [6] categorised the symptoms of nasopharyngeal cancers in their published article into four categories:

- Symptoms caused by the tumor occupying the nasopharynx (nasal obstruction, epistaxis, nasal discharge),
- Symptoms resulting from Eustachian tube dysfunction (hearing loss, serous otitis media, otalgia),
- Symptoms caused by the upward spread of the tumor (headaches, diplopia, facial pain and numbness),
- Palpable neck mass.

Examining the nasopharynx (NP) is challenging due to its anatomical structure. However, NP examination can be easily performed using fiberoptic endoscopes under topical anesthesia to obtain biopsies in cases suspected of benign masses or cancer. NP biopsy is the easiest and safest diagnostic tool for diagnosing NP masses.

Since NP cancers often exhibit submucosal localization, taking multiple biopsies that include both the mucosa and submucosa may be necessary to obtain an accurate diagnosis.

In our study, the aim was to analyze the age, gender, and clinical findings of patients who underwent biopsy due to suspicious lesions/masses in the nasopharynx, retrospectively evaluate their histopathological data, determine the benign/malignant ratio of these lesions, and present the distribution of histopathological diagnoses.

Materials and Methods

A retrospective study included 126 cases (47 females, 79 males) who underwent nasopharyngeal endoscopic punch biopsy at our hospital's Ear, Nose, and Throat clinic between 2018 and 2023. The study was conducted in accordance with the principles of the Helsinki Declaration and Good Clinical Practice Guidelines and with approval from the hospital's ethics committee (Ethics committee no: [insert number]). The included cases' demographic information and pathology results were obtained by scanning the hospital's medical records system.

The age, gender, reason for biopsy and biopsy results were evaluated for all cases. The biopsy procedure performed was the same for all cases and is defined as follows. Nasopharyngeal endoscopic biopsies were performed on all cases under local anesthesia in the outpatient clinic. After providing local anaesthesia with a nasal spray containing lidocaine, the nasopharyngeal mucosa, torus tubarius, pharyngeal orifice of the Eustachian tube, and Rosenmuller's fossa were evaluated. Biopsies were taken to rule out nasopharyngeal cancer in adult cases with recurrent nosebleeds, nasal obstruction, lymphadenopathy unresponsive to medical treatment in the cervical region, headaches, and unilateral serous otitis media. In cases with a lesion occupying space identified during the endoscopic examination, biopsies were taken from the lesion, and in patients with no mucosal pathology detected, multiple deep punch biopsies were taken from different areas. All pathology specimens obtained from the cases were sent to the pathology clinic, and the pathology results were recorded.

The pathological diagnoses were evaluated and classified into malignant and benign categories.

Statistical Analysis

The data obtained from our study were analyzed using the SPSS 22.0 software package. Descriptive statistics were reported as frequency and percentage for categorical variables and median value (minimum-maximum) for numerical variables. Nominal variables were evaluated using the chi-square and Fisher's exact probability tests. Multinomial logistic regression analysis was performed to determine the risk factors affecting malignancy. A p-value < 0.05 was considered statistically significant.

Results

Demographic characteristics of the cases are given in Table 1.

Table 1. *Demographic characteristics of the cases and general distribution of symptoms*

Gender	Male	79	62,70%
	Female	47	37,30%
Benign, Malign	Benign	106	84,10%
	Malign	20	15,90%
Symptom	headache	6	4,80%
	mass in the neck	18	14,30%
	epistaxis	1	0,80%
	nasal obstruction	87	69,00%
	serous otitis	14	11,10%

A total of 126 patients were included in the study. Among the patients who underwent NP biopsy, 47 (37.3%) were female, and 79 (62.7%) were male. The mean age of male patients was 42.16 ± 17.62 (range: 12-79), while the mean age of female patients was 39.53 ± 17.87 (range: 13-82). There was no statistically significant difference observed between males and females.

When benign and malignant pathologies were evaluated according to age, the mean age in the benign pathology group was 38.87 ± 16.12 (range: 12-84), while in the malignant pathology group, it was 53.45 ± 20.82 (range: 22-82), and this difference was statistically significant. (Table 2). No statistically significant difference was observed in the gender distribution of cases with malignant and benign pathologies (p=0.431).

Table 2. *Relationship between age and benign-malignant pathology*

Age	**Count**	**Minimum**	**Maximum**	**Mean**	**Standard Deviation**	**p**
Benign	106	12	84	38,87	16,12	**0,004**
Malign	20	22	82	53,45	20,82	

Of 126 patients, 106 (84.10%) had benign pathologies, including lymphoid hyperplasia, chronic lymphoid process, and Tornwald cyst. In 20 cases (15.90%), nasal pharyngeal carcinoma was diagnosed due to suspicion of malignancy and further investigation. Among these 20 cases, two were diagnosed as keratinizing squamous cell carcinoma (WHO Type 1), 12 were diagnosed as non-keratinizing squamous cell carcinoma (WHO Type 2), and the remaining 6 cases were classified as other categories, including five lymphomas and one adenocarcinoma.

When evaluating the symptoms, neck mass and nasal congestion (n=7) were the most commonly observed symptoms in malignant lesions, followed by ear symptoms such as serous otitis and otalgia (n=3). Headache was present in 2 patients, and nasal bleeding was observed in 1 patient (Table 3). No significant association existed between the reported malignancies (WHO Type 1, Type 2, and Other malignant pathologies) and the symptoms (p=0.424).

Table 3. *The relationship between symptoms and benign-malignant pathology*

Symptoms	**Benign**	**Malign**	**Total**
Headache	4	2	6
	66,70%	33,30%	100,00%
Mass in the neck	11	7	18
	61,10%	38,90%	100,00%
Epistaxis	0	1	1
	0,00%	100,00%	100,00%
Nasal obstruction	80	7	87
	92,00%	8,00%	100,00%
EOM	11	3	14
	78,60%	21,40%	100,00%
	106	20	126
	84,10%	15,90%	100,00%

Discussion

The nasopharynx (NF) is an irregular cuboidal space behind the nasal cavity, below the base of the skull. It opens into the nasal cavity through the posterior choanae. Its roof, known as the fornix, is situated beneath the body of the sphenoid bone. The posterior wall is formed by the clivus (part of the skull base) and the first two cervical vertebrae, while the inferior wall is formed by the soft palate (palatum molle). The lateral and posterior walls consist of the parafascial tissue that extends bilaterally from the apex of the petrous pyramid, located medially to the carotid canal. The pharyngeal orifices of the Eustachian tubes open into the lateral walls. There is a curved structure called the torus tubarius behind the Eustachian orifices. Above and behind the torus, the Rosenmüller fossa is present, the most common site for developing nasopharyngeal cancer. The mucosa of the NF is lined with non-keratinizing columnar ciliated epithelium containing areas of widespread squamous metaplasia. The connective tissue beneath the epithelium is rich in lymphoid cells [7].

This detailed description provides an understanding of the anatomy of the nasopharynx, including its location, boundaries, and associated structures. It emphasizes the significance of the Rosenmüller fossa as a common site for nasopharyngeal cancer development and highlights the presence of lymphoid-rich tissue in the subepithelial layer. This information contributes to a comprehensive understanding of the nasopharynx and its relevance in various pathological conditions.

Indeed, the diagnosis of nasopharyngeal cancer cannot be excluded solely based on endoscopic examination. Nasopharyngeal cancer can spread submucosally, so the mucosa may appear normal during endoscopic examination. This can delay the diagnosis of nasopharyngeal cancer and result in the cancer being diagnosed at a more advanced stage. Early diagnosis of these aggressive cancers not only prolongs the survival of patients but also increases the success of treatment [8].

In this study, the age, gender, clinical findings, and histopathological data of patients who underwent biopsy due to suspicious lesions/masses in the nasopharynx were retrospectively evaluated. The rate of benign diagnoses was found to be higher compared to malignant diagnoses. Nonkeratinizing undifferentiated carcinoma was the most commonly detected type among the malignant diagnoses.

The nasopharyngeal epithelium comprises approximately 60% stratified squamous epithelium, while the remaining consists of respiratory-type epithelium and intermediate/transition epithelium. Any clinical symptoms caused by a nasopharyngeal lesion can originate from the epithelium, lymphoid tissue, or salivary glands [9]. The most common benign pathology observed in the nasopharynx is reactive lymphoid hyperplasia. Patients with this condition typically present with symptoms such as hearing problems, nasal congestion, nasal discharge, and recurrent infections [10]. In our study, a high proportion (84.10%) of benign pathologies was attributed to reactive lymphoid hyperplasia. However, due to being a tertiary healthcare center, the incidence of malignancy was also found to be significantly high (15.90%).

The findings of our study highlight the importance of considering both benign and malignant pathologies in evaluating patients with nasopharyngeal lesions. The high prevalence of reactive lymphoid hyperplasia underscores its significance as a common benign cause of symptoms in this region. However, the substantial malignancy rate reinforces the need for thorough evaluation and consideration of potential malignant etiologies in clinical practice.

NK is more commonly observed in males than females, with a ratio of 3:1. The regional variations and temporal changes in carcinogens and environmental factors can influence the gender distribution of the disease [11,12]. In our study, the male-to-female ratio among malignant patients was determined to be 1.85. This finding aligns with the general trend of males having more prevalent NK. However, it is important to consider that other factors may also contribute to the observed gender distribution in our study population.

NK is a neoplasm that tends to grow silently and is often diagnosed at an advanced stage due to its anatomical location. Approximately 70-90% of patients have locally advanced disease and cervical lymph node metastases [11-13]. Symptoms can vary but commonly include nasal obstruction/discharge due to mass effect, ear symptoms related to dysfunction of the Eustachian tube, headache associated with involvement of the fifth and sixth cranial nerves and the skull base, diplopia, facial numbness/pain, and neck swelling/mass. These

symptoms can also be seen in both benign and malignant conditions of the nasopharynx. They are also common symptoms in neighbouring areas such as the nasal cavity, paranasal sinuses, middle ear pathologies, and skull base pathologies. In our study, patients with suspected nasopharyngeal lesions underwent a biopsy to rule out or confirm malignancy. The most common symptoms observed in malignant cases in our case series were palpable neck mass and nasal obstruction, consistent with the literature. Additionally, three patients presented with unilateral serous otitis media and otalgia, while one patient presented with epistaxis as a symptom.

In our study, non-keratinizing and undifferentiated types accounted for 60% of malignant cases. No malignancy was observed in patients under the age of 18. In the non-keratinizing type, variable reactive lymphoplasmacytic cells accompany the inflammation, and scattered, non-cohesive, undifferentiated neoplastic cell groups are seen in irregular islands. The differentiated type resembles a high-grade urothelial carcinoma. Less than 10% of cases show rare morphological variants, such as spindle cells, pleomorphic (Reed-Sternberg-like cells), and papillary types. Therefore, it enters the differential diagnosis with lymphoma, and immunohistochemical examination is required. The differentiation between differentiated and undifferentiated types is highly subjective and has no clinical significance [14]. However, suppose the non-keratinizing undifferentiated nasopharyngeal carcinoma shows a layer-like pattern composed of poorly differentiated neoplastic cells (i.e., Régaud pattern). In that case, it should be considered an aggressive and malignant lymphoma in the differential diagnosis. Immunohistochemical panels should be applied for further evaluation.

The keratinising type of nasopharyngeal carcinoma (NPC) contains cells showing histopathologically variable keratinisation and squamous differentiation, thus exhibiting similar histological features to squamous cell carcinoma (SCC). Both tumours have a similar immunohistochemical profile [11,12]. Our study diagnosed two individuals (10%) with keratinizing type NPC.

The basaloid subtype of NPC cannot be morphologically distinguished from basaloid SCC in other body regions. We did not encounter any cases of this subtype in our study.

In addition to NPC, lymphomas are the second most common tumours observed in the nasopharynx [14,15]. Consistent with the general literature, we found that lymphomas accounted for 20% of the tumour group in our study, with the most common subtype being diffuse large B-cell lymphoma (80%).

Conclusion

Histopathological correlation is required for the differential diagnosis of patients with a suspicious mass/lesion in the nasopharynx. In our study, the malignancy rate was determined as 15.9%. According to the literature, this high rate emphasises the need to rule out malignancies. Even in the absence of an occupying mass during the nasopharyngeal endoscopic examination, obtaining a punch biopsy that includes the mucosa and submucosa will enable early diagnosis and treatment of nasopharyngeal cancer.

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DETERMINATION OF THE RELATIONSHIP BETWEEN NURSES' CARE BEHAVIORS AND PATIENTS' PERCEPTION OF CARE BEHAVIORS AFTER CANCER SURGERY

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ABSTRACT

Objective

The aim of this study was to investigate the relationship between nursing care behaviors following cancer surgery and the perception of these care behaviors by patients.

Methods

This descriptive research was conducted in the surgical oncology and general surgery departments of an educational and research hospital. The study sample consisted of 31 nurses working in the general surgery and surgical oncology clinics and 310 patients who had undergone cancer surgery. Data were collected using the Patient Information Form, Nurse Information Form, and Care Behaviors Inventory-24 (CBI-24). Data analysis included numerical summaries, percentages, means, standard deviations, *t*-tests for independent and dependent groups, one-way ANOVA tests, and Pearson's correlation analysis.

Results

The mean age of the participating patients was 46±2.74, while the mean age of the nurses was 34.08±2.02. Statistically significant differences were observed between patients and nurses in some demographic variables and CBI-24 score averages ($p<0.05$). The total mean CBI-24 score for patients was 3.60±0.82, whereas for nurses, it was 3.83±0.92. In the correlation analysis between nurses and patients' CBI-24 subscale and total scores, a statistically significant positive relationship was found in all CBI-24 subscales and total scores ($p<0.05$).

Conclusion

In conclusion, it was determined that the level of nursing care behaviors exhibited by both nurses and patients ranged from moderate to high. The care behaviors demonstrated by nurses yielded positive patient perceptions of care behaviors. Additionally, a positive relationship was identified between the care behaviors of nurses and patients.

Keywords: *Cancer, surgery, patient, nurse, care behavior*

Introduction

Nursing, being a care-based profession, centers around the individual [1]. The scope of care is not limited to nursing alone, but it holds a special place within the context of nursing [2]. Care encompasses various aspects, such as meeting the individual's unmet needs, providing information about procedures, assisting in problem-solving, and enhancing interpersonal communication [3,4]. Care, intertwined with trust, hope, faith, respect for human dignity, and scientific knowledge, emphasizes the need for a professional approach to nursing care [5]. Professional nursing care includes behaviors like being with the patient at all times and performing necessary

tasks for them, and how nurses interact with healthy/ill individuals is also crucial in gradually developing this perception [6]. Nursing care behaviors, which constitute a significant portion of the services provided to patients during this period [7], are an important factor influencing overall patient satisfaction with healthcare [6]. Therefore, evaluating nursing care behaviors by both nurses and patients is of great importance. This is because the perception of care outcomes and the fulfillment or non-fulfillment of expectations can be defined differently by different individuals and even by the same individuals at different times [8]. The concept of care, being abstract and difficult to measure, is also influenced by culture and values. Research on specific, structured efforts among nurses to improve nursing care behaviors is also insufficient. Therefore, this research was conducted with the aim of determining the perceptions of patients and nurses in the general surgery and surgical oncology services regarding the quality of nursing care and the factors influencing it, with the belief that it would contribute to the improvement and implementation of nursing care quality.

Method

Study Design and Sample

This study is of a descriptive type. The research was conducted at the Sivas Cumhuriyet University Health Services Application and Research Hospital in the general surgery and surgical oncology services from April 1, 2022, to April 1, 2023. The population of the study included nurses (34 individuals) working in the general surgery and surgical oncology services of the Sivas Cumhuriyet University Health Services Application and Research Hospital, as well as cancer surgery patients over 18 years of age, able to speak and understand Turkish, without mental health problems. The sample of the study consisted of a total of 31 nurses who agreed to participate in the study and a total of 310 patients who met the study criteria. Before starting the study, the sample size was determined as 96 individuals when an effect size of 0.50, a power of 92%, and a significance level of 0.05 were taken using the G-power 3.1 program. A larger patient group was included in our study than the determined minimum sample size.

Measurments

Three data collection forms were used in the study. These were the Patient Information Form, the Nurse Information Form, and the Care Behaviors Scale-24.

- **Patient Information Form:** This form contained a total of 10 questions concerning the patients included in the study, including their age, gender, marital status, education level, presence of chronic illness, previous hospital and surgical experience, reasons for surgery-cancer type, length of stay in the hospital, and room characteristics, in line with the literature [4,6,7].
- **Nurse Information Form:** The form included a total of 9 questions about the socio-demographic characteristics of the nurses included in the study, such as age, gender, marital status, education level, as well as professional life characteristics such as years of experience, choosing the profession willingly, working willingly in the clinic, working duration in the clinic, and work style, within the scope of the study.
- **Care Behaviors Inventory -24 (CBI-24):** The CBI-24, developed by Wu et al. [9], was used to allow nurses to self-evaluate and compare their perceptions with those of patients. The Turkish validity and reliability study of the scale was conducted by Kurşun and Kanan [10]. The CBI-24 consists of 4 subscales, including Assurance (8 items = 16,17,18,20,21,22,23,24), Knowledge-Skill (5 items = 9,10,11,12,15), Respectfulness (6 items = 1,3,5,6,13,19), and Commitment (5 items = 2,4,7,8,14), and a total of 24 items. A 6-point Likert-type scale (1 = never, 2 = almost never, 3 = sometimes, 4 = often, 5 = most of the time, 6 = always) was used for responses. The internal consistency of the scale for both patients and nurses was found to be between 0.82 and 0.92 for subscales and 0.96 for the total scale. For this study, Cronbach's Alpha coefficient for nurses' CBI-24 was calculated as 0.92, and for patients, it was calculated as 0.87. To calculate scale scores, the scores of the 24 items were summed to obtain the total scale score, then divided by 24 to obtain a scale score between 1 and 6. For each subscale, the scores of the items in each subscale were summed, and the subscale score between 1 and 6 was obtained by dividing the obtained score by the number of items in the subscale. As both subscale and

total scale scores increase, the level of perception of nursing care quality by patients or nurses increases. A high score obtained from the scale indicates a more positive perception of nursing care quality [9,10].

Data Collection

Data were collected through face-to-face interviews with patients undergoing cancer surgery in the general surgery and surgical oncology services from April 1, 2022, to April 1, 2023. Before starting the study, it was explained that both nurses and patients voluntarily participated in the study, and their written consents were obtained. Filling out the forms took approximately 15-20 minutes for each individual.

Data Analysis

Data were analyzed using the SPSS 23.00 software package. The normality of the data was assessed with the Kolmogorov-Smirnov (*K-S*) test. Since the data showed a normal distribution, parametric tests were used for analysis. Descriptive statistics, including numbers, frequencies, and means, were used to determine the characteristics of the participants. Independent sample *t*-test was used to examine differences between groups, and the *F* test (ANOVA) was used for more than two groups. The relationship between nurse care behavior and patient perception of care behavior was determined using Pearson correlation analysis. The level of statistical significance was accepted as $p<0.05$.

Ethical Approvel

Before starting the study, approval was obtained from the Sivas Cumhuriyet University Non-Interventional Clinical Research Ethics Committee (Decision no: 2022-03/14, Date: 23.03.2022).

Results and Discussion

Table 1 presents the comparison of patients' demographic characteristics and mean scores of the CBI-24. In the table, it can be observed that the average age of the patients was 46±2.74, 65.8% were female, 92.3% were married, and 76.8% had an elementary school education. Furthermore, 96.8% had chronic illnesses, 96.1% had previous hospital experience, 63.2% had undergone surgical procedures in the past, 32.9% had surgery due to rectal cancer, 62.6% stayed in the hospital for 1-7 days, and 71% were accommodated in four-person patient rooms. There was a statistically significant difference found between patients' gender, marital status, previous hospital experience, history of surgical procedures, reason for surgery (cancer type), length of hospital stay, and room characteristics with CBS-24 mean scores ($p<0.05$).

Table 1. Patients' demographic characteristics and mean scores of the Care Behaviors Inventory-24 (n=310)

Demographic Characteristics						
	Mean±SD					
Age	46±2.74			**CBI-24**		
		n	**%**	**Mean±SD**	**Test**	***p***
Gender	Female	204	65.8	3,34±0,74	*t*= 5.825	0.000**
	Male	106	34.2	4,10±0,75		
Marital status	Not married	24	7.7	3,56±0,84	*t*= 2.002	0.040*
	Married	286	92.3	4,07±0,25		
Educational status	Literacy	50	16.1	3,36±0,29	*F*= 1.685	0.189
	Primary school	238	76.8	3,67±0,90		
	Secondary school	22	7.1	3,37±0,48		
Chronic disease	Yes	10	3.2	3,50±0,06	*t*= 1.631	0.442
	No	300	96.8	3,77±0,58		
Past hospital experience	Yes	298	96.1	3,64±0,81	*t*= 2.838	0.033*
	No	12	3.9	2,72±0,77		

Prior surgical intervention	Yes	196	63.2	3,72±0,97	*t*= 2.525	0.013*
	No	114	36.8	3,37±0,34		
Reason for surgery – type of cancer	Rectum	102	32,9	4,31±0,82	*F*= 23.533	0.000**
	Breast	68	21,9	2,85±0,66		
	Stomach	69	22,3	3,45±0,30		
	Thyroid	34	10,9	4,14±0,40		
	Pancreas	9	2,9	3,70±0,37		
	Colon	28	9,1	2,64±0,59		
Length of stay in hospital	1-7 days	194	62,6	4,22±0,32	*t*= 2.782	0.002*
	8 days over	116	37,4	3,65±0,47		
Patient room feature	Private room	36	11.6	2,70±0,20	*F*= 45.631	0.000**
	Double	54	17.4	2,88±0,80		
	Four-person	220	71.0	3,93±0,65		

**p<0.05, **p<0.001, CBI-24: Care Behaviors Inventory-24*

Table 2 provides a comparison of nurses' demographic characteristics and mean scores of the CBI-24. When examining the table, it can be observed that the average age of the nurses was 34.08±2.02, 80.6% were female, 61.3% were married, 45.2% had a bachelor's degree in nursing, 74.2% had been practicing nursing for 1-5 years, 38.7% chose the nursing profession willingly, 51.6% willingly worked in their current clinic, and 87.1% worked in a shift-based schedule. There was a statistically significant difference found between nurses' education level, willingness to choose the nursing profession, willingness to work in their current clinic, and duration of working in the current clinic with CBS-24 mean scores (p<0.05).

Table 3 provides the mean scores of the CBI-24 for both nurses and patients, including total scores and subscale scores. Upon reviewing the table, it can be observed that patients had an average total CBS-24 score of 3.60±0.82. The subscale mean scores for patients were as follows: Assurance subscale: 3.54±0.86, Knowledge-Skill subscale: 3.64±0.88, Respectfulness subscale: 3.52±0.85, and Commitment subscale: 3.74±0.81. The table also includes the mean scores of nurses for the total CBS-24 and its subscales.

Table 2. *Nurses' demographic characteristics and mean scores of the Care Behaviors Inventory-24 (n=31)*

Demographic Characteristics						
	Mean±SD					
Age	34,08±2.02			**CBI-24**		
		n	**%**	**Mean±SD**	**Test**	***p***
Gender	Female	25	80.6	3,75±0,85	t= 1.013	0.336
	Male	6	19.4	4,18±1,11		
Marital status	Not married	12	38.7	4,21±0,94	t= 1.839	0.078
	Married	19	61.3	3,62±0,85		
Educational status	High school	8	25.8	3,20±0,49	F= 9.284	0.000**
	Associate degree	5	16.1	3,03±0,64		
	Licence	14	45.2	4,13±0,70		
	Master's degree	4	12.9	4,90±0,92		
Curation of working	1-5 years	23	74.2	3,71±0,91	F= 1.112	0.360
	6-10 years	5	16.1	3,73±0,86		
	11-15 years	1	3.2	3,58±0,74		
	16 years	2	6.5	5,00±1,17		
Willingness to choose the nursing profession	Yes	12	38.7	4,39±0,92	t= 3.428	0.002*
	No	19	61.3	3,41±0,66		

willingness to work in their current clinic	Yes	16	51.6	4,32±0,87	t= 4.368	0.000**
	No	15	48.4	3,22±0,55		
Duration of working in the current clinic	Less than 1 year	9	19.4	4,39±0,96	F= 4.415	0.011*
	1-5 years	22	74.2	3,55±0,73		
	6-10 years	1	3.2	3,58±0,34		
	11-15 years	1	3.2	5,83±0,51		
How it works	During the day	4	12.9	4,46±1,19	t= 1.125	0.333
	Shift	27	87.1	3,77±0,87		

**p<0.05, **p<0.001, CBI-24: Care Behaviors Inventory-24*

Table 3. The Subscale and Mean Scores of the Care Behaviors Inventory-24 for Nurses and Patients

CBI-24 subscales	**Patients**		**Nurses**	
	Mean±SD	**Min-max**	**Mean±SD**	**Min-max**
Assurance	3.54±0.86	2-5	2.94±0.72	1,5-4,5
Knowledge-Skill	3.64±0.88	2-5	3.87±0.94	2-6
Respectfulness	3.52±0.85	2.17-5	3.82±0.91	2-6
Commitment	3.74±0.81	2.20-5	3.76±0.91	2-6
Total CBI-24	3.60±0.82	2.08-5	3.83±0.92	2-6

CBI: Care Behaviors Inventory-24

Table 4 presents the Pearson correlation analysis showing the relationship between nurses' and patients' mean scores on the CBI-24. According to the table, there is a statistically significant positive correlation at a high level (p<0.05) between nurses' and patients' mean scores on the CBS-24 subscales and the total scores. In other words, as the average scores for nurses' care behaviors increase, the average scores for patients' perception of care behaviors also increase.

Table 4. *The Relationship Between Nurses' and Patients' Care Behaviors Inventory-24 Mean Scores*

		Nurses' CBI-24 Sub-Dimensions and Total Average Scores				
Patients' BDI-24 Sub-Dimensions and Total Average Scores		Assurance	Knowledge-Skill	Respectfulness	Commitment	Total CBI-24
Assurance	r	1	0.893	0.689	0.687	0.874
	p		0.03*	0.000**	0.000**	0.04*
Knowledge-Skill	r	0.893	1	0.947	0.768	0.593
	p	0.03**		0.000**	0.000**	0.000**
Respectfulness	r	0.689	0.947	1	0.647	0.750
	p	0.000**	0.000**		0.000**	0.000**
Commitment	r	0.687	0.768	0.647	1	0.748
	p	0.000**	0.000**	0.000**		0.000**
Total CBI-24	r	0.874	0.593	0.750	0.748	1
	p	0.04*	0.000**	0.000**	0.000**	

**p<0.05, **p<0.001, CBI: Care Behaviors Inventory-24*

The concept of care and care behaviors are perceived differently among patients served in various situations [11]. This study was conducted with the aim of determining the relationship between nurses' care behaviors after cancer surgery and patients' perception of care behaviors.

The findings of this study indicate that nurses exhibit care behaviors above a moderate level, and patients have a similar level of perception of care behaviors. Furthermore, a statistically significant positive relationship was found between nurses' care behaviors and patients' perception of care behaviors. This suggests that nurses' care behaviors are tangible and observable by patients and that these behaviors are positively reflected in patients' perceptions. While some studies support the findings of our study [12-14], others, in contrast, show that patients' perceptions of care do not always align with nurses' perceptions [15-16]. At this point, it can be said that there is a need for more relational studies on patient and nurse care behaviors and further evidence.

In this study, it was found that there was a difference between patients with a history of previous hospital experience and those who had undergone previous surgical procedures in their perception of care behaviors. Similar results were published by Kabaroğlu and colleagues [17]. This difference may be attributed to the quality of nursing care being good in previous hospital experiences or nurses exhibiting positive patient care behaviors before.

There was also a difference in the perception of care behaviors based on the reason for surgery (cancer type) among patients. Previous studies have shown that patients' perception of care behaviors varies based on the diagnosis they receive and the type of surgical procedure they undergo [18,19]. In another study [20], it was found that patients diagnosed with cancer had a higher perception of care behaviors. In this study, all patients were cancer patients, and according to the results of the study, it is believed that the size of the surgical procedure and the patients' perception of cancer affected the perception of care behaviors. Additionally, there was a statistically significant difference in perception of care behaviors based on the length of hospital stay and room characteristics. A shorter length of hospital stay and having fewer roommates may have influenced patients' comfort, thereby affecting their perception of care behaviors.

Nurses' education level is an important factor influencing care behaviors. It was found that there was a difference in care behaviors based on nurses' education level, with nurses exhibiting higher-level care behaviors as their education level increased. These findings are consistent with the results of Zakerimoghadam and Rezaei [22] but not with Mobley and colleagues [23]. As can be seen, the literature contains conflicting results.

Some studies [23, 24] have suggested a negative relationship between nurses' years of service and their affection for the profession with care behaviors. In the present study, there was a significant difference in care behaviors among nurses who chose the profession willingly, willingly worked in their current clinic, and had 1-5 years of experience in the clinic. It can be said that nurses' professional experience leads to mental transformations over time, and having a shorter length of service may make nurses more sensitive to patients. Additionally, nurses in this study may have positively influenced their care behaviors by choosing and enjoying their profession. Indeed, this may have also been reflected in patients' perception of care behaviors.

The authors suggest that activities aimed at meeting the basic needs of patients undergoing cancer surgery in nursing care have become routine, and patients are satisfied with these practices. Furthermore, these activities form the foundation of the nursing care concept, which may create a positive perception of care behaviors in patients by meeting their expectations.

Conclusion

In this study, it was concluded that there is a positive relationship between nurses' care behaviors and patients' perception of care behaviors. Additionally, it was determined that nurses' care behaviors and patients' perceived care behaviors were above a moderate level. It was observed that patients' demographic characteristics did not affect their perceived care behaviors and satisfaction levels. It was also found that nurses' care behaviors were relatively higher than patients' perceptions of care behaviors. In line with these findings, further research should be conducted to explore approaches that can increase the perceived care behaviors by patients, and various strategies should be developed. Healthcare institutions should regularly assess the care behaviors exhibited by nurses and the level of care behaviors perceived by patients using valid and reliable instruments. The results should be shared with the institution's nursing staff.

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INVESTIGATION OF ANTI-TUMOR ACTIVITY OF β - GLUCAN ON CHRONIC MYELOID LEUKEMIA CELL LINE

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ABSTRACT

Background

Chronic myeloid leukemia (CML) is a clonal myeloproliferative neoplasm driven by BCR-ABL1 oncoprotein [1]. The development of the tyrosine kinase inhibitor (TKI) imatinib allows patients with CML to experience near-normal life expectancy. Specific point mutations that decrease drug binding affinity can produce TKI resistance, and second- and third-generation TKIs largely mitigate this problem. Some patients develop TKI resistance without known resistance mutations, with significant heterogeneity in the underlying mechanism. TKI treatment are short lived in advanced phases of the disease or in BCR-ABL1-positive acute lymphoblastic leukemia, with relapse driven by both BCR-ABL1 kinase-dependent and -independent mechanisms [2]. Glucans are part of a group of biologically active natural molecules and are steadily gaining strong attention not only as an important food supplement, but also as an immunostimulant and potential drug [3]. The aim of this study was to investigate the antitumoral efficacy of beta-glucan on the CML cell line.

Methods

Using XTT test, the efficacy of β -glucan on the survival of CML K562 cell line was investigated. These cells were cultivated at a concentration of 1×10^4 cells per well and incubated overnight before the addition of β -glucan. After that the different concentrations (25, 50, 100, 250, 500 µM) of β -glucan were applied to cells for 24 h. Cells that had not been treated were used as a control. Following 4-hour incubation, the cells were shaken and the absorbance was measured using a microplate reader at 450 nm. Cell viability was evaluated as a percentage of live cells versus untreated cells after each experiment was done three times. Cell viability was evaluated as a percentage of live cells versus untreated cells after each experiment was done three times. Statistical evaluation of the data was performed by One Way ANOVA, statistical significance was defined at $p<0.05$.

Results

There was no significant decrease in the viability of CML K562 cells in treated-groups compared to the control.

Conclusions

β -glucan did not produce antitumoral effect against chronic myeloid leukemia. More clinical trials are needed for new therapeutic agents in the treatment of CML.

Keywords: *β -glucan, chronic myeloid leukemia, XTT, K562 cell line*

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IS EVERY DISTANT ORGAN INVOLVEMENT SEEN ON PET/CT IMAGING A METASTASIS? CASES REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Cancer is a leading cause of global and national mortality, second only to cardiovascular diseases. The diagnosis, staging, and treatment of cancer often involve various radiological diagnostic tools, including X-ray, ultrasound, CT, MRI, and PET/CT scans. Among these, PET/CT has gained significance in tumor localization, detecting distant metastases, and postoperative follow-up. However, despite its reliability, PET/CT results can be influenced by factors like increased tissue perfusion, inflammation, and muscle contractions, potentially leading to misinterpretations by clinicians. This report presents a case involving a 57-year-old female patient scheduled for gastric cancer surgery. During the PET/CT scan, an unusual radionuclide uptake caused by rectum muscle contraction led to the false impression of metastasis.

Introduction

Cancer ranks among the most common causes of mortality worldwide and in our country, following cardiovascular diseases [1]. In the diagnosis, staging, and treatment of cancer, in addition to laboratory tests, a variety of radiological diagnostic tools such as X-ray, ultrasound (USG), computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography-computed tomography (PET/CT) are utilized [2], [3]. Among these, PET/CT has increasingly become one of the most important imaging modalities due to its applications in tumor localization, detection of distant metastases, and postoperative follow-up [4]. However, despite its widespread use and reliability, PET/CT can sometimes be affected by various factors, such as increased tissue perfusion, inflammation, and intense muscle contractions, which can occasionally mimic tumor metastasis and lead to misinterpretation by clinicians [5], [6].

In this report, we aim to present a case of a 57-year-old female patient scheduled for surgical intervention due to gastric cancer. The PET/CT imaging performed for staging revealed an erroneous positivity in the rectum attributed to muscular contraction despite the absence of distant organ metastasis and the lack of any tumoral lesion during perioperative evaluation.

Case Report

A 57-year-old female patient applied to the gastroenterology clinic in an external center with complaints of abdominal pain, swelling, nausea, and weight loss that had been present for about three months. Biopsy was taken from the tumoral mass seen in the stomach antrum during upper gastrointestinal endoscopy. The pathology department reported the histopathological examination of the biopsy material as stomach adenocarcinoma. The patient applied to our clinic for a surgical procedure. Laboratory tests did not reveal any abnormal findings except for hypochromic microcytic anemia. In PET/CT taken for staging in the preoperative preparation period, the SUVmax value of the tumor formation in the anterior surface of the stomach antrum was measured as 7.4 (Figure 1 A). However, interestingly, there was no pathological radionuclide uptake in the abdomen, thorax, bones, and brain, while an uptake with an SUVmax value of 14.2 was observed in the lower rectum (Figure 1 B). The patient's rectum and colon were evaluated as normal in colonoscopy. Thin-section pelvic MRI was taken for a more detailed examination. The rectum was normal, with surrounding soft tissues on MRI images (Figure 2).

The patient was taken to surgery. The operation was started laparoscopically, and all organs in the abdomen were explored. On exploration, a mass of approximately 3x4cm was seen on the anterior surface of the stomach antrum (Figure 3 A). During the surgical exploration, no pathological finding suggestive of a tumor was found in the rectum (Figure 3 B). The patient was accepted as primary gastric cancer, and Subtotal Gastrectomy + Billroth II gastrojejunostomy + D2 dissection was performed. After one day, the patient was taken to the ward in the postoperative general surgery intensive care unit. Oral was started on the 5th postoperative day. His drains were removed at the later follow-ups, whose yield decreased, and he was discharged on the 7th postoperative day without complications. Histopathological evaluation was reported as gastric adenocarcinoma.

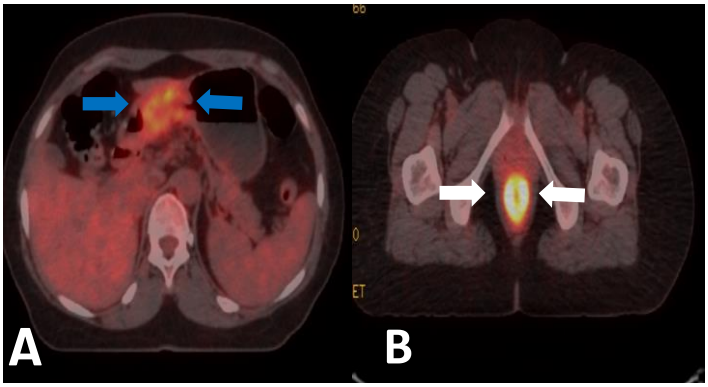

Figure 1. *In the PET-CT axial and coronal sections, it is seen that radionuclide material is more intensely uptake in the rectum (white arrow) (B) in the lower pelvic region, as well as the primary tumoral (blue arrow) (A) uptake in the stomach antrum at the upper abdomen level.*

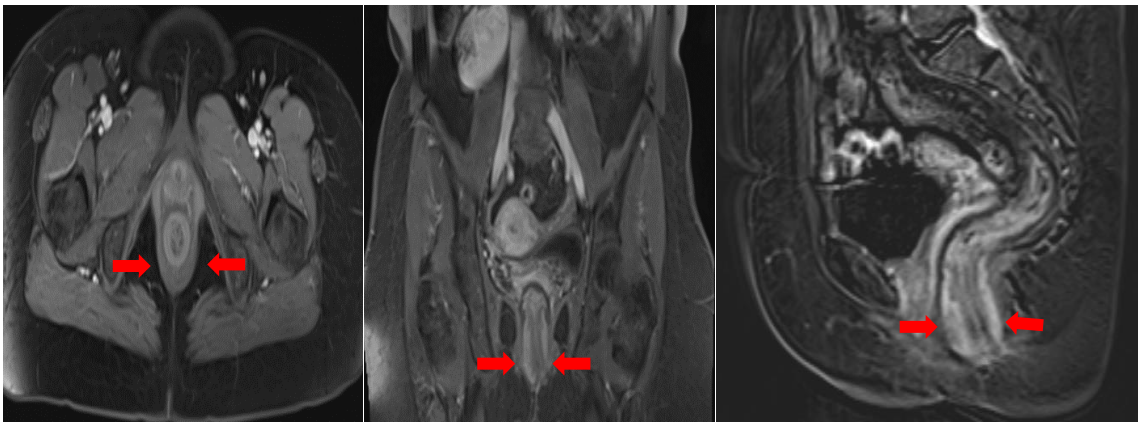

Figure 2. *Axial and coronal sections of MRI show that the ultrastructural of the rectum and surrounding tissues are normal (blue arrows)*

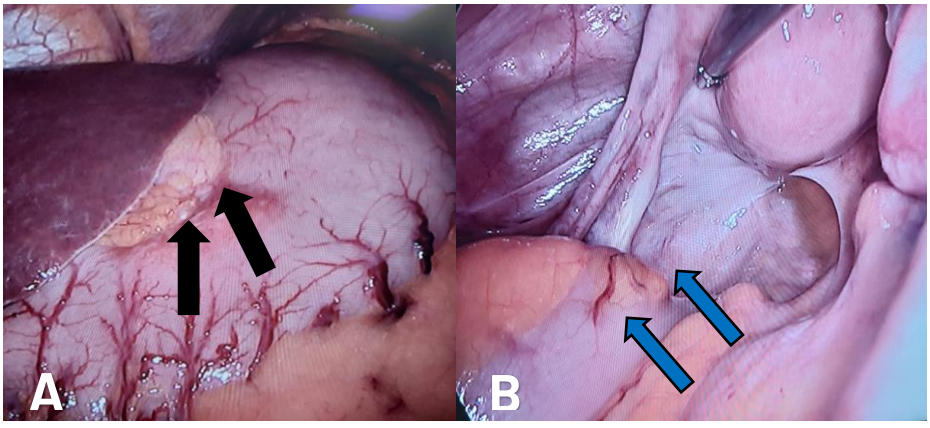

Figure 3. *In the intraoperative images, there is a tumoral appearance on the anterior surface of the antral region of the stomach (A) (black arrows). At the same time, the rectum appears to be normal together with the surrounding tissues (B) (blue arrows)*

Discussion

Gastric adenocarcinoma is a malignancy originating from the epithelial cells of the stomach lining [7]. It is a relatively common cancer worldwide, with varying incidence rates among different geographic regions and populations [8]. In this case, we present a 57-year-old female patient with complaints of abdominal pain, swelling, nausea, and weight loss, which prompted further investigation. The diagnosis of gastric adenocarcinoma was established through histopathological examination of a biopsy taken from the tumoral mass in the stomach antrum during upper gastrointestinal endoscopy [9]. This procedure remains a crucial diagnostic tool for the evaluation of gastric lesions, allowing for both tissue sampling and visual assessment [7]. One noteworthy aspect of this case is the absence of pathological radionuclide uptake in the abdomen, thorax, bones, and brain during the preoperative PET/CT scan, despite the clear presence of gastric adenocarcinoma. Interestingly, an abnormal uptake with an SUVmax value of 14.2 was observed in the lower rectum, even though colonoscopy revealed no apparent abnormalities in the rectum and colon. This discrepancy between imaging findings and clinical evaluation posed a diagnostic challenge. To further investigate the rectal uptake, thin-section pelvic MRI was performed, which did not reveal any abnormalities in the rectum or surrounding soft tissues. This discrepancy between the PET/CT and MRI findings underscores the importance of a comprehensive diagnostic approach, including both imaging modalities and endoscopic evaluation. The primary treatment strategy for gastric adenocarcinoma typically involves surgical resection [10]. In this case, the patient underwent Subtotal Gastrectomy with Billroth II gastrojejunostomy and D2 lymph node dissection. The decision to perform surgery was based on the laparoscopic exploration findings, which confirmed the presence of a mass on the anterior surface of the stomach antrum. The absence of pathological findings suggestive of a tumor in the rectum during exploration led to the conclusion that the rectal uptake observed in PET/CT was unrelated to the gastric adenocarcinoma. The patient's postoperative course was uneventful, and they were discharged without complications. Histopathological evaluation confirmed the diagnosis of gastric adenocarcinoma, consistent with the preoperative biopsy findings. This case highlights the complexity of diagnosing and managing gastric adenocarcinoma and emphasizes the importance of a multidisciplinary approach involving gastroenterologists, radiologists, and surgeons. It also underscores the limitations of imaging modalities in certain cases and the need for complementary diagnostic tools such as endoscopy and histopathological examination to guide clinical decision-making.

In conclusion, this case report illustrates the challenges and diagnostic nuances encountered in the evaluation and management of gastric adenocarcinoma. The atypical imaging findings in this case serve as a reminder of the importance of integrating clinical, radiological, and histopathological information to make accurate diagnoses and treatment decisions in the context of gastric cancer. Further studies and larger case series may shed light on the incidence and significance of discordant imaging findings in gastric adenocarcinoma.

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THE RELATION BETWEEN MEDIASTINAL LYMPH NODE DENSITY AND RADIOTRACER UPTAKE IN PATIENTS WITH LUNG CANCER

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ABSTRACT

Lung cancer is common worldwide and a frequent cause of cancer-related deaths. [1]. Positron emission tomography (PET/CT) is the gold standard in many studies for noninvasive lymph node (LN) classification in patients with lung cancer. [7-10]. This study investigated the correlation between Maximum standardized uptake value (SUVmax) and LN density. Thus, we aimed to increase the sensitivity in determining suspicious LN with density criteria on unenhanced thorax CT.

This study included 46 patients diagnosed with lung cancer who had PET/CT between January 2023 and July 2023. 29 PET +, 28 PET - LN detected. An ROI area was determined according to the shape of the LN node on the non-contrast base images of PET/CT, and LN density was measured. (Figure 1). The density of LNs and Suv max ratios were compared. LNs with prominent fatty hilus, central necrosis, calcified LNs, and LNs with unclear borders from neighboring anatomical structures were excluded from the study because it would cause erroneous results in density evaluation (Figure 2). In eligible persons, PET + and PET - LN were tried to be obtained from the same patient (Figure 3).

LN short axis was 13.7 (±5) mm in the PET + group and 8.4 (±2.55) mm in the PET - group and was significantly higher in the PET + group ($p<0.001$) (Table 1). HU değeri pet + grupta 41.1 (±14,3), pet – grupta 26,3 (±14,1) olup pet + grupta anlamlı yüksekti ($p<0,001$) (Table 2).

In conclusion, we found that adding density to the LN short axis and shape criteria on non-contrast thorax CT of patients with lung cancer increases the sensitivity for metastatic LN.

Keywords: *Lung cancer, positron emisson tomography (PET/CT), computed tomography, Hounsfield unit, lymph node metastasis*

Introduction

Lung cancer is common worldwide and a frequent cause of cancer-related deaths [1]. Positron emission tomography (PET/CT) is the noninvasive routine imaging modality in lung cancer. In addition, mediastinal lymph node (LN) evaluation is also performed with this method [2]. Correct mediastinal LN staging is necessary because the involvement of contralateral or widespread mediastinal lymph nodes can make the patient inoperable and is associated with a bad prognosis [3]. In diagnosing mediastinal LN metastasis, density measurement on CT can be a guide, as well as radiotracer uptake, because the LN's hilar fatty tissue is lost due to metastasis [2]. Therefore, we investigated the relationship between LN density and Maximum standardized uptake value (SUVmax) in this study.

Method

Patients diagnosed with lung cancer who had PET/CT between January 2023 and July 2023 were retrospectively screened. A PET/CT scan was made with a GE Discovery 600 device. 68Ga-DOTATATE PET/CT was used in neuroendocrine tumors and 18F-FDG PET/CT in others. 68Ga-DOTATATE, 18F-FDG was given at the required dose 60±5 minutes before acquisition. Patients' first PET CT images before treatment were taken as the basis for avoiding treatment effects. We used the unenhanced base image of the PET/CT to avoid the

contrast effect. LN's long axis greater than 10 mm was selected to make PET/CT meaningful regarding radioactive material uptake. An ROI area was determined according to the shape of the LN on the PET/CT base images, and LN density was measured (Figure 1). The SUVmax value of the same LN was also taken, and correlation analysis was performed. PET + was considered when the SUVmax value was more than three times the blood pool, and PET – was considered when it was equal to or less. LNs with demarcated borders from adjacent anatomical structures were selected for accurate density measurement. LNs with unclear borders from neighboring anatomical structures were excluded from the study (Figure 2).

LNs with prominent fatty hilus and central necrosis and calcified LNs were excluded from the study because it would cause erroneous results in density evaluation. (Figure 2).

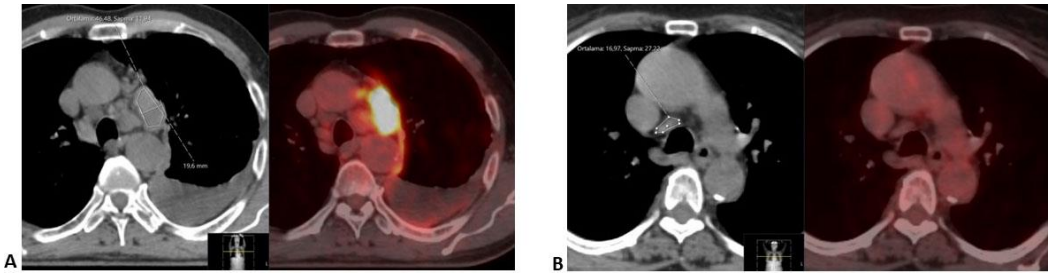

Figure 1. *Density measurement with ROI circle in non-contrast CT base images of PET + LN in the aorticopulmonary window (A) and PET – LN in the right paratheca l (B)*

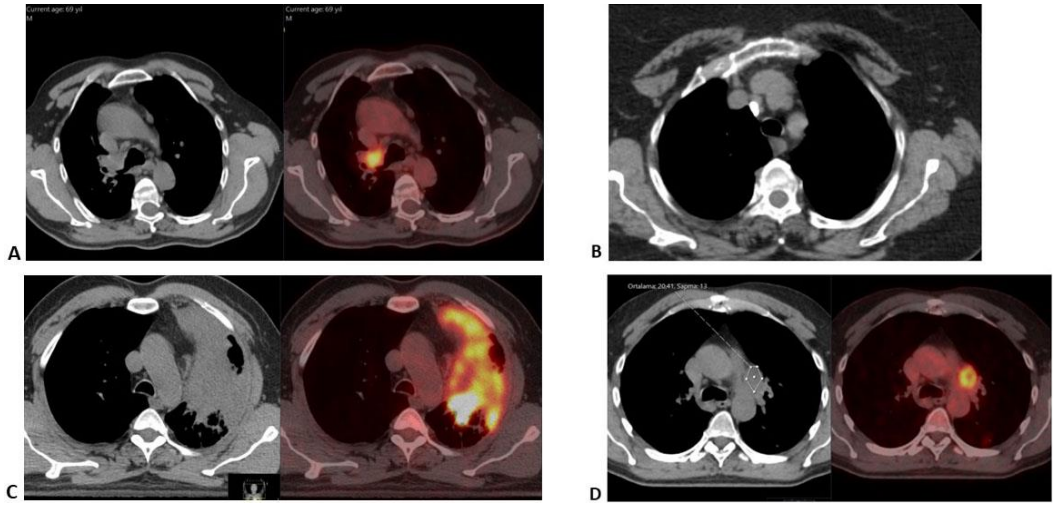

Figure 2. *LN with unclear borders with adjacent anatomical structures (A), calcified LN (B), LN with prominent fatty hilus (C) and necrotic LN (D)*

PET + and PET - LNs were taken from the same patient in suitable people. (Figure 3). Thus, the person factor was also reduced.

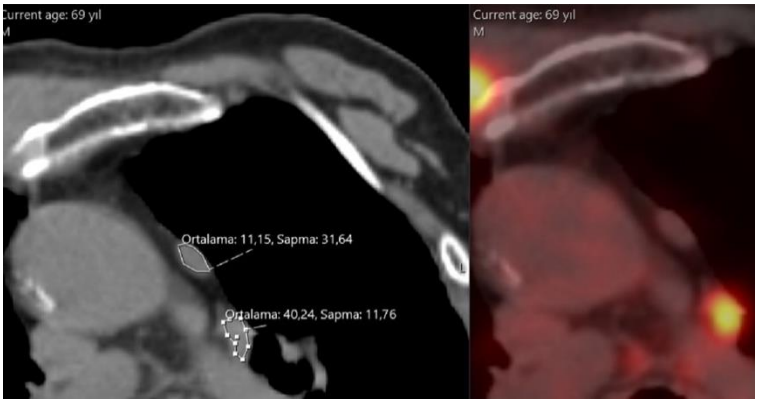

Figure 3. *Density measurements of PET + (anterior) and PET – (posterior) LN from the same patient*

Descriptive statistics; for quantitative variables, it was presented as mean ± standard deviation or median (IQR) according to compatibility with normal distribution, and frequency (percent) for qualitative variables. The test of Shapiro-Wilk was determined the normality of the data. If the data was distributed normally, an independent samples t-test was used, and if it was distributed non-normally, the Mann-Whitney U test was used. Analyses were made with SPSS statistical software version 25.0. P values less than 0.05 were taken into account as statistically significant.

Results and Discussion

29 PET + and 28 PET - LNs from 46 patients were included in the study. PET + and PET - LNs were obtained from the same person in 11 patients. The PET + group had 15 adenocarcinomas, 11 squamous cell cancer, 2 small cell lung cancer, and 1 neuroendocrine tumor. The PET - group had 10 adenocarcinomas, 9 squamous cell cancers, 1 mesothelioma, 2 neuroendocrine tumors, 4 pneumonia, and 1 lung nodule. The mean age of the PET + group was 66.6 (10±), and the PET - group was 63.7 (11.5±), and there was no significant difference (p=0,32). LN short axis diameter (SAD) was 13.7 (±5)mm in the PET + group and 8.4 (±2.55) mm in the PET - group and was significantly higher in the PET + group (p<0,001) (Table 1).

The HU value was 41.1 (±14.3) in the PET + group and 26.3 (±14.1) in the PET - group, and it was significantly higher in the PET + group (p<0,001) (Tablo 2).

No significant correlation was found between SUV value and HU in the PET+ group (r=-0,14, p=0,45).

Radiologically, CT diagnostic criteria for metastatic LNs are primarily size, shape, margin, density, and contrast enhancement patterns. Among these, size is the most common criterion. In most studies, a SAD above 1 cm is generally considered the threshold for malignancy [4]. However, metastatic LNs of normal size cause false negativity [5,6]. Thorax CT is a commonly used imaging modality in diagnosing and following up lung cancer. However, although short axis and shape criteria are frequently used to evaluate LN in Thorax CT, false negativity is not rare. CT sensitivity for mediastinal LN staging is low at 57% [7]. PET/CT is the gold standard for noninvasive lymph node classification in lung cancer patients due to its high accuracy, proven in multiple studies [7-10].

Table 1. *Comparison of patient age and LN SAD in PET+ and PET- groups*

Independent Sample t Test					
	Groups	**n**	**Mean**	**Std. Deviation**	**P (Sig.)**
Age	PET +	29	66,6	10	0,32
	PET -	28	63,7	11,5	
LN short axis	PET +	29	13,7	5	<0,001
	PET -	28	8,4	2,5	

Table 2. *Comparison of LN density in PET + and PET- groups*

Mann Whitney U Test					
	Groups	**n**	**Median**	**Std. Deviation**	**P (Sig.)**
HU	PET +	29	41,1	14,3	<0,001
	PET -	28	26,3	14,1	

A study in patients with lung cancer showed that PET positivity with 89% sensitivity and 84% specificity is a significant measure for malignant LN infiltration [11]. In this study, we accepted pet ct as a reference. Therefore, we aimed to increase the diagnosis of metastatic LN by adding density criterion to the size criterion on non-contrast CT and to achieve the sensitivity of PET CT. 27 of 38 LNs above 26 Hu were PET +, and 5 of them had a SAD less than 10 mm. There were only 2 PET + LNs smaller than 26 HU, and their SAD was over 10 mm. Using 26 hu and 10 mm as the threshold, sensitivity and specificity were 76% and 89%, respectively, and both showed a significant increase. This information showed us that LN density increases the sensitivity of

malignant LN on CT, and 26 HU was the threshold value for malignant LN in our study. Nevertheless, not every LN above 26 HU was PET+. Therefore, HU evaluation increases the sensitivity of CT LN but is inferior to PET CT.

In a study, Lee et al. found the median HU values of metastatic LNs in the 25-45 HU range. Accordingly, 71.0% (115/162) of malign LNs were between 25 and 45 HU. 78.9% (86/109) of median HU values of the benign nodes were outside the 25-45 hu range [12]. In a study conducted with 60 LN (36 metastatic, 24 non-metastatic) from 43 patients with lung cancer, the density of malignant LNs was higher in contrast-negative CT. The mean density of malignant LNs was 33,2, and benign LNs was 10,1 HU. This study observed no significant difference between malignant and benign LNs on contrast-enhanced CT [2].

Conclusion

If we add density to the LN's SAD and shape criteria in the CT of patients with lung cancer, we will increase the sensitivity of CT in the detection of malignant LN.

Acknowledgments

I want to thank Dr. Zekiye Hasbek for her contributions to this study.

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GASTROINTESTINAL SYSTEM LYMPHOMAS: A SINGLE CENTER EXPERIENCE

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ABSTRACT

Objective

Non-Hodgkin Lymphoma (NHL) is a hematological malignancy characterized by abnormal clonal proliferation of lymphoid cells originating from lymph nodes or extranodal lymphatic tissues. It often presents with enlarged lymphadenopathy. Extranodal involvement can also be detected frequently. The most common extranodal involvement is detected in the gastrointestinal tract. Our aim in this study is to share the follow-up and treatment findings of patients with gastrointestinal lymphoma in our clinic.

Materials-methods

Our aim in this study was to present the diagnosis, prognosis and vital data of 10 patients with gastrointestinal system involvement that we followed in our clinic for the last 5 years.

Results

The patients in our study consisted of a total of 10 patients, 5 females and 5 males. The minimum age of the patients was 46 and the maximum age was 86, with a median of 62 years. Three of the patients were diagnosed from stomach, 2 from small intestine, 3 from colon, 1 from rectum, and 1 from pancreas. All patients received combined chemotherapy with Rituximab. Complete remission was achieved in 7 patients.

Conclusion

Gastrointestinal involvement is the most common extranodal involvement of Non-Hodgkin lymphoma, and very good responses are obtained with Rituximab-based treatments.

Keywords: *Gastrointestinal tract, lymphadenopathy, non-hodgkin lymphoma*

Introduction

Non-Hodgkin Lymphoma is a heterogeneous group of tumors caused by the malignant transformation of mature and immature cells of the lymphoid system, caused by 85-90% of B lymphocytes and to a lesser rate T lymphocytes and natural killer (NK) cells (1). NHL has more than 30 subtypes originating from B-cell, T-cell, and NK cells. Most common NHL subtypes in developed countries; Diffuse large B-cell lymphoma (~ 30%) and Follicular lymphoma (~ 20%). Although it is difficult to use in clinical practice, we can divide the disease into two groups according to its behavior as indolent (low-grade, slow-progressing) form and aggressive (moderate-high-grade) form. Diffuse large B-cell lymphoma (DLBCL) is the most common aggressive NHL subtype, while follicular lymphoma is the most common subtype among indolent NHLs (2).

The most common clinical presentation of NHL is asymmetric, painless, enlarged lymphadenopathy. Approximately two-thirds of patients present to clinicians with peripheral (cervical, axillary, inguinal) lymphadenopathy. Although B symptoms (fever, night sweats and weight loss) are seen in approximately 40% of patients, they are mostly observed in advanced stage patients or aggressive tumors and indicate poor prognosis. Extranodal lymphoma; It is defined as the involvement of organs and structures other than lymph nodes, such as the spleen, thymus, and pharyngeal lymphatic ring. Gastrointestinal system, bone, skin, lung,

central nervous system are the most common extranodal involvement sites. Primary extranodal disease occurs in approximately 10-35% of NHLs and most commonly involves the gastrointestinal tract (44%) and upper respiratory tract (19%). Bone (8%) and central nervous system (5%) involvement is observed to a lesser extent. However, approximately 50% of patients may develop extranodal involvement during the course of their disease (3). Lymphomas involving the gastrointestinal tract are seen in approximately 30-40% of extranodal lymphomas; Nausea, vomiting, aversion to food, weight loss, abdominal fullness, early satiety and visceral obstruction may present with symptoms. Patients may apply to clinics with acute perforation, gastrointestinal bleeding, and sometimes even malabsorption syndrome (3).

Material-Methods

Our study included 10 patients diagnosed with Non-Hodgkin lymphoma from the gastrointestinal tract, who were diagnosed and followed up in our clinic between 2017-2022 in Sivas Cumhuriyet University Faculty of Medicine Hematology clinic. The data of the patients were scanned retrospectively from their files. Demographic data, pathology results, laboratory data, and treatment protocols of the patients were recorded.

Results

A total of 10 patients, 5 female and 5 male, diagnosed with Non-Hodgkin lymphoma from the gastrointestinal tract were included in our study. The median age of the patients was 62 years. Histologic subtype was Diffuse Large B-cell lymphoma in 8 of 10 patients and Follicular lymphoma in 2 patients. Three of the patients were diagnosed from stomach, 2 from small intestine, 3 from colon, 1 from rectum, and 1 from pancreas.

Table 1. *Demographic data of patients, treatment and prognostic data*

	Age	**Gender**	**Subtip**	**involvement site**	**Stage**	**Bulky**	**BM involvement**	**IPI**	**Treatment**	**latest status**	**living situation**
Case 1	56	M	DLCBL	Rectum	4XB	+	-	1	R-CHOP + İT MTX	Remission	Alive
Case 2	60	M	DLCBL	Small intestine	4B	-	+	2	R-CHOP	Remission	Alive
Case 3	76	M	DLCBL	Transverse colon	3B	-	-	3	R-CHOP + İT MTX	Died during treatment	Ex
Case 4	48	M	DLCBL	Pancreas	3EXB	+	-	3	R-CHOP	Remission	Alive
Case 5	72	M	DLCBL	Stomach	4B	-	-		R-CHOP	Remission	Ex
Case 6	72	F	DLCBL	Transverse colon	3EB	-	-	4	R-CHOP	Died during treatment	Ex
Case 7	86	F	DLCBL	Stomach	3EB	-	-	3	R-miniCHOP	Died during treatment	Ex
Case 8	48	F	DLCBL	Stomach	2B	-	-	0	R-CHOP + İT MTX	Remission	Alive
Case 9	46	F	FL	Colon	3EA	-	-	1	R- Benda	Remission	Alive
Case 10	55	F	FL	small intestine	2A	-	-	0	R- Benda	Remission	Alive

DLBCL: *Diffüz Large B-cell lymphoma* ***FL:*** *Follicular Lymphoma* ***R-CHOP:*** *Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisolo* ***R-BENDA:*** *Rituximab, Bendamustine* ***İT-MTX:*** *Intrathecal Methotrexate,* ***IPI:*** *International Prognostic Index,* ***BM:*** *Bone marrow*

Rituximab-based combined chemotherapy was given to all patients. 8 of the patients were given R-CHOP/mini CHOP, 2 of them were given R-Bendamustine. Intrathecal methotrexate was administered to 3 patients.

Demographic data, treatment and prognostic data of the patients are given in Table 1. The laboratory data of the patients at the time of diagnosis are also given in Table 2. After the treatment, 7 patients went into remission, 3 patients died during the treatment. The follow-up of the patients is still ongoing in our clinic, and one of the patients who went into remission during the follow-ups died due to non-disease reasons.

***Table 2**. Laboratory data of patients at the time of diagnosis*

	WBC	**Neu**	**Lymph**	**Monocyte**	**Hgb**	**PLT**	**AST**	**ALT**	**ALP**	**GGT**	**LDH**	**ESR**
Case 1	8.72	5.75	2.03	0.63	15.3	224000	17	13	113	52	224	10
Case 2	7.54	5.72	0.86	0.57	12.9	308000	20	16	88	80	190	21
Case 3	7.86	5.59	1.07	1.09	12.3	650000	14	8	59	18	247	39
Case 4	6.93	4.72	1.42	0.65	14.6	246000	69	84	169	89	280	52
Case 5	11.41	7.66	1.96	1.60	14	527000	19	15	74	16	252	55
Case 6	10.98	8.48	1.37	0.92	9.9	505000	13	6	191	129	617	102
Case 7	4.70	2.92	1.17	0.46	11.4	265000	11	2	95	9	150	20
Case 8	9.56	7.38	1.66	0.45	10.6	437000	15	12	84	17	163	36
Case 9	5.46	2.82	2.13	0.39	13.9	200000	15	10	58	13	181	2
Case 10	1.94	0.65	0.97	0.25	9.1	239000	26	50	143	33	183	13

***WBC:** White Blood Cell **Neu:** Neutrophil **Lymph:**lymphocyte **Hgb:** Hemoglobin **PLT:** Platelet, **ALT:** Alanine amino transferase, **AST:** Aspartate amino transferase, **ALP:** Alkaline phosphatase, **GGT:** Gamma glutamyl transferase, **LDH:** lactate dehydrogenase, **ESR:** Erythrocyte sedimentation rate*

Discussion

Primary gastrointestinal tract (GIS) lymphomas are the most common type of primary extranodal lymphomas, accounting for 5-20% of all non-Hodgkin lymphomas (NHL) and 30-45% of extranodal lymphomas. In addition, it constitutes 1-4% of all GIS malignancies (4). T

The majority of primary GIS lymphomas occur between the 4th and 7th decades, and the mean age of onset is 55. It is more common in men. In our study, the mean age was 62 and the ratio of men and women was equal. The most common site of involvement in primary GIS lymphomas is the stomach, and it ranges from 24-75% in series (5). This is followed by the small intestine and colon, respectively. In our data, it was detected most frequently in the stomach and colon.

In conclusion, primary GI lymphoma is a heterogeneous disease in terms of clinical and demographic characteristics. However, with the right treatment and follow-up, very good results are obtained.

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CAN FOLLICULAR LYMPHOMA, AN INDOLENT LYMPHOMA, BE AGGRESSIVE?; A CASE REPORT

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ABSTRACT

Non-Hodgkin Lymphoma is a heterogeneous group of diseases that occur as a result of malignant transformation of the lymphoid system. Non-Hodgkin lymphomas are classified as B, T and NK cell. In addition, it can be classified as indolent and aggressive according to its clinical course. Follicular lymphoma is the most common among indolent lymphomas, that is, lymphomas with a silent course. Patients with follicular lymphoma are usually diagnosed at an advanced stage because of its silent and slow course. We wanted to share the treatment and prognosis of a patient who was diagnosed with follicular lymphoma, which is actually an indolent lymphoma, which we followed in the Hematology clinic of Sivas Cumhuriyet University Faculty of Medicine, and who progressed very aggressively during the follow-up .

Keywords: *Aggressive, indolent, lymphoma*

Introduction

Non-Hodgkin Lymphoma (NHL); It is a heterogeneous group of tumors originating from 85-90% of B lymphocytes and to a lesser extent from T lymphocytes and natural killer (NK) cells, resulting from malignant transformation of lymphoid system cells. Diffuse large B-cell lymphoma is the most common aggressive NHL subtype, and follicular lymphoma is the most common subtype among indolent NHLs. Follicular lymphoma (FL) is a slowly progressing disease originating from germinal center B cells and is the second most common NHL subtype. FL is characterized by widespread lymphadenopathy, bone marrow involvement, spleen enlargement and, to a lesser extent, extra-nodal involvement (1).

FL usually follows an indolent course and most patients are asymptomatic despite widespread disease. Most patients are diagnosed in advanced stages (III and IV). There is no curative treatment in the majority of FL patients with advanced stage III and IV disease. There is a possibility of spontaneous regression seen in 10-20% of the natural history of FL. Treatment should be initiated when symptoms such as B-symptoms, cytopenia, mass disease, organ dysfunction, ascites, pleural effusion, or rapid lymphoma progression develop. Modified GELF criteria are generally used to initiate treatment. The GELF criteria are given in Table 1(2).

Table 1. *Modified GELF criteria*

GELF criteria
Involvement in ≥3 cm and ≥3 sites each
≥7 cm nodal or extranodal mass
Presence of B symptoms
Symptomatic splenomegaly
Pleural effusion or ascites in the peritoneum
Cytopenias (leukocytes <1.0 x 10^9 /L and/or platelets <100 x 10^9 /L)
Leukemia (> 5.0 x 10^9 /L malignant cells)

Although the prognosis is good in low-grade lymphomas and the prognosis is poor in high-grade lymphomas, various systems have been developed over time to better predict the prognosis and make a

treatment recommendation. Since follicular lymphoma patients have a lower performance status and/or involvement in a large number of extranodal regions, the International Prognostic Index FLIPI-1 and FLIPI-2 are used in Follicular Lymphoma (3).

Table 2. *Prognosis scoring systems in Follicular Lymphoma*

Parametre	**FLIPI-1**	**FLIPI-2**
Lymph node	>4 lymph node sites	The long diameter of the widest lymph node is >6 cm
Age	>60	>60
Serum marker	Higher than normal LDH	High β2 microglobulin
Phase	Ann Arbor III-IV	Bone marrow involvement
Hemoglobin	<12 g/dl	<12 g/dl
Five-year survival (%)		
Low risk (0-1)	91	79
Medium risk (2)	78	51
High risk (3-5)	53	20

FLIPI: *Follicular lymphoma international prognostic index,* ***LDH:*** *Lactate dehydrogenase*

Case Report

The 36-year-old female patient applied to another clinic outside our hospital with complaints of mass and weight loss under the armpit. As a result of excisional lymph node biopsy taken from the patient's armpit, grade 3 follicular lymphoma was diagnosed. The patient's pathology blocks were again consulted by the pathology clinic at our hospital and reported as grade 2 follicular lymphoma. Bone marrow aspiration and biopsy were performed on the patient for staging purposes. Bone marrow involvement was detected. PET/CT was performed on the patient for staging purposes. In Figure 1, PET/CT images are available before treatment. The patient was admitted as stage 4 B and the R-CHOP protocol was started for the patient. Salvage treatment was planned due to insufficient partial regression in the interim PET/CT evaluation after 3 cycles. R-ICE (Ifosfamide+Carboplatin+Etoposide) protocol was given as salvage treatment. Rituximab+lenalidomide treatment was started due to insufficient response in the patient who was evaluated by PET/CT again after 2 cycles. Stem cells were collected and stored in order to perform autologous stem cell transplantation (OKHN) in the patient who had a nearly complete metabolic response in the control PET/CT. PET/CT images are given in figure 2.

At the stage of transplantation, COVID infection was detected in the patient during the COVID 19 pandemic period. In Figure 3, PET/CT images compatible with covid pneumonia of the patient are given. The transplant was delayed, but new lesions appeared in the patient during this process. At the stage of transplantation, covid infection was detected in the patient during the COVID 19 pandemic period. The transplant was delayed, but new lesions appeared in the patient during this process.

In Figure 3, PET/CT images compatible with the patient's covid pneumonia are given.

The patient was accepted as relapsed and Rituximab+Bendamustine treatment was started. Gemcitabine + Oxaliplatin + Ifosfamide protocol was started to the patient after the disease progression was detected after 3 cures. OKHN was planned for the patient who responded in the control PET/CT. However, due to the detection of invasive fungal infection in the lung, the transplant was postponed and fungal treatment was started. During the follow-up, lymphadenopathy was detected in the right inguinal region of the patient. Re-excisional lymph node biopsy was performed to confirm the diagnosis in the patient whose disease progressed very aggressively. Because the patient's clinical course was more like an aggressive lymphoma rather than an indolent lymphoma.

Was The Diagnosis Correct?

The biopsy was reported as classical follicular lymphoma. Progression was detected in the control PET/CT. PET/CT images are given in Figure 4. Obinituzumab+Rituximab protocol was given to the patient. Then, maintenance lenalidomide treatment was started. Figure 5 shows PET/CT images while under maintenance lenalidomide treatment. During the follow-up, the patient died due to urosepsis due to urinary tract infection. In Table 3, the laboratory values of the patient at the time of diagnosis and the most recent laboratory values are given.

Table 3. *Laboratory data of the patient at the time of diagnosis and the latest laboratory data*

	Examinations at the time of diagnosis	**The latest examinations**
WBC (x10^9/L)	11860	1920
Neutrophils (x10^9/L)	3240	400
Lymphocyte (x10^9/L)	7900	1340
Hemoglobin (Gr/dL)	11,5	8
Platelet (x10^9/L)	149000	3000
Kreatinin (mg/L)	0,62	4,72
ALT (U/L)	8	11
AST (U/L)	13	242
ALP (U/L)	79	108
GGT (U/L)	24	35
LDH (U/L)	292	1545
ESR (mm/H)	12	82
CRP (mg/L)	14,1	395,94

WBC: *White blood cell,* ***ALT:****Alanine amino transferase,* ***AST:****Aspartate amino transferase,* ***ALP:*** *Alkaline phosphatase,* ***GGT:****Gamma glutamyl transferase,* ***LDH:****lactate dehydrogenase,* ***ESR:****Erythrocyte sedimentation rate,* ***CRP:****C reactive protein*

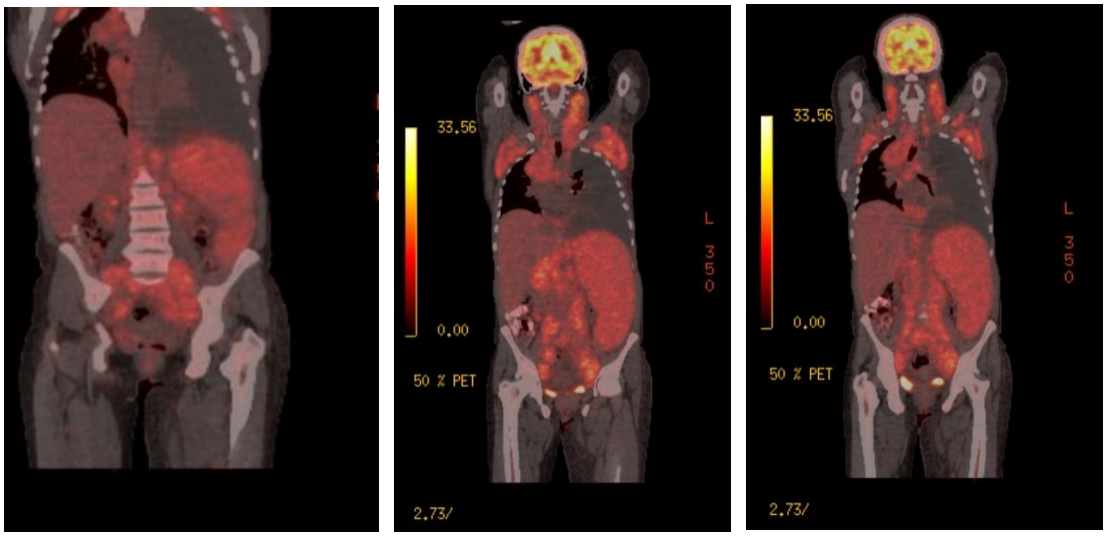

Figure 1. *PET/CT images of the patient at the time of diagnosis (Involvement in almost all lymphatic tracts and spleen in the examination area, diffuse pleural effusion in the left hemithorax)*

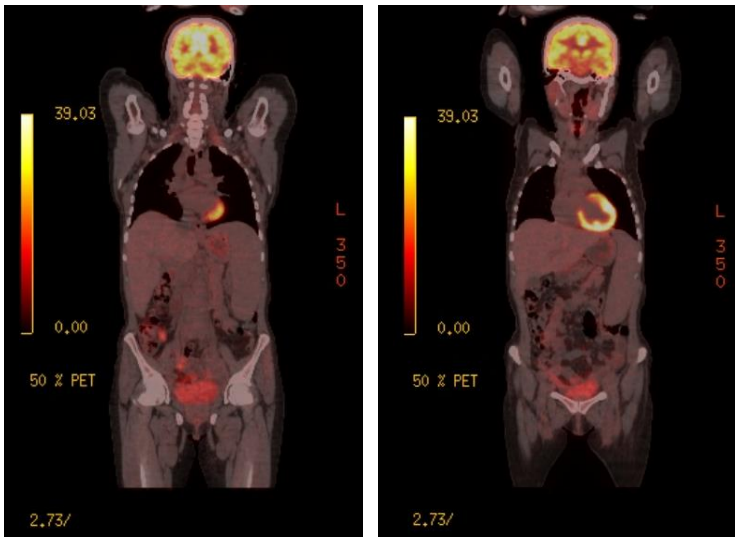

Figure 2. *PET/CT images showing the patient's almost complete metabolic response after the third-line treatment (almost complete metabolic response in supra/infradiaphragmatic lymph nodes, significant regression in spleen involvement, complete recovery in pleural effusion in the left hemitarox)*

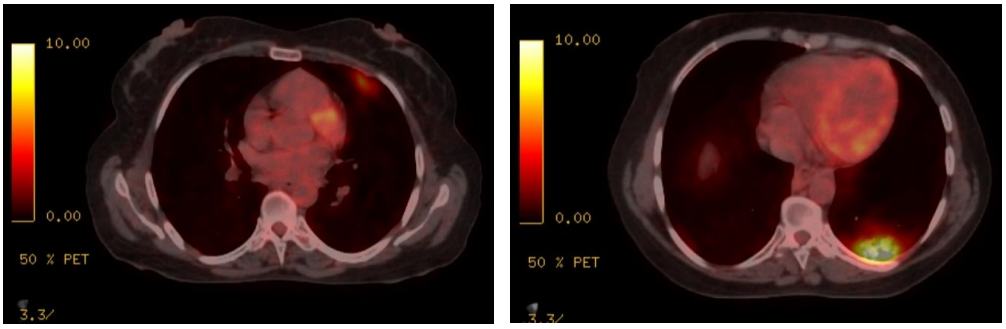

Figure 3. *PET/CT images compatible with the patient's Covid pneumonia*

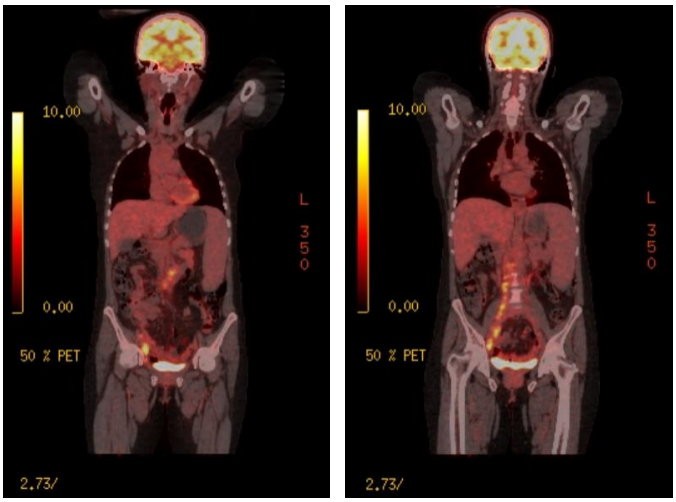

Figure 4: *PET/CT images of the patient before the 4th line treatment (recurrence) New lesions in the abdominopelvic and mediastinal area)*

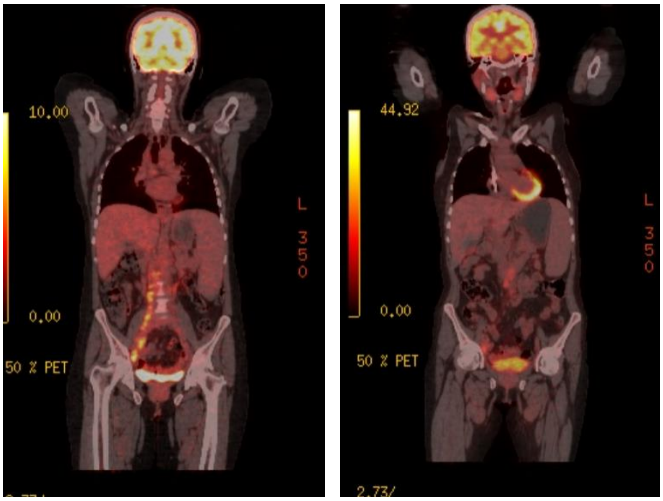

Figure 5: *PET/CT images of the patient while on maintenance lenalidomide therapy (Slight involvement of lymph nodes in the right upper paratracheal area with significant regression in abdominopelvic and mediastinal lymph nodes)*

Discussion

NHL is the most common hematological malignancy in the world, characterized by abnormal clonal proliferation of lymphoid cells originating from lymph nodes or extranodal lymphatic tissues. Most common NHL subtypes in developed countries; Diffuse large B-cell lymphoma (~ 30%) and Follicular lymphoma (~ 20%). Different behaviors are also observed among the subgroups of NHL. This is also observed in treatment responses. The disease can occur in an aggressive (moderate-high-grade) or indolent (low-grade) form (3).

Unlike high-grade lymphomas, indolent lymphomas are not considered curable with conventional treatment methods. An exception is the small number of patients with silent lymphoma presenting with localized lymphadenopathy. These patients can be treated with surgical excision or radiotherapy. However,

most diseases are diagnosed at an advanced stage and their treatment is managed as a lifelong chronic disease. Most patients with asymptomatic, painless disease are treated with a "wait and watch" approach (3).

Treatment is indicated in cases of systemic symptoms, bulky mass, progressive nodal enlargement and vital organ dysfunction. Treatment usually consists of an outpatient immunochemotherapy regimen lasting four to six months. Typical first-line drug regimens consist of R-CHOP and R-Bendamustine. After chemotherapy is completed, patients characteristically follow a relapsing-remission course lasting several years (4).

Rituximab given bimonthly for two years after initial immunochemotherapy increases the duration of remission. The length of first remission is an important determinant of outcome, especially in follicular lymphoma; Better results are obtained in patients with a first remission of more than two years. What should not be forgotten in the "wait and watch" approach; some of the low-grade lymphomas will develop into high-grade disease over time (4). Our patient was stage 4 at the time of diagnosis. Although he had indolent lymphoma, his clinical course was very aggressive. A repeat excisional biopsy was performed to ensure the diagnosis during follow-up. However, the diagnosis of our patient was correct.

As a result, indolent lymphomas are mostly diagnosed in advanced stages due to their silent clinic. It is very difficult to achieve a full cure in these patients and their clinics are aggressive.

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CHALLENGES IN DIAGNOSING AND MANAGING INSULINOMAS: TWO CASE REPORTS AND REVIEW OF THE LITERATURE

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ABSTRACT

Insulinomas, very rare among pancreatic endocrine tumors, are functional neuroendocrine lesions of the pancreas with endogenous hyperinsulinemia, fasting hypoglycemia, and neurological findings. Insulinomas, the most common cause of organic hyperinsulinemic hypoglycemia in adults, occur at 1-4 per million in the general population and represent 1-2% of all pancreatic neoplasms. The etiology and pathogenesis of insulinomas are unknown. Diagnosis is made by the support of clinical signs by laboratory and radiological findings. Surgical resection is the primary treatment for insulinomas; therefore, accurate tumor localization before or during surgery is essential. Intraoperative manual palpation of the pancreas by an experienced surgeon and intraoperative ultrasonography are sensitive methods for localizing insulinomas. Here, we present two cases with neuroglycopenic symptoms such as behavioral and personality changes, seizures, sweating, tremors, palpitations, and visual disturbances.

Introduction

Insulinomas, very rare among pancreatic endocrine tumors, are functional neuroendocrine lesions of the pancreas with endogenous hyperinsulinemia, fasting hypoglycemia, and neurological findings [1]. Insulinomas, the most common cause of organic hyperinsulinemic hypoglycemia in adults, occur at 1-4 per million in the general population and represent 1-2% of all pancreatic neoplasms [2], [3]. Its incidence generally increases between 30 and 60, and the female-to-male ratio is 3:2 [4]. The literature has reported that 90% of insulinomas are benign, 90% are solitary, more than 90% are localized in the intra-pancreatic regions, and 90% are less than 2 cm in diameter [5]. The etiology and pathogenesis of insulinomas are unknown [5]. Diagnosis of insulinoma is made with clinical and laboratory data as well as radiological diagnostic tools such as ultrasonography (USG), magnetic resonance imaging (MRI), Ga-SSTR positron emission tomography-CT (PET/CT) [2], [6]. Common autonomic symptoms of an insulinoma include sweating, tremor, and palpitations, while neuroglycopenia symptoms include confusion, behavioral changes, personality changes, visual disturbances, seizures, and coma [7], [8].

The classic diagnosis of insulinoma depends on meeting the criteria for the Whipple triad, which remains the cornerstone of the screening process: (1) hypoglycemia (plasma glucose < 50 mg/dL); (2) neuroglycopenic symptoms; and (3) rapid resolution of symptoms following administration of glucose [9]. Surgical resection is the primary treatment for insulinomas; therefore, accurate tumor localization before or during surgery is essential [10]. Intraoperative manual palpation of the pancreas by an experienced surgeon and intraoperative ultrasonography are sensitive methods for localizing insulinomas [11]–[13]. Here, we present two cases with neuroglycopenic symptoms such as behavioral and personality changes, seizures, sweating, tremors, palpitations, and visual disturbances.

Case 1

A 46-year-old male patient with a history of neurofibromatosis was admitted to the endocrine service with complaints of not being able to wake up in the morning, fainting, myalgia, irritability, and excessive hunger and tachycardia mostly occurring in the morning or after physical exercise. A prolonged fasting test was applied to

the patient when a blood glucose 43 C-peptide: 1.6 insulin: 4 was found in the initial tests. When blurred consciousness and hypoglycemia developed during the application, the patient's complaints improved when glucose infusion was started. In the MRI of the abdomen, it was interpreted that there was a mass of approximately 25 mm x 16 mm in the tail of the pancreas that did not clearly separate from the pancreas. A surgical operation was planned because the patient's clinical findings and MRI results were compatible with insulinoma. In the perioperative USG, approximately 3 cm of insulinoma tissue was seen at the junction of the pancreatic body-tail, and the mass was excised from the pancreatic tissue by the radiologist during the surgery. Perioperative USG also revealed a submucosal mass in the second part of the duodenum adjacent to the pancreatic head. Thereupon, an endoscopy was performed during the operation. Multiple biopsies were taken from the mass in the duodenum at endoscopy. Close blood glucose monitoring was performed during the operation. Histopathological results were well-differentiated neuroendocrine tumors for the pancreatic lesion, and the duodenum biopsy result was leiomyoma. The patient did not have any problems in the postoperative period. Plasma insulin values soon returned to normal, but transient hyperglycemia occurred and lasted for approximately 48 hours. The patient was discharged asymptomatically one week later.

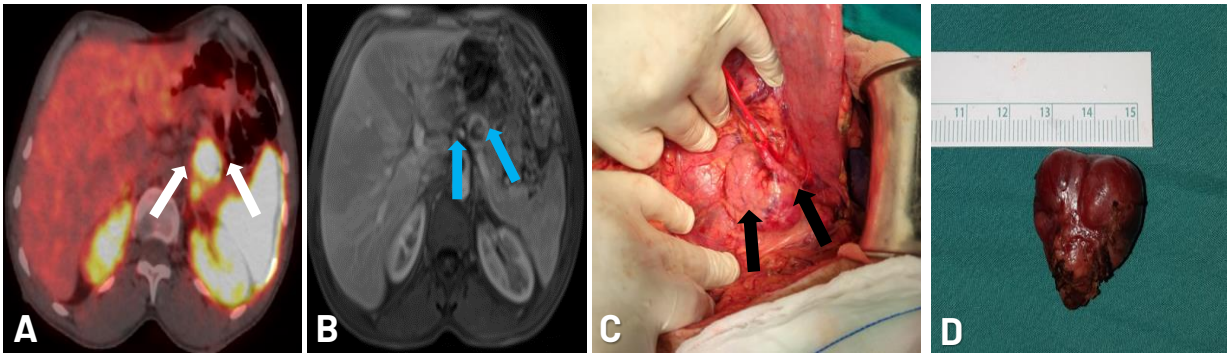

Figure 1: *Axial sections of PET/CT and MRI showing insulinoma in the body of the pancreas (white arrow) (A) and (blue arrow) (B). Insulinoma mass (black arrow) (A) and specimen image (B) which has a different color and appearance from the intraoperative pancreatic tissue.*

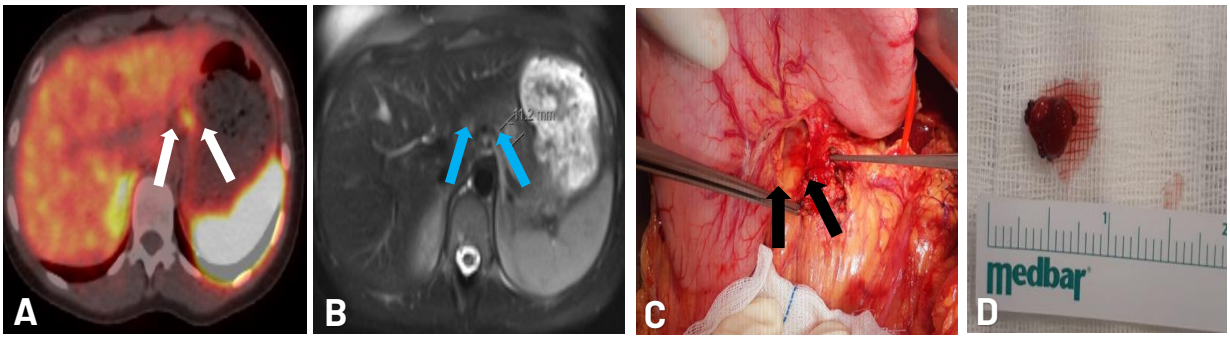

Figure 2: *Axial sections of PET/CT and MRI showing insulinoma in the body of the pancreas (white arrow) (A) and (blue arrow) (B). Insulinoma mass (black arrow) (A) and specimen image (B) which has a different color and appearance from the intraoperative pancreatic tissue.*

Case 2

A 26-year-old female patient, especially in the morning, fainting was added to the complaints of blurred consciousness and sleepiness. Her blood sugar measured by the 112 emergency teams, measured by the 112 emergency teams, reached 40, and her clinic partially improved when her sugar was intervened at home. The patient was brought to the hospital and admitted to the endocrine service. In the examinations performed on the patient, C-peptide: 1.14 (>0.6) insulin: 3.74 (>3), insulinoma was considered in the foreground. An abdominal MRI was taken to the patient. No insulinoma-like mass was seen on MRI. An approximately 1.32x2.12 cm lesion was detected in the pancreatic body-tail junction in Endoscopic USG, and PET/CT was taken to the patient. Thereupon, the patient was taken to a surgical operation. Intraoperative USG was performed because the mass

was very small. The enucleation method removed the mass, whose location was determined exactly on USG. Histopathological examination of the mass was reported as a well-differentiated pancreatic neuroendocrine tumor. After the operation, the patient was normoglycemic and had no complaints related to hypoglycemia. The patient was discharged on the 5th postoperative day with good recovery.

Discussion

Insulinomas, as illustrated by these two cases, are rare neuroendocrine tumors of the pancreas that present with a wide spectrum of clinical manifestations. They are characterized by endogenous hyperinsulinemia and various neurological symptoms, making their diagnosis and management challenging [7], [8].

One of the key diagnostic criteria for insulinoma is the Whipple triad, which includes hypoglycemia (plasma glucose < 50 mg/dL), neuroglycopenic symptoms, and rapid symptom relief upon glucose administration [9]. These cases exemplify the importance of recognizing this triad, even when it manifests with diverse neurological and autonomic symptoms, such as behavioral changes, seizures, sweating, tremors, and palpitations.

Accurate localization of insulinomas is crucial for effective surgical management [10]. In both cases, preoperative imaging played a pivotal role in identifying the lesions. However, it's worth noting that insulinomas can sometimes be challenging to visualize, as seen in Case 2, where MRI nearly failed to detect the tumor. However, complementary techniques such as endoscopic ultrasound (EUS) and PET/CT provided critical information for diagnosis and surgical planning [2], [6].

Intraoperative procedures, including manual palpation of the pancreas and intraoperative ultrasonography, were instrumental in precisely locating and excising the tumors [11]–[13]. In Case 1, a submucosal mass in the duodenum adjacent to the pancreatic head was discovered during surgery, underscoring the importance of thorough intraoperative evaluation.

Histopathological examination confirmed well-differentiated neuroendocrine tumors in both cases, highlighting the typical pathological features of insulinomas. Additionally, the incidental finding of a leiomyoma in Case 1 emphasizes the importance of thorough examination during surgery.

Both patients experienced transient hyperglycemia postoperatively, which is a common occurrence as the body adjusts to normal insulin levels. However, this resolved within a relatively short time frame, and both patients were discharged in good condition.

These cases emphasize the significance of a multidisciplinary approach involving endocrinologists, radiologists, surgeons, and pathologists in diagnosing and managing insulinomas. Additionally, they highlight the value of combining various imaging modalities and intraoperative techniques to ensure successful tumor localization and excision. Timely diagnosis and surgical intervention remain the mainstay of treatment, offering the best chances of a favorable outcome for patients with insulinomas.

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THE RELATIONSHIP BETWEEN CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH BREAST CANCER AND BONE SCINTIGRAPHY RESULTS

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ABSTRACT

Breast cancer is the most common type of cancer in women. The correct staging of the disease ensures the selection of the correct treatment methods and the effective use of resources. For this purpose, whole body bone scintigraphy has been used for a long time. Bone scintigraphy is one of the oldest conventional modalities of nuclear medicine. Due to its cost-effectiveness, it is still widely used in the management of breast cancer. Radiation exposure is an important deterrent in scintigraphic examinations. Therefore, it should be carefully considered in which patients it should be applied or not. In this study, it was aimed to examine the relationship between clinical and histopathological features of patients with breast cancer and bone scintigraphy results. Introducing features that help predict the outcome of bone scintigraphy can prevent unnecessary radiation exposure and unnecessary cost.

This study was conducted retrospectively. Patients referred to our clinic for whole body bone scintigraphy for staging due to breast cancer were examined. Patients with available breast cancer histopathology results were included in the study. According to the histopathology results, the patients were divided into 5 different groups. In addition, groupings were made according to hormone receptor status as estrogen receptor positive and negative, progesterone receptor positive and negative, HER2 receptor positive and negative. According to these receptor positivity, 4 different subgroups were formed. In addition, T stage, N stage and general pathological stage were determined according to the histopathology results of the patients. Bone scintigraphy results were compared separately according to the stage groups, histopathology groups, receptor groups, and subgroups formed according to the receptor status of the patients. Obtained results were analyzed statistically.

In our study, 185 patients were evaluated. Forty-one patients were included in the study. The mean age of the patients was 56 (39-81). In our study, the rate of bone metastasis positivity in scintigraphy was 46%. There was a statistically significant difference in age, menstrual status, T stage, N stage and general pathological stage between the groups with positive bone metastasis and negative groups according to bone scintigraphy. On the other hand, histopathology groups, molecular subgroups formed according to receptor status, estrogen receptor status, progesterone receptor status and HER2 receptor status did not significantly affect bone scintigraphy results.

In conclusion, in our study, bone metastasis was found to be low probability in patients with breast cancer detected in the early stages and at a young age. Therefore, the application of bone scintigraphy should be carefully considered in order to prevent unnecessary radiation exposure and unnecessary cost in every patient.

Keywords: *Estrogen receptor, progesterone receptor, HER2, luminal A, luminal B, triple negative*

Introduction

Breast cancer is the most common type of cancer in women [1]. Its incidence is increasing due to the development of cancer screening programs and diagnostic methods [2]. The correct staging of the disease ensures the selection of the correct treatment methods and the effective use of resources [3]. After the lymph nodes, breast cancer most commonly metastasizes to the bones. Detection of the presence of bone metastases

during staging changes the treatment protocol [4,5]. For this purpose, whole body bone scintigraphy has been used for a long time [6].

Bone scintigraphy is one of the oldest conventional modalities of nuclear medicine [7]. With the widespread use of positron emission tomography, it is less preferred in the staging of oncological diseases. However, due to its cost-effectiveness, it is still widely used in the management of cancers such as breast cancer and prostate cancer [8]. Radiation exposure is an important deterrent in scintigraphic examinations. Therefore, it should be carefully considered in which patients it should be applied or not. Thanks to the development of screening programs and diagnostic methods, breast cancers are detected at earlier stages and at earlier ages. Radiation exposure, which will increase cumulatively in the follow-up of the disease, although not at very high doses for diagnostic purposes, may also increase the risk of developing other cancers in the rest of the patient's life at an early age. Determining which patient is at higher risk of bone metastases at this stage may prevent unnecessary radiation exposure of low-risk and/or younger patients.

In this study, it was aimed to examine the relationship between clinical and histopathological features of patients with breast cancer and bone scintigraphy results. Introducing features that help predict the outcome of bone scintigraphy can prevent unnecessary radiation exposure and unnecessary cost.

Method

This retrospective study was performed between 01.06.2023 and 31.08.2023 in Sivas Numune Hospital Department of Nuclear Medicine. Patients referred to our clinic for whole body bone scintigraphy for staging due to breast cancer were examined. Patients with available breast cancer histopathology results were included in the study.

Patients were injected with 15-25 mCi Technetium-99m Methylene Diphosphonate or Technetium-99m Hydroxy Diphosphonate for bone scintigraphy. Whole body scan planar images and Single Photon Emission Computed Tomography images were taken 2-4 hours after the radiopharmaceutical injection. The resulting images were evaluated on the InterView XP 2.11.003.0000 (Mediso Medical Imaging, Budapest, Hungary) workstation.

According to the histopathology results, the patients were divided into 5 different groups as apocrine breast cancer, intraductal carcinoma, intralobular carcinoma, mucinous cancer and mixed type cancer. In addition, groupings were made according to hormone receptor status as estrogen receptor positive and negative, progesterone receptor positive and negative, HER2 receptor positive and negative. According to these receptor positivity, 4 different subgroups were formed. These subgroups were as follows;

- Luminal A: Estrogen receptor and/or progesterone receptor positive, HER2 receptor negative
- Luminal B: Estrogen receptor and/or progesterone receptor positive, HER2 receptor positive
- Triple Negative: Estrogen receptor, progesterone receptor and HER2 receptor negative
- HER2 Type: Estrogen receptor and progesterone receptor negative, HER2 receptor positive

In addition, T stage, N stage and general pathological stage were determined according to the histopathology results of the patients. Bone scintigraphies of all patients included in the study were re-evaluated. Bone scintigraphy results were compared separately according to the stage groups, histopathology groups, receptor groups, and subgroups formed according to the receptor status of the patients. Obtained results were analyzed statistically.

Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Descriptive statistics specified numbers and percentages (%) for categorical variables. The mean and standard deviation were specified for the normally distributed continuous variables. The median was specified for continuous variables that did not show normal distribution. The conformity of the variables to the normal distribution was examined using histograms, probability charts, and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk test). Quantitative data according to the normal distribution characteristics were evaluated with the Mann Whitney U test or Student's t-test. Qualitative data were analysed with the chi-square test. The statistical significance level was chosen at a two-sided p-value of 0.05 or less.

Results and Discussion

In our study, 185 patients were evaluated. According to the inclusion criteria, 41 patients were included in the study. The clinical and histopathological features of the patients are summarized in Table 1. The mean age of the patients was 56(39-81). Twenty patients were premenopausal while 21 patients were postmenopausal. Nineteen of the patients were at T1 stage, 14 at T2 stage and 3 at T3 stage. Twenty patients were in N0 stage, 12 patients were in N1 stage and 9 patients were in N2 stage. Of the patients, 14 were Stage 1, 19 were Stage 2, and 8 were Stage 3 (general pathological stage). According to the histopathology results, apocrine breast cancer was found in 1 patient, intraductal carcinoma in 28 patients, intralobular carcinoma in 10 patients, mucinous carcinoma in 1 patient, and mixed type carcinoma in 1 patient. According to their receptor status, 16 patients were in the luminal A group, 12 patients were in the luminal B group, 9 patients were in the Triple negative group, and 4 patients were in the HER2 type group. Estrogen receptor was positive in 27 patients and negative in 14 patients.

In our study, bone scintigraphy showed an appearance compatible with metastasis in 19 patients, while there was no metastasis in 22 patients. There was a statistically significant difference in age, menstrual status, T stage, N stage and general pathological stage between the groups with positive bone metastasis and negative groups according to bone scintigraphy. On the other hand, histopathology groups, molecular subgroups formed according to receptor status, estrogen receptor status, progesterone receptor status and HER2 receptor status did not significantly affect bone scintigraphy results.

There are different studies in the literature reporting the incidence of bone metastasis of breast cancer [9-12]. Butzelaar et al. evaluated 90 breast cancer patients with stages T1-2 and N0-1a in their study and found bone scintigraphy positive in 3 of the patients [13]. Another study followed 465 breast cancer patients for 2-9 years and found an abnormality in bone scintigraphy in 9.5% of the patients [14]. Koizumi et al [15] evaluated 5538 breast cancer patients in their retrospective study. They found the incidence of bone metastasis to be 2.13%. In our study, the rate of bone metastasis positivity in scintigraphy was 46%. The reason for this inconsistency with the studies in the literature may be that we gave a substantial number of suspicious results because the gamma camera in our clinic is not hybrid and we accept the suspicious results in bone scintigraphy as positive.

Table 1. *Clinical and histopathological features of the patients*

	Bone Scintigraphy			
	All(n:41)	**Positive(n:19)**	**Negative(n:22)**	**p value**
Age				
Mean±SD	56±10.94	61.73±8.53	51.04±10.51	0.001
Range	39-81	46-81	39-77	
Menstrual Condition, n(%)				
Premenopausal	20(48.8)	3(7.3)	17(41.5)	<0.001
Postmenopausal	21(51.2)	16(39.0)	5(12.2)	
T, n(%)				
1	19(46.3)	4(9.8)	15(36.6)	
2	14(34.1)	7(17.1)	7(17.1)	0.001
3	8(19.5)	8(19.5)	0(0.0)	
N, n(%)				
0	20(48.8)	2(4.9)	18(43.9)	<0.001
1	12(29.3)	8(19.5)	4(9.8)	
2	9(22.0)	9(22.0)	0(0.0)	
Pathological Stage, n(%)				
1	14(34.1)	1(2.4)	13(46.3)	<0.001
2	19(46.3)	10(24.4)	9(22.0)	
3	8(19.5)	8(19.5)	0(0.0)	
Histopathology, n(%)				
Apocrine	1(2.4)	0(0.0)	1(2.4)	

Intraductal carcinoma	28(68.3)	14(34.1)	14(34.1)	0.354
Intralobular carcinoma	10(24.4)	3(7.3)	7(17.1)	
Mixt	1(2.4)	1(2.4)	0(0.0)	
Mucinous	1(2.4)	1(2.4)	0(0.0)	
Estrogen receptor, n(%)				
Positive	27(65.9)	11(26.8)	16(39.0)	0.318
Negative	14(34.1)	8(19.5)	6(14.6)	
Progesterone receptor, n(%)				
Positive	19(46.3)	7(17.1)	12(29.3)	0.257
Negative	22(53.7)	12(29.3)	10(24.4)	
HER2 receptor, n(%)				
Positive	16(39.0)	9(22.0)	7(17.1)	0.309
Negative	25(61.0)	10(24.4)	15(36.6)	
Molecular Subgroup, n(%)				
Luminal A	16(39.0)	5(12.2)	11(26.8)	
Luminal B	12(29.3)	7(17.1)	5(12.2)	0.477
Triple Negative	9(22.0)	5(12.2)	4(9.8)	
HER2 Type	4(9.8)	2(4.9)	2(4.9)	

Koizumi et al. [15] found that tumor size, nodal involvement, and histopathology were correlated with bone metastasis in their multivariate logistic regression analysis. In parallel with the results of this study, we also found that the T stage and nodal stage of the disease, which reflect the tumor size, significantly changed the results of bone scintigraphy. However, contrary to the findings of Koizumi et al. [15], in our study, the histopathology groups were similar in terms of bone scintigraphy results. Breast cancers of all histopathology types do not have the same risk for bone metastasis. The reason for the inconsistency of our results in our study may be the small number of patients we included in our study.

The aim of our study was to examine the relationship between the clinical and histopathological features of the patients and the results of bone scintigraphy in patients with breast cancer. Thus, we aimed to determine the characteristics of patients that help predict the results of bone scintigraphy. There are studies stating that bone scintigraphy is unnecessary in the initial staging of low-risk, early-stage, small-sized breast cancers [16-20]. However, the same cancer types may show different behavioral characteristics in different societies. In our study, we examined breast cancers seen in the Central Anatolian Turkish population. However, due to the limited number of patients and the lack of service continuity in our center, our findings may not reflect the whole society.

About half (48.8%) of the patients we examined in our study were premenopausal. Metastasis was detected in 3/19 patients in the premenopausal group. In the postmenopausal group, metastases were detected in 16/21 patients. It may be considered normal for breast cancers detected at an early age, and therefore perhaps in the early stages, to show low bone metastasis. However, inconsistent with our findings, there are studies stating that menstrual condition does not have a significant correlation on bone metastasis [15].

Our study includes some limitations. In our study, hospital information management system and e-Nabız system were used to reach the clinical data of the patients we examined. However, e-Nabız data of most of the patients could not be accessed. The study design also aimed to correlate tumor markers and bone scintigraphy findings. However, the laboratory results of most of the patients for whom e-Nabız data could be accessed could not be obtained. The number of patients for whom tumor marker results could be obtained was very few. Therefore, the correlation between tumor markers and bone scintigraphy findings was not included in the statistical analysis. It is thought that the reason for this situation is the update made in the e-Nabız system. As a result, the number of patients included in our study is low. This number of patients may not accurately reflect the general population. This may have affected the results of the study. Bone scintigraphies of the patients included in our study were evaluated by a single nuclear medicine physician. This may also have affected the results.

Conclusion

In our study, bone metastasis was found to be low probability in patients with breast cancer detected in the early stages and at a young age. Bone metastasis is less common in premenopausal women instead of early age. Therefore, the application of bone scintigraphy should be carefully considered in order to prevent unnecessary radiation exposure and unnecessary cost in every patient.

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Author Contributions

The author declares that he has all participated in the design, execution, and analysis of the paper and that he has approved the final version.

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PRELIMINARY STUDY: OPTIMIZATION of the SAMPLE PREPARATION PROCESS for COMPARISON of SERUM COPPER, ZINC, and MANGANESE LEVELS of INDIVIDUALS WITH and WITHOUT ENDOMETRIUM CANCER

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ABSTRACT

Endometrial disease (EC) is one of the most well-known gynecological malignant growths with a rising frequency [1]. Most cases are analysed at a beginning phase in any case, have a good patient prognosis. One of the first manifestations of EC is uterine bleeding, which occurs after menopause in more than 80% of patients. However, only 10% of these postmenopausal bleedings are associated with EC [2]. Studies have revealed that estrogen and progesterone assume a functioning part in the pathogenesis of endometrial polyps [3]. Oestrogen is thought to have an effective role in the growth and development of endometrial polyps similar to the endometrium [4]. Heavy metals with estrogenic effects in the human body are called metalestrogens [5]. Heavy metals with estrogenic effects in the human body are called metalestrogens. Heavy metals describe metals or semi-metals (metalloids) often associated with contamination, exposure or ecotoxicity. Inorganic heavy metal ions that bind and activate estrogen receptors are called metalloestrogens. Aluminum, antimony, arsenate, barium, cadmium, chromium, cobalt, copper, lead, mercury, nickel, selenite, tin and vanadium have metalloestrogenic properties [6]. In addition to their toxic effects, metalloestrogens have also been associated with the etiology of estrogen-dependent diseases such as breast, endometriosis and endometrial cancer [6-8].

The point of this study was to examine, serum metalloestrogen levels such as copper (Cu), zinc (Zn), manganese (Mn) and Cu/Zn ratio and their possible relationship with the formation of endometrial cancer. In addition, it is aimed to reach the right measurement methods with the optimization of the sample preparation method.

A total of 20 individuals, including 10 patients diagnosed with endometrial cancer (EC) in Sivas Cumhuriyet University Faculty of Medicine, Department of Obstetrics and Gynecology, and 10 women without malignant disease, ovarian cyst and uterine leiomyoma as the control group, and who did not use oral contraceptives, were incorporated in the study. Two unique preliminary stages were performed in one randomly selected sample from the collected samples and Cu, Zn and Mn levels were measured advanced spectroscopic techniques. The same method was applied to the remaining samples after the preliminary preparation process, which gave more accurate results than the % correct readings of the internal standard in the samples, and Cu, Zn and Mn levels were determined in both groups.

This study is a starter study to decide the importance of trace elements in the development and progression of endometrial cancer. This study will contribute to our understanding of the complex relationship between trace element homeostasis and endometrial cancer and will support paving the way for new preventive and therapeutic strategies targeting trace element imbalances in potentially susceptible populations.

Keywords: *Endometrium cancer, heavy metals, sample prepration, AAS*

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IN VITRO EVALUATION OF THE EFFECTS OF CITRUS AURANTIUM L. ON BREAST CANCER

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ABSTRACT

Cancer is one of the leading causes of death worldwide. Thus, cancer studies are considered to be one of the key areas of health research. Finding new anticancerogenic compounds for therapeutic application require extensive research.

Several *Citrus* L. species grow wild in Asia's tropical regions, and are very useful economically. A variety of ailments can be prevented and treated using the fruits of the *Citrus* species. In perivous studies, it was shown that these species, which contain a wide variety of bioactive compounds, had antibacterial, anti-inflammatory, and antioxidant effects.

Citrus fruit peels could be beneficial for treating tumors since they contain compounds that have a variety of molecular skeletons. In this study, the cytotoxic activity of peel extracts from *Citrus aurantium* L. were assessed against MCF-7 cell line. The most active extract was found to be the ethyl acetate extract with the IC_{50} value of 0,768 ± 0,16 µg/mL. According to *in vitro* cytotoxic activity-guided fractionation assay, sephadex LH-20 and silica gel column chromatography techniques were used. The IC_{50} values of the active fraction and sub-fraction were 50,20 ± 8,450 and 31,43 ± 1,44 µg/mL, respectively. Four compounds namely isomeranzin, nobiletin, 3-methoxy nobiletin and tengeretin were isolated form the active sub-fraction. Nobiletin exerted the highest cytotoxic effect with the IC_{50} value of 18,87 ± 4,73 µg/mL, among the other isolated compounds. We would like to thank The Scientific and Technological Research Council of Türkiye (TÜBİTAK) for the financial support of the present study with the project number of 220S197.

Keywords: *Citrus aurantium, cytotoxicity, MCF-7, phytochemistry*

DIFFUSE LARGE B-CELL LYMPHOMA OF THE ORAL CAVITY: A CASE REPORT

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ABSTRACT

Introduction

Although non-Hodgkin lymphoma is the most common neoplasm in the oral and maxillofacial region after squamous cell carcinoma, they are rare malignancies.Diffuse large B-cell lymphomas (DLBCL) in adults constitute the largest group of histological types of non-Hodggin lymphomas. Waldeyer's ring, maxilla, mandible, palate, and parotid glands are the areas most commonly affected by oral DLBCL. DLBCL usually presents as ulcerations or swellings in the oral region. In this case report, a 54-year-old male patient diagnosed with DLBCL is presented.

Case

A 54-year-old immunocomponent male patient presented with a non-healing ulcerated lesion at the extraction site of a right maxillary first molar extracted due to mobility. A case with pathological diagnosis of DLBCL as a result of histopathological and immunohistochemical evaluations after biopsy is presented. Chemotherapy was applied to the patient in the oncology department. Complete haematologic remission was recorded and the patient has a 36-month follow-up.

Conclusion

The clinical and radiographic findings of oral lymphomas are non-specific and difficult to distinguish from odontogenic conditions. Because belated diagnosis of oral lymphomas negatively affects the prognosis of patients, dentists should suspect malignancy and take a biopsy in the presence of any lesion lasting more than two weeks that does not respond to standard treatment procedures, following exclusion of local irritants of traumatic or inflammatory origin.Although lymphoma in the oral cavity is rare, dentists should consider lymphoma as an important differential diagnosis in persistent progressive lesions during examination.

Keywords: *Lymphoma, early diagnosis, biopsy, tooth extraction*

Introduction

Lymphoid malignancies originating from the extra medullary lymphoid tissues of the immune system are called lymphoma. Lymphomas represent 3.5% of all intra oral malignancies of the head and neck [1].Lymphomas are divided into two groups according to their differences in histology, clinical features and prognosis: Hodgkin lymphoma (HL) and Non-Hodgkin lymphomas (NHL).While HL often presents as a nodal disease involving the neck and mediastinal nodes [2], NHL shows extranodal involvement up to 48% [3].

The head and neck region is the second most common anatomic area of extra nodal NHL after the gastrointestinal tract [3].Although NHLs represent the second most common oral cavity malignancy after squamous cell carcinoma [4], NHL is very rare in the oral cavity. NHL represents 2-5% of all oral malignant neoplasms [5] and the majority are located in the submucosal of the hard or soft palate, tongue, and gingiva [6].The most common intra oral regions are Waldeyer's ring, maxilla, mandible, palate, and gingiva [5]. Lymphomas of the nasal cavity, paranasal sinuses, and nasopharynx are very rare and represent less than 5% of all extra nodal

lymphomas [7].In immunocompetent individuals, the major histologic type of NHLs of the oral cavity and maxillofacial region is the DLBCL subtype [5]. In addition, DLBCL is the most common subtype of adult NHL worldwide [8].It represents approximately 68% of lymphoma cases, occurring on average in the seventh decade of life in the oral and maxillofacial region and with a 2:1 female to male ratio [9]. In the oral and maxillofacial region, DLBCL most commonly involves the tonsils, palate, maxilla, mandible, and parotid glands [5].

The clinical and radiographic signs of DLBCL in the oral cavity is not disease specific and often presents with clinical features similar to an odontogenic inflammatory process. This leads to difficulties in the diagnosis of the disease. Oral lymphoma lesions can involve both hard and soft tissue. Hard tissue lesions present as painful expanding lesions that cause asymmetry in the jaws.Soft tissue lesions usually present as single or multiple rapidly growing, painless or symptomatic swellings covered with intact or ulcerated mucosa [5]. Numbness, paresthesia, tooth mobility, and lymphadenopathy may also accompany patient findings [10]. Intra oral lesions usually grow rapidly and may affect the mandible and maxilla.Radiographically, the most common radiological finding is radiolucency, which indicates bone resorption [11]. Radiographic findings of DLBCL include well-circumscribed multilocular lesions, diffuse moth-eaten pattern or pathologic fracture [12,13].Radiographic signs can be interpreted as periodontal diseases, dental abscesses or bone diseases such as osteomyelitis. In addition, tooth root resorption, radiolucent areas similar to dental pathology, widening of the periodontal ligament space, loss of lamina dura and osteolytic lesions with unclear borders can be observed on radiographic images [1,14].The most common complaints in the head and neck region of patients are painless swelling, tooth mobility of unknown cause, or bone pain [1].

Oral findings can present as the first and only sign of disease, therefore correct diagnosis is important. Delayed or misdiagnosed diagnosis can lead to inappropriate treatment with unnecessary tooth extraction, prescribing antibiotics, or dental treatment. A correct diagnosis can be made by prolonging the symptoms or by investigating atypical findings. When examining the symptoms of mandible and maxilla pain, tooth mobility and swelling, differential diagnosis should take into account conditions of malignant etiology.

Case Report

In this case report, a 54-year-old immunocompetent male patient diagnosed with DLBCL is presented.The patient has a non-healing, progressively enlarging ulcerated lesion extending in the buccopalatal direction in the extraction region of the maxillary first molar.The lesion was followed up by the dentist after 2 weeks of anti-inflammatory and antibiotic use. The patient was referred to Sivas Oral and Dental Health Hospital Periodontology clinic for further evaluation because the expected therapeutic effect was not observed during the follow-up period and irregular resorption areas were observed in the bone in his x-rays.

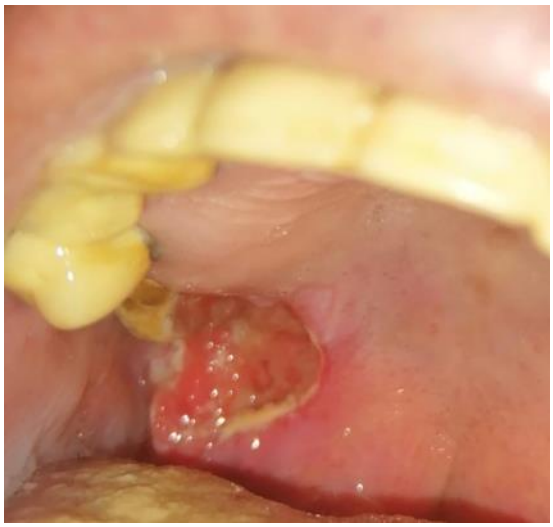

Figure 1. *Clinical appearance of ulcerated lesion extending to the palatal region in the right maxillary posterior region*

On detailed clinical evaluation of the patient, there was no weight loss, loss of appetite, increased fatigue, no family history of hematological malignancy or a regular drug use.

The patient had the habit of smoking 1 pack a day. In his anamnesis, it was learned that the right first molar tooth was extracted due to tooth mobility in the maxilla.

In the intraoral examination, a poorly circumscribed, white pseudo-membrane-covered ulcero-proliferative lesion extending in the buccopalatinal direction was observed in the right extraction socket mucosa. In radiographic evaluation, panoramic radiograph showed an area of radiolucency that was not very specific but raised suspicion for malignancy.

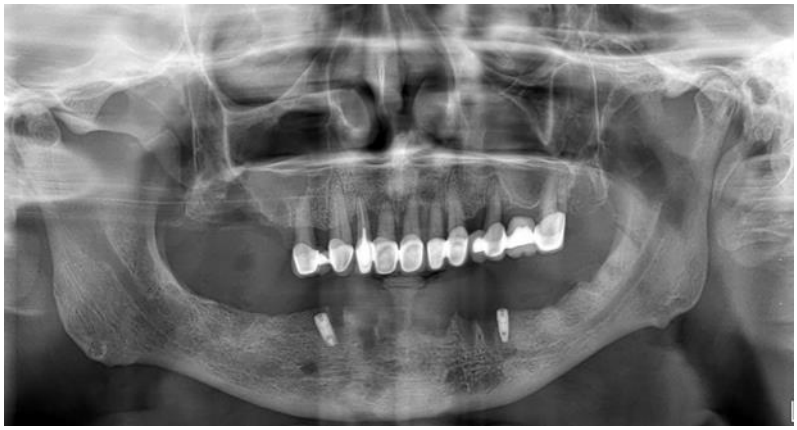

Figure 2. *Panoramic radiograph of the patient after the tooth extraction. Radiolucency with irregular borders extending to the maxillary sinus is observed in the relevant region*

Cone-beam computed tomography (CBCT) was taken for further examination. When CBCT sections were evaluated, damage to the lateral wall of the right maxillary sinus and destructive and expanding soft tissue density extending to the extraction socket were detected.Incisional biopsy was taken from the soft tissue edges of the lesion, considering it to be a pathology due to the atypical clinical and radiographic appearance of the patient and the characteristic features of the clinical history. Three tissue samples were taken from the buccal, palatal and distal surfaces of the lesion, including intact and suspicious areas, and sent for pathological examination. Histopathological and immunohistochemical findings are compatible with DLBCL.The biopsy result was specified as lymph node secondary malignant neoplasm / CD20 + DLBCL. The patient was referred to the oncology department for treatment. Chemotherapy treatment was started. The patient is currently in a healthy 36-month follow-up.

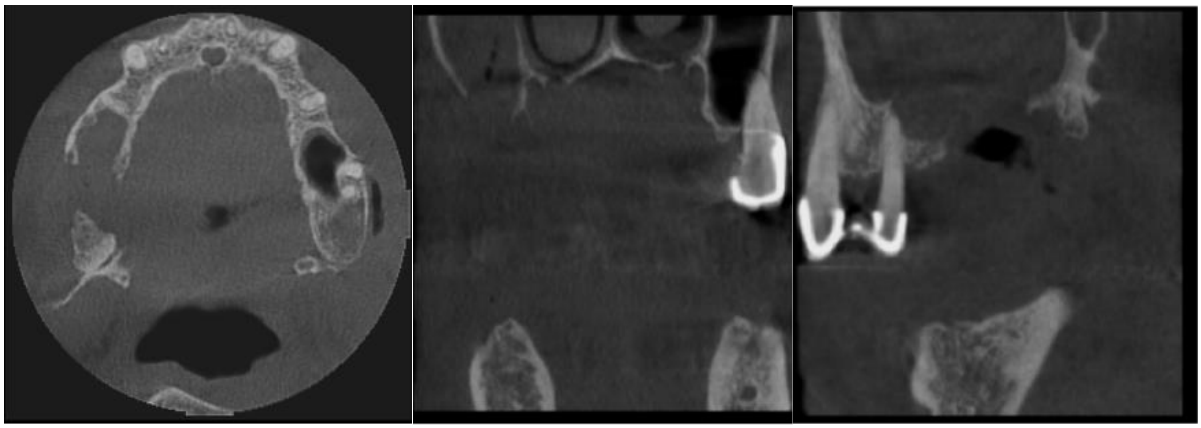

Figure 3. *The ragyoopaque image of the right maxillary sinus in CBCT sections.*

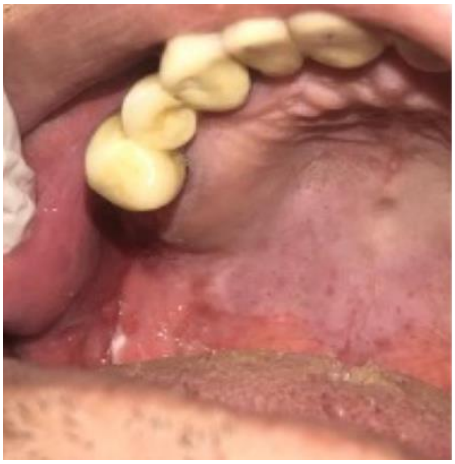

Figure 4. *Intraoral image at 36-month follow-up*

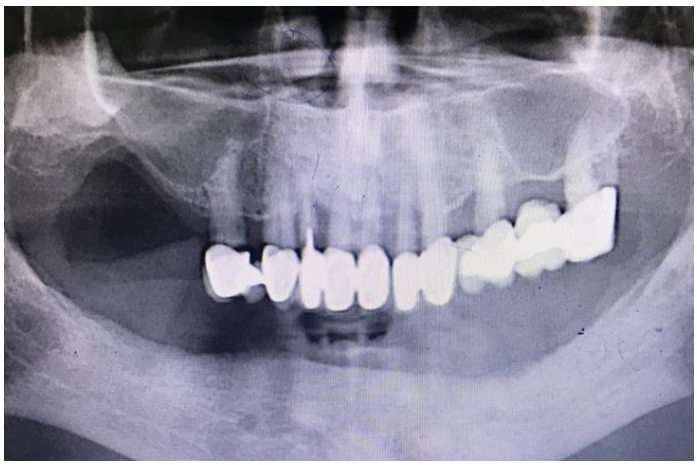

Figure 5. *Panoramic radiography image at 36 months follow-up. Regular borders of the right maxillary sinus are observed.*

Discussion

Although it is very rare for lymphomas to involve the oral cavity, the incidence of the disease is increasing [11,15]. Intra oral malignancies represent approximately 2.5% of lymphoma cases [16].Only 2% of oral cavity cases are diagnosed with NHL [16].A lymphoma that develops in the oral cavity is usually a component of disease dissemination involving regional lymph nodes or may have primary extra nodal disease in the oral cavity or jaws [17,18,19] .The rarity of oral lymphoma and the scarcity of available literature limit the understanding of the clinical course and subsequent outcomes. Due to the progressive course of the disease, it is important to evaluate clinical, radiographic and histological findings together in order to reach the correct diagnosis.

The rare incidence and common signs and symptoms in the oral cavity make the diagnosis of NHL difficult because its clinical and radiographic presentation in the oral cavity is nonspecific.Oral lymphoma is difficult to distinguish from other common infectious or inflammatory conditions that can lead to misdiagnosis and/or delay in treatment.Late diagnosis of the disease may delay the treatment and negatively affect the prognosis of the patients. Therefore, the differential diagnosis of odontogenic infections and tumoural lesions is important for appropriate treatment. The differential diagnosis should include malignancies of the oral cavity, salivary gland tumours and other lymphoid lesions.

Careful examination of the oral and maxillofacial region is necessary for early detection of suspicious lesions. Although careful clinical and medical history and evaluation may lead to a possible clinical diagnosis in many cases, biopsy and/or additional ancillary testing may be necessary to confirm the diagnosis or exclude neoplastic sources.In oral mucosal lesions that may suggest malignancy, histopathological examination/biopsy is indicated if no improvement is observed after a 2-week observation period, despite the exclusion of traumatic or inflammatory local irritants and appropriate treatment [20]. Tissue biopsy, immunophenotyping technique and molecular studies are used to confirm the diagnosis of lymphomas in the oral and maxillofacial region [5]. Appropriate examinations such as computed tomography imaging, CBCT or magnetic resonance imaging, immunohistochemical and histopathological analyzes are very important in the diagnostic process. Clinical and pathologic findings should be evaluated together for the correct diagnosis of lesions.

Dentists and specialists should maintain high suspicion of malignancy when inflammatory lesions do not respond to standard treatment procedures. In addition, recurrence of lymphomas in the oral and maxillofacial region may occur during or after treatment. At the end of treatment, careful evaluation of patients by dentist at regular intervals is necessary to identify recurrence of the disease or other formation in the area.

In summary, to limit misdiagnosis and diagnostic delay of oral lymphoma, careful evaluation of non-specific signs such as mucosal ulceration, bleeding and tooth motility is necessary, and lymphomas should be considered in the differential diagnosis of lesions that do not respond to standard therapy. Early referral for histopathology and immunohistochemistry analyzes can lead to early diagnosis and appropriate treatment.

The main limitation of this study is that it is a descriptive study of only one patient presented in a specialized dentistry and periodontology department.This report describes how a case that could easily be dismissed as periodontal disease was diagnosed with the rare oral DLBCL disease and provides an example that haematological malignancies such as lymphoma can occur in extranodal areas of the oral and maxillofacial region. However, further studies are needed to define the characteristics of oral lymphomas and their occurrence in the oral cavity.

Conclusion

Although lymphoma in the oral cavity is rare, dentists should consider lymphoma as an important differential diagnosis in the presence of pain, swelling, tooth mobility or radiographic radiolucency, especially in the presence of long-standing progressive lesions. A high index of suspicion is required for diagnosis, as delayed diagnosis affects prognosis. Careful examination of the oral and maxillofacial region by dentists and specialists, considering malignant lesions in the differential diagnosis, taking early biopsy, and meticulous follow-up are necessary for the diagnosis and staging of lymphomas. Therefore, dentists should take biopsy when they suspect and refer patients to hematology and oncology departments for further evaluation and treatment.

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I would like to thank the patient for consenting to be presented as a case in the report.

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EFFECTS OF MOLECULAR AND HISTOLOGICAL CHARACTERISTICS ON PROGNOSIS IN SYNCHRONOUS ENDOMETRIAL AND OVARIAN CANCER CASES

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ABSTRACT

Introduction

In synchronous of the ovary(OC) and endometrium(EC) (SEOC), the correct diagnosis is made both by histopathological and molecular examinations(1). Our aim was to investigate the patients with histopathological diagnosis of SEOC, with the homologuous recombination deficiency(HRD) genes analyzing, detecting genetic changes in tumors and evaluating their effects on the prognosis.

Material and Method

Among 1673 patients who were operated for EC and OC in Gazi University between 2005 and 2021, 7 patients with a histopathological diagnosis of SEOC with a life expectancy of 5 years or more were included. DNA from patients' FFPE blocks was isolated using the Promega ReliaPrep FFPE gDNA Miniprep System kit. Sequence analysis was performed with Illumina staining-based sequencing. Samples were sequenced using the Sophia homologous recombination solution DNA Kit. Data analysis was performed with Sophia DDM platform and in silico vehicles (Franklin, ClinVar), and variants were classified according to ACMG criteria.

Results

EC and OC most commonly had the Likely pathogen (LP) and pathogen (P) mutations, detected in the *ATM* gene. In addition to histopathological features, DNA sequence analysis results confirmed the diagnosis of SEOC, except for one patient.

Discussion

The use of pathology alone to distinguish between SEOC and MC may reveal potential risks such as misstaging and mismanagement of patients(1). Clonality analyzes have been performed to differentiate between MCs and SEOCs, and there are limited studies on whether genetic changes in SEOCs are predictive of biological behavior(2,3). In our study, molecular evaluation in the HRD genes supported the diagnosis of SEOC, and the prognosis of these patients was good. These data should be supported by larger patient series.

Conclusion

Mutations that did not adversely affect the prognosis were detected in the HRD gene panel in SEOC patients.

Table 1: *DNA sequence analysis results with clinical findings of patients with ovarian and endometrioid type tumor histology*

	AN	AE	GK	SG
Age	47	49	49	38
Ca-125 (IU/ml)	16	12	11	90
EC Grade	2	2	2	2
MI	< ½	< ½	Only endometrium	< ½

Endometrial hyperplasia/polyp	-/-	-/-	-/-	-/-
Mutation in EC	-	-	ATM[1]	CHEK[2]
OC Grade	2	1	2	2
Ovarian endometriosis	(+)	(+)	(+)	(+)
Mutation in OC	ATM	ATM BRCA2 TP53	ATM[1]	ATM
Adjuvant therapy	RT + KT	RT + KT	KT	RT + KT
Recurrence	-	-	-	-
Death	-	-	-	-
OS	65	128	114	121
RFS	65	128	114	121

[1] Different mutations in the same gene in EC and OC [2] Same motations in the same gene in EC and OC

Table 2: *DNA sequence analysis results with clinical findings of patients with ovarian and endometrial nonendometrioid type tumor histology*

	MA⁺	**DU⁺**	**SÇ⁺**
Age	64	57	64
Ca-125 (IU/ml)	776	14	361
EC Grade	1	3	1
MI	< ½	< ½	Only endometrium
Endometrial hyperplasia/polyp	-/-	-/-	-/-
Mutation in EC	CHEK2	ATM[2] TP53[2] BRCA2	-
OC Grade	3	3	3
Ovarian endometriosis	(+)	(+)	(+)
Mutation in OC	ATM	ATM[2] TP53[2]	TP53
Adjuvant therapy	RT + KT	KT	KT
Recurrence	Liver	-	-
Death	-	-	-
OS	65	101	70
RFS	13	101	70

[1] Different mutations in the same gene in EC and OC [2] Same motations in the same gene in EC and OC
⁺ Same histologyin EC and OC (seroun) [2] Different histology in EC and OC (endometriod in EC, serous in OC)

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ANTI-CANCER ACTIVITIES OF THE NEW TRIAZINE COMPOUNDS IN LUNG CANCER CELL (A549)

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ABSTRACT

Every year, millions of people around the world get cancer, and more than half of cancer patients die from this disease [1]. For the last decade, lung cancer has been the most common type of cancer in the world [2, 3]. Many clinical trials for targeted therapy and immunotherapy agents in lung cancer are ongoing, and promising results have been shown to date [4]. Triazine derivatives may show properties such as anti-tumour, antibacterial and antifungal, depending on the substituted groups. There is data that triazine compounds suppress cell proliferation in various cancer cells, have cytotoxic effects, arrest the cell cycle, are ER stress antagonists and cause cell death [5, 6].

The effects of the synthesized compounds on cell viability, cell cycle, ER stress and cell death were investigated at the molecular level in lung cancer cells. The anti-cancer activities of the compounds in the A549 cell line were examined at the cell, gene, and protein level.

Cytotoxic activity, gene, and protein studies of the new triazine compounds on lung cell lines have yielded effective results. It was concluded that these drug candidate compounds have anticancer activity. It is thought that the detection of targeted therapies in lung cancer and a clearer understanding of molecular biomarkers may increase the treatment options.

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A CASE OF CHRONIC MYELOID LEUKEMIA WITH THALASSEMIA TRAIT PRESENTING WITH HIGH PLATELET/EOSINOPHIL/LEUKOCYTE LEVELS AND SPLENOMEGALY

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ABSTRACT

A 53-year-old woman (born in 1970) was referred to the hematology department in August 2023 by her family doctor for hypereosinophilia, lymphocytosis, elevated basophil and platelet counts, leukocytosis, and anemia. Patient reported that her sister had died of a hematologic disease. Peripheral blood smear showed a blast rate below 1% and the presence of myelocytes. Additionally, the patient exhibited elevated levels of vitamin B12 and normal IgE levels. She also experienced B symptoms. Laboratory results were as follows: EPO: 14.3 IU/L (within the normal range), LDH: 867.15 U/L (elevated), HBA2: 6.1 % (elevated), WBC: 155800/µL, platelet count: 539000/µL, MCV: 65.5 fL. Further analysis through T(9:22) FISH revealed the presence of the Philadelphia translocation, leading to the commencement of imatinib treatment.

Chronic myeloid leukemia (CML) has become a treatable condition through tyrosine kinase inhibitors that target specific molecular pathways. Hemogram tests can exhibit elevated white blood cell counts, eosinophil levels, and platelet counts, which were observed in our patient. Her low hemoglobin levels were attributed to her status as a thalassemia carrier. It is crucial to consider the possibility of CML in patients presenting with elevated leukocyte, eosinophil, basophil, or platelet counts in their hemogram tests. In this case, the coexistence of thalassemia trait and CML was regarded as a coincidental finding.

EXAMINING THE INTERACTION: CORRELATIONS BETWEEN ZINC, COPPER, AND MANGANESE LEVELS IN RELATION TO THE RISK OF OVARIAN CANCER

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ABSTRACT

Ovarian cancer is a complex and multifactorial disease with a growing body of research exploring potential risk factors and biomarkers [1]. This study investigates the association between trace elements, specifically zinc, copper, and manganese levels, and ovarian cancer risk. The role of these trace elements in cancer progression has garnered significant interest due to their involvement in essential cellular processes, including oxidative stress, DNA repair, and immune response modulation. A case-control study was conducted involving 10 of cases ovarian cancer patients and 10 of controls age-matched healthy individuals. Blood samples were collected and analysed for zinc, copper, and manganese levels using state-of-the-art spectroscopic techniques. Statistical analysis, was performed to assess the potential correlation between trace element levels and ovarian cancer risk.

This study is a preliminary study to determine the importance of trace elements in the development and progression of ovarian cancer. Further research is required to elucidate the underlying molecular mechanisms governing the observed relationships. This study will contribute to our understanding of the complex interplay between trace element homeostasis and ovarian cancer and will help pave the way for new preventive and therapeutic strategies targeting trace element imbalances in potentially susceptible populations.

Keywords: *Ovarian cancer, trace elements, zinc, copper, manganese, risk factors, biomarkers, case-control study*

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A RARE CASE OF LUNG ADENOCARCINOMA IN A PATIENT WITH PULMONARY ALVEOLAR PROTEINOSIS

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ABSTRACT

Pulmonary alveolar proteinosis is a rare disease characterised with lipoproteinous material deposition in alveoles and alveolar macrophages . The most common symptoms are dyspnea and dry cough. The radiographic finding is bilateral, symmetric alveolar consolidation or ground-glass opacity. The diagnosis is mostly made by positive staining of transbronchial biopsy or bronchoalveolar lavage (BAL) material with periodic- acid-Schiff method accompanied by clinical and radiological findings.In this article, it is aimed to lung adenocarcinoma detected in a patient followed up with pulmonary alveolar proteinosis in the light of the literatüre.

Keywords: *Pulmonary alveolar proteinosis, lung adenocarcinoma*

Introduction

Pulmonary alveolar proteinosis (PAP) is a rare diffuse lung disease characterized by the accumulation of amorphous, periodic acid–Schiff (PAS)-positive lipoproteinaceous material in the alveolar spaces. These lipoproteinaceous materials are composed principally of the phospholipid surfactant and surfactant apoproteins. PAP are usually categorized in three clinically diverse forms: congenital, secondary, and autoimmune PAP(1-3).Although it varies by country the prevalence is estimated to be 3.7 -40/1000000 and the incidence is 0.2/1000000 per year (2). The congenital PAP involves a heterogeneous group of disorders, which are characterized mainly with gene mutations in encoding surfactant protein B or C or the β_C chain of the receptor for granulocyte–macrophage colony-stimulating factor (GM-CSF). Secondary PAP occurs with respect to other underlying causes. Currently, recognized conditions include hematologic malignancies, immunodeficiency disorders, inhalation of inorganic dust (e.g., silica), and certain infections(4,14,15). Autoimmune PAP, the most common form, develops in adults, usually as an isolated idiopathic lung disease without a definite aetiology. The majority of autoimmune PAP patients had elevated serum levels of neutralizing anti-GM-CSF antibodies, which were not seen in patients with congenital and secondary PAP. In this article, it is aimed to lung adenocarcinoma detected in a patient followed up with pulmonary alveolar proteinosis in the light of the literature.

Case Report

A 55 year old ,60 pack/year cigarette, 14 year ex-smoker,farmer male patient was diagnosed with autoimmune PAP in an external center in 2009 with bronchoalveolar lavage and Chest tomography (CT) finding.The initial chest radiography (CXR) in 2009 disclosed bilateral symmetrical ground glass opacity in the lower lung field. Chest tomography (CT) revealed a bilateral symmetrical, crazy-paving appearance with geographic distribution, mainly in the lower lung field. He applied to our clinic in July 2023 with complaint of shortness of breath, fatigue, cough, hemoptysis, night sweats.On admisson ,his general condition was good ,he was conscious, oriented and cooperative. On physical examination, palpable lymphadenopathy in the right neck was observed. Other physical examination and vital finding were normal. The patient laboratory values were CRP 65, Sedim 58 ,D-dimer 7.74. CA-15-3 202 U/ml , CA-19-9 191 U/ml and CA -125 261 U/ml. Sft FEV1/FVC %75 ,FEV1 4,19LT % 106,FVC 5.54LT %111 ve DLCO %115.

As a result of neck USG, a large number of lymph nodes with a conglomeration tendency are observed, approximately 1 cm in size on the left and right.Fine neesle aspiration biopsy was performed from the right lymph node.Pan CK: Positive and TTF-1: Positive in pathology,first of all,poorly differantiated adenocarcinoma

metastasis of primary lung origin was found to be compatible.In 2023, follow-up chest CT revealed multiple lymph nodes in the mediastinal area,the largest in the left hilar region, witfh a short axis of 24 mm which was not found in the previous examination.Mediastinal lymphadenopathies not seen in thorax CT in 2013 and 2015 draw attention in 2023 (Figure 1).

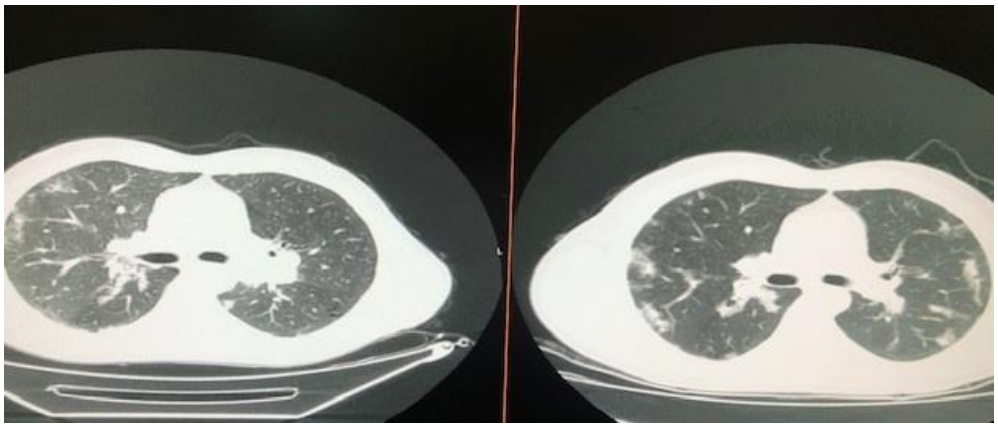

Figure 1. *Serial chest CT shows gradual resolution of ground glass opacities, but newly developed mediastinal lymphadenopathy*

In the PET-CT imaging of the patient, increased 18F-FDG uptake was observed in the lymph nodes with a metabolic size of 25x19 mm in the mediastinum (the highest SUVmax:8.3).The bronchoscopic biopsy revealed no specific finding. Incisional biopsy was planned from the right neck for molecular testing.

Discussion

Pulmonary alveolar proteinosis is a rare disease characterised with lipoproteinous material deposition in alveoles and .It was first described by Samuel H. Rosen et al. in 1958. PAP is usually seen at the age of 30-60 years and 2 times more in men, but it can be seen at an earlier age in women than in men(2,5,6,7).53-85% of patients have a history of smoking(2,3). Pulmonary surfactant is released from type 2 epithelial cells and consists of 90% phospholipids (phosphotidyl choline, phosphatidyl protein) and 10% protein (SP A, B, C, D). After the surfactant is synthesized, it is released into the alveolar space and lays the inner surface of the alveolar wall. Phospholipid, the main ingredient of surfactant, is critical in reducing surface tension at the air-liquid interface. In this way, collapse of alveoli is prevented at the end of expiration, its size is stabilized and elastic recoil decreases (8,9). It has been shown that surfactant accumulates in the alveoli similar to the human PAP phenotype in mice with the GM-CSF gene disabled (10,11). The majority of idiopathic PAP patients had elevated serum levels of neutralizing anti-GM-CSF antibodies, which were not seen in patients with congenital and secondary PAP. Friemann has demonstrated that intratracheal instillation and inhalation of quartz in rats induced alveolar proteinosis and a dose- and time-dependent increase of type II pneumocytes proliferation. As mitogenesis increases carcinogenesis, the likelihood of malignant transformation of PAP may be obligatory to enhanced tumor development (18). Athanassiadou and his colleagues reported that patients with primary lung cancer had an increase in the number of macrophages that were functionally incompetent (19). Sulkowska demonstrated the coexistence of PAP-like changes in the vicinity of non-small cell lung cancer. These morphological changes were partly attributed to the increase in desquamation and disintegration of type II pneumocytes, which were subjected to damage(20). In our patient, he was also diagnosed with PAP years ago, but in the following years, although there were additional underlying factors, it suggested that PAP disease may be a risk factor for a lung adenocarcinoma and suggested that patients should be followed closely, especially through the mediastinal window. Whether PAP and solid organ cancer have a causal relationship or are two independent diseases requires further investigation.

HRCT findings seen in PAP patients are not specific for PAP. Similar images; It can also be seen in pulmonary edema, alveolar hemorrhage, organizing pneumonia, acute respiratory distress syndrome (ARDS), Pneumocystis Jiroveci pneumonia and lipoid pneumonia(16,17). In our patient, acute clinical picture such as pulmonary edema, hemorrhage, ARDS and comorbidities were excluded, so these clinical pictures were

excluded. There was no reproduction or acute picture for PCP. Organized pneumonia was excluded by the characteristics of the patient's BAL fluid.

Conclusion

It should be considered that lung adenocarcinoma may develop together, before, after or coincidentally in a patient followed up with PAP. A PAP patient should not be followed up. Further aggressive studies are needed when a nodule is found in PAP patients.

Conflict of interest statement: The authors have no conflicts of interest to disclose.

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GENOMIC VARIATIONS IN PRIMARY AND METASTATIC PROSTATE CANCER TISSUE SAMPLES

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Objective

To uncover genomic variations in primary and metastatic prostate cancer tissue samples

Materials and Methods

Data of patients diagnosed with prostate adenocarcinoma were included from the "GENIE Cohort v13.1" database, which is a project of the American Association for Cancer Research (AACR). Demographic information, clinicopathological and genomic data of the patients were anonymized and extracted.[1-4]

Results

Data of 5581 prostate adenocarcinoma patients were evaluated. A single pathology sample was available in 4541 (89.5%) of the patients. The number of samples varied from 1 to 5 in the rest of it. 3075 samples from primary tumor tissue and 2187 from metastatic tissue were obtained. The race was significantly different between those sampled in primary site and metastatic site($q<0.05$).

The median (min-max) age of the patients who were sampled from the primary site was 63 (43.5-87.5), and the median age (min-max) was 68 (46.5-88) in those who were sampled from the metastatic site.

Genomic alterations differed between primary and metastatic tumor tissue samples in prostate cancer patients ($q<0.01$) (Figure 1).

Gene amplification differed between primary and metastatic tumor tissue samples in prostate cancer patients ($q<0.01$) (Figure 2).

AR amplification was seen in 27.69% of metastatic tumor tissue and 1.42% of primary tumor tissue. MYC amplification was seen in 9.97% of metastatic tumor tissue and 2.55% of primary tumor tissue (Figure 2).

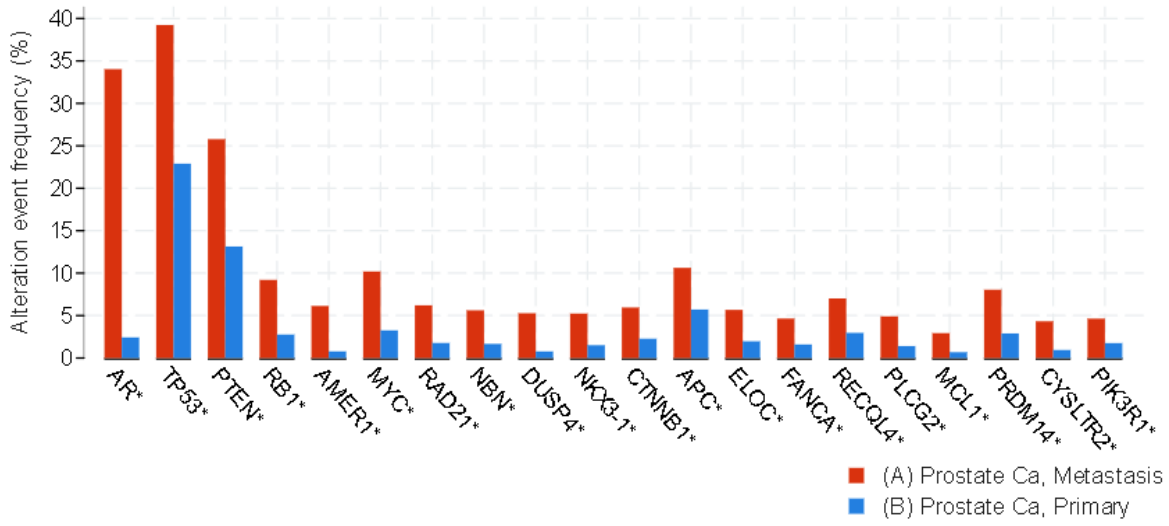

Figure 1. *Comparative Genomic Alterations in Primary and Metastatic Tumor Tissue Samples of Prostate Adenocarcinoma*
**Significant statistical difference between groups ($q<0.01$)*

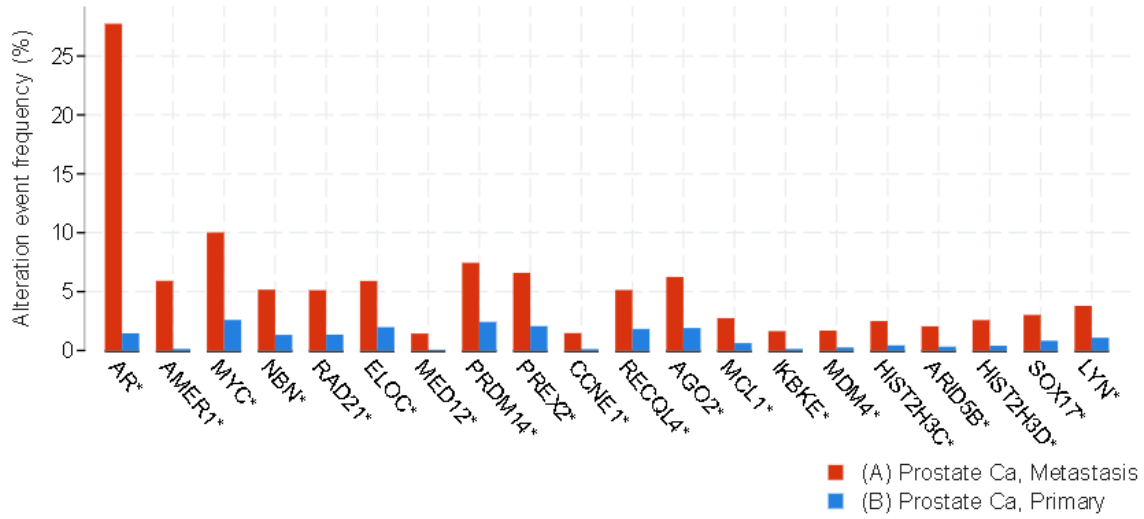

Figure 2. *Gen Amplifications in Primary and Metastatic Tumor Tissue Samples of Prostate Adenocarcinoma. *Significant statistical difference between groups (q<0.01)*

Gene mutations differed between primary and metastatic tumor tissue samples of prostate cancer patients (q<0.01) (Figure 3).

AR mutation was in 9.55% of metastatic tissue and 1.13% of primary tissue, TP53 mutation was in 35.03% of metastatic tissue and 21.8% of primary tissue.

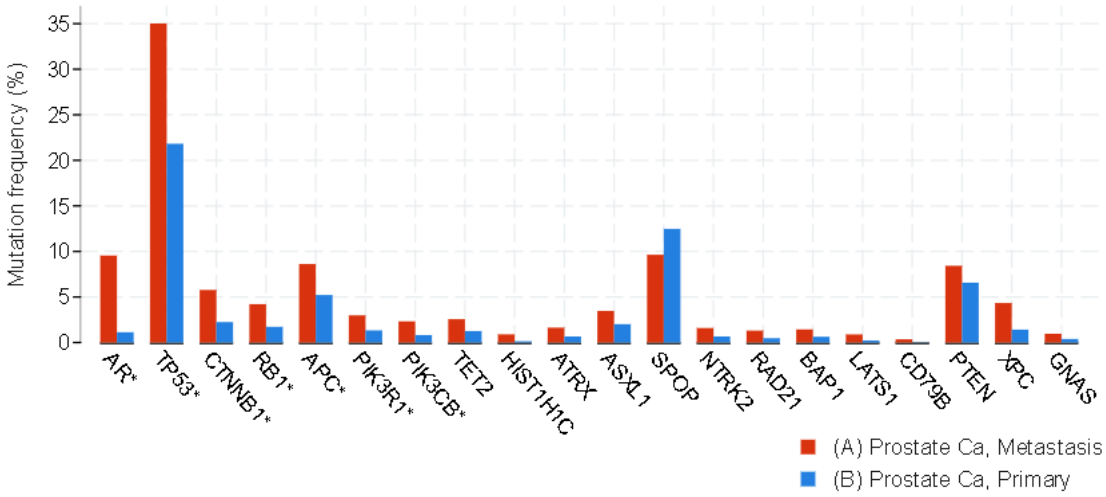

Figure 3. *Gen Mutations in Primary and Metastatic Tumor Tissue Samples of Prostate Adenocarcinoma *Significant statistical difference between groups (q<0.01)*

Conclusion

This study showed significantly heterogeneity in primary and metastatic prostate cancer tissue samples. Alterations in AR signaling underlie resistance to androgen deprivation therapy. In this study, alterations in the AR gene were shown to be more frequent in metastatic tissue samples. Alterations in RB1, AR, and TP53 genes are associated with more aggressive disease that are less dependent on AR signaling [5,6]. Advanced treatment options should be created by taking into account the differences in these genomic alterations in personalized treatment planning.

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THE RELATIONSHIP BETWEEN BMI AND SURGICAL MARGIN POSITIVITY IN PATIENTS WITH PROSTATE CANCER

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ABSTRACT

Background

Prostate cancer is one of the most common forms of cancer in men around the world, with an estimated 1,600,000 cases and 366,000 deaths per year [1]. The optimal treatment is surgical intervention, with various factors influencing postoperative survival. Body mass index (BMI) is a parameter that researchers have linked to mortality rates in prostate cancer [2]. In this study, we aimed to investigate the relationship between BMI and positive surgical margins (PSM).

Methods

A total of 95 patients undergoing surgery for prostate cancer were included in the study. Patients were divided into two groups according to their BMI, normal (BMI < 25 kg/m2) and overweight (BMI > 25 kg/m2). The groups were compared for positive surgical margins, PSA levels, age, number of positive cores, stage, recurrence, presence of diabetes mellitus (DM), hypertension and metabolic syndrome .

Results

The mean age of the 95 patients included in the study was 64.1±5.7 years and the median PSA level was 7.6 ng/mL. There were 24 patients with a BMI < 25 kg/m2 and 74 patients with a BMI > 25 kg/m2. No significant correlation was found between the groups in terms of age, PSA, biopsy pathology result, number of positive cores, surgical pathology result, stage, recurrence, presence of hypertension and DM. However, surgical margin positivity and presence of metabolic syndrome were statistically significantly higher in the BMI>25 kg/m2 group (49.3% vs 23.8% for surgical margin positivity, p=0.038; 24.7% vs 4.8% for presence of metabolic syndrome, p=0.036).

Conclusion

Preoperative BMI was associated with positive surgical margins in our study. This may be due to the procedural difficulty of surgery in overweight patients or the association of obesity with the aggression of the tumourWe believe that more comprehensive studies are needed to explain the reasons for these results.

Keywords: *Prostate cancer, surgical margin positivity, BMI*

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EFFECT OF ALOGLIPTIN ON DNA DAMAGE IN STOMACH CARCINOMA BY IN-VITRO METHOD

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ABSTRACT

Cancer is an undesirable pathological condition where cells acquire autoimmunity and begin to proliferate uncontrollably, causing irreversible health problems and ultimately resulting in death. Alogliptin is used with diet and exercise to improve glycaemic control. Although Alogliptin used in type 2 diabetes mellitus is associated with DNA damage, and there is a close relationship between DNA damage and cancer, no study has been conducted in the field of stomach cancer yet. For this reason, the effectiveness of Alogliptin, which has an inhibitory effect on DNA damage, on stomach cancer cell lines was investigated for the first time in this study using cell viability tests and immunofluorescence methods. It was determined that 100 µM, 1, and 10 mM concentrations of Alogliptin significantly reduced viability in the SNU-1 cell line, which was not treated (control group). In terms of DNA damage, it was determined that while the positivity was higher in SNU-1 cells without any application in immunofluorescence staining with 8-OhDG, the positivity was decreased in SNU-1 cells treated with Alogliptin and therefore, Alogliptin reduced DNA damage. As a result, it was revealed that Alogliptin may have a positive role in treating stomach cancer.

Keywords: *Stomach cancer, alogliptin, SNU-1, XTT assay, 8-OhDG*

Introduction

Stomach Cancer

Cancer: Any of the cells in the organism is a new mass formation that gains autonomy and multiplies unlimitedly without being influenced by the control mechanisms of the living thing, proliferates, and continues to develop even after its causes are eliminated [3]. The leading causes of cancer are activation of oncogenes, inactivation of tumor suppressor genes, impairment of DNA repair ability, inability to undergo apoptosis, reprogramming of cell energy metabolism, and protection of the tumor cell from the immune system. The main factors that activate cancer's causes are hereditary, physical, chemical, and biological (such as bacteria viruses) carcinogens [4]. Stomach cancer, related to these factors like other cancers, is one of the leading causes of cancer deaths worldwide [5]. Although the distribution of stomach cancer in men and women is equal, the peak age is determined as 60. It is more common in some geographical regions depending on genetics and diet. When diagnosed, distant metastasis usually occurs in 50% of cases [4]. Causes of stomach cancer: diet, inflammation, Helicobacter pylori, alcohol and tobacco habits [6]. Clinical symptoms seen in stomach cancer are persistent pain that increases after meals, vomiting, loss of appetite, weight loss and discomfort, fullness, burning, and pain in the epigastrium [4]. Cancer in the stomach begins with damage to the stomach epithelium and then occurs with the induction of carcinogenesis [5].

Apart from various etiological factors that lead to stomach cancer, The effects of DNA damage and Reactive Oxygen Species (ROS) cannot be ignored. The production of ROS is known as one of the essential factors that cause DNA damage. Living cells cause the production of ROS under physiological conditions as a result of their aerobic metabolism. Harmful effects caused by ROS and other free radicals are known as

Oxidative Stress (OS) [6]. Reactive oxygen species and oxidative stress are essential in the aging process's pathophysiology and degenerative diseases such as cancer [5]. Oxidative DNA damage occurs as a result of ROS attack, and as a result of this situation, malignant transformation develops due to defects in the epithelium of the stomach mucosa [6]. Reactive oxygen species produced in this process are associated with mitochondria. Mitochondria are known as an organelle responsible for semi-autonomous ATP production that contains its DNA. It is also one of the sources of ROS by contributing to the oxidative state of the cell. Increased mitochondrial ROS production is a pathological mechanism in some degenerative diseases and many types of cancer [5].

8-hydroxy-2'deoxyguanosine (8-OHdG)

8-hydroxy-2 deoxyguanosine (8-OHdG) is an essential marker in detecting DNA damage. It is also one of the most common DNA modifications and is often used as a specific marker of oxidative DNA damage. It has been determined that the mutagenic base 8-OHdG is significantly increased in many tumor cells compared to normal cells. Studies have shown that 8-OHdG in the urine of patients with stomach cancer increases approximately tenfold compared to its ordinary course. 8-OHdG levels in the urine of affected patients have been reported to decrease after tumor resection. Significant increases in 8-OHdG in stomach tumors have been accepted as reflecting high OS status [6]. Within the framework of this information, investigating the 8-OHdG level to detect DNA damage in stomach tumors is a significant issue for our study.

Alogliptin

Alogliptin is an anti-hyperglycemic agent used to achieve glycemic control in combination with diet and exercise. Alogliptin is a selective inhibitor of the enzyme dipeptidyl peptidase-4 (DPP-4), thus having the ability to control hyperglycemia [1,2]. This enzyme is abundant on the surface of most cells and rapidly inactivates some incretin hormones, such as glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). Both of these hormones are released by intestinal cells after eating. By antagonizing DPP-4 after its release, it raises active postprandial incretin levels, resulting in increased insulin synthesis and release as well as decreased glucagon secretion. This entire cycle helps regulate glucose homeostasis [2]. Inhibition of the DPP-4 enzyme increases the level of incretin hormones such as GLP-1 and GIP. Increasing insulin secretion is dependent on these hormones [1]. Taking Alogliptin suppresses oxidative stress, adipose tissue inflammation, activation of the DPP-4 enzyme and prothrombic state. Alogliptin also inhibits stress-induced free radical production and thus reduces the expression of 8-OHdG, which is essential for DNA damage in adipose tissues [7]. One of the agents in the DPP-4 group is alogliptin and is used in the treatment of type 2 diabetes mellitus (Figure 1) [8].

In type 2 diabetes mellitus, insulin production in the pancreas is sufficient. However, insulin insensitivity develops because the receptors that detect the insulin hormone in the cells do not work. Although Alogliptin used in type 2 diabetes mellitus is associated with DNA damage, and there is a close relationship between DNA damage and cancer, a practical study has not yet been conducted in cancer areas [9]. For this reason, the effectiveness of Alogliptin, which has an inhibitory effect on DNA damage, on gastric cancer cell lines in vitro was investigated for the first time in this study.

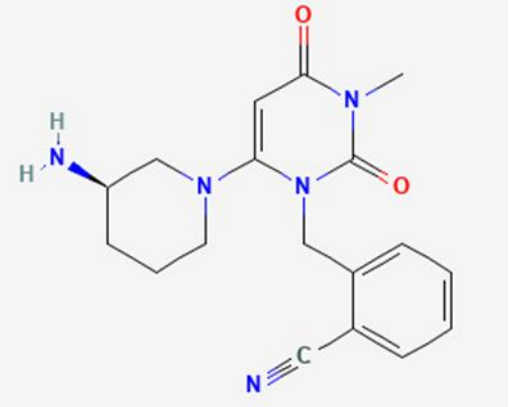

Figure 1. *Chemical structure of Alogliptin*

Method

Cell Culture

The SNU-1 cell line was obtained from the American Type Culture Collection. These cells were treated with 10% Fetal Bovine Serum (FBS) (Sigma-Aldrich Co., St Louis, MO, USA), 1% penicillin/streptomycin (Sigma Aldrich Co., St Louis, MO, USA), and 1% RPMI medium containing L-glutamine (Thermo Fisher Scientific, Altrincham, UK) was cultured. Prepared cells under suitable conditions; incubated with an incubator at 37 °C and a humidified

atmosphere with 5% CO_2. Cells were treated by preparing stock solutions of different concentrations of Alogliptin (0.1, 1, 10, 100 µM, 1 and 10 mM), RPMI (Sigma-Aldrich Co., St Louis, MO, USA) [10].

Cell Viability Assessment (XTT)

Cell viability was evaluated using the XTT test (Roche Diagnostic, MA, USA). Initially, SNU-1 cells were seeded in 96-well plates at a density of 1 × 104 cells in 50 µL of DMEM per well. Stocks of alogliptin at various concentrations (0.1, 1, 10, 100 µM, 1, and 10 mM) were prepared and applied to cell culture for 24 h. The next day, 50 µL of XTT solution was added to all wells and incubated at 37 °C for 4 hours. The absorbance of the groups was measured at 450 nm using an ELISA microplate reader (Thermo Fisher Scientific, Altrincham, UK). All experiments were repeated three times, and cell viability was measured as the percentage of live cells compared to the control group (cells without Alogliptin treatment). All experiments were repeated three times, and cell viability was measured as the percentage of live cells compared to the control group (cells without Alogliptin treatment) [10].

Determination of DNA Damage by Immunofluorescence Staining Method

Fixation step with paraformaldehyde: The cells in the cell culture (6 chambers) were placed on a slide and dried. Fixation of cells with methanol at -20°C for 15 minutes was carried out.

Permeabilization stage: 400 µL of 0.1% Triton X-100 was added to 500 µL of Phosphate Buffer Solution (PBS) on the cells, and the cells were incubated in this solution for 15 minutes at room temperature.

Blocking step: 500 µL of 2% Bovine Serum Albumin (BSA) was added to 500 µL of PBS, and the cells were incubated in this solution for 60 minutes at room temperature.

Immunostaining phase: At this stage, the monoclonal 8-OhDG primary antibody (Santa Cruz, Catalog no. sc-393871), which is compatible with the human cell line in previous studies, is added to 0.1% BSA at an appropriate rate (1/100 dilution ratio) was left at room temperature for 3 hours. After taking the primary antibody solution, it was washed three times with PBS. Fluorescence-linked Goat anti-Mouse IgG was compatible with monoclonal 8-OhDG primary and secondary antibody was used. For this purpose, secondary antibody (1/50 dilution ratio) and nuclear dye 4',6-Diamidino-2-Phenylindole, Dihydrochloride (DAPI) (Thermofischer, Catalog no: D1306) were added into 0.1% BSA at the appropriate dilution rate. It was incubated for 45 minutes in the dark at room temperature. Finally, the cells were washed three times with PBS and examined under a Fluorescence Microscope (ZEISS Axio Vert.A1) [10].

Statistical Analysis

Results were expressed as mean ± SEM. Data analyses were performed with SPSS Version 23.0 for Windows. Data were evaluated using one-way analysis of variance (ANOVA). The Post Hoc Tukey test was used to determine the differences between the experimental groups [10].

Results and Discussion

Effects of Alogliptin on SNU-1 Cell Viability

To evaluate the effects of alogliptin on SNU-1 cell viability, an XTT cell viability assay was performed. The XTT viability test is one of the most commonly used tests measuring cell death/proliferation based on the measurement of metabolic activity. In these tests, in which cell viability is determined by spectrophotometer. The viability of the untreated cells is accepted as 100%, and the viability of the treated cells is determined as a percentage (%) according to these cells [11]. Atabay et al. investigated the elemental analysis and anti-tumor activity of propolis samples in glioblastoma cell lines and used the XTT test to evaluate the cytotoxicity of the cells [12].

Alogliptin 100 µM, 1, and 10 mM concentrations showed that cell viability was significantly reduced compared to the control group. (***P<0.001), (Figure 2). It was determined that Alogliptin did not show an anti-proliferative effect at 0.1, 1, or 10 µM concentrations (Figure 2) (P>0.05).

With this finding, Shigematsu et al. studied Alogliptin on oxaliplatin-induced peripheral neuropathy in vivo and in vitro. They revealed that Alogliptin, used in cell culture, reduced the viability of cells [13]. Alogliptin acts primarily on glucose metabolism and insulin regulation. Cancer cells generally need more glucose than normal cells. Alogliptin may prevent the cells from receiving adequate nutrition by reducing the glucose level needed by the cell, thus causing the death of the cancerous cell. However, this is a prediction; there is no clear evidence yet regarding the mechanism by which Aloglipt reduces cell viability.

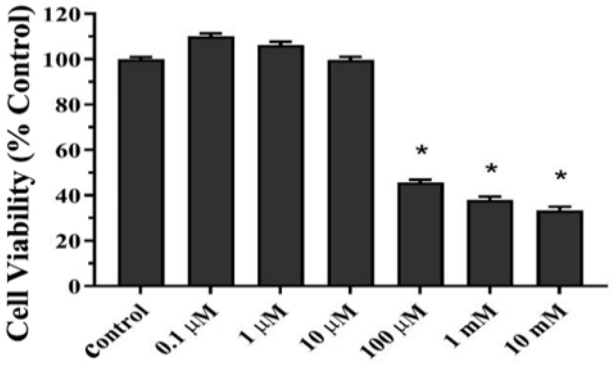

Figure 2. Effects of Alogliptin on SNU-1 cell viability. Values are presented as mean ± SEM (***P<0.001).

Effect of Alogliptin on DNA Damage

In terms of DNA damage, while the positivity in immunofluorescence staining with 8-OhDG was high in SNU-1 cells (control) without any application (Figure 3), positivity decreased in SNU-1 cells treated with Alogliptin, indicating that Alogliptin reduces DNA damage and is thus beneficial for cancerous cells. It was seen that it was (Figure 4). In a study similar to the results of this study, Kamur et al. determined DNA damage with 8-OhdG in squamous cell carcinoma of the head and neck, and found that the level of 8-OhdG was much higher than in normal cells [14]. In another similar study conducted on human esophageal cancer, DNA damage was determined by 8-OhDG, and it was reported that this level was much higher than average [15]. DNA damage occurs in cancer cells due to various factors. For this reason, this value is high in various cancer studies.

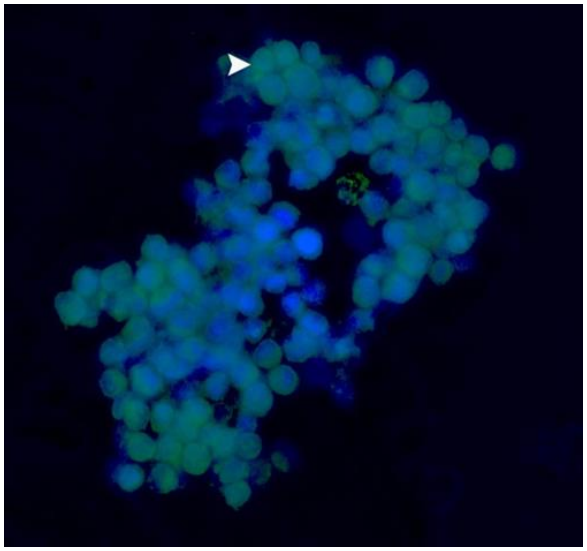

Figure 3. *Advanced positivity in the SNU-1 group (arrow).*

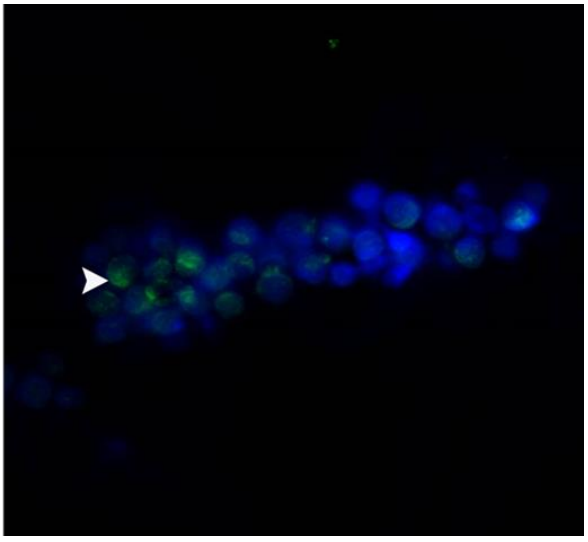

Figure 4. *Mild positivity in SNU-1 cells treated with alogliptin (arrow).*

Conclusion

Nowadays, cancer cases are increasing every day and cause significant deaths. Stomach cancer, one of these cancer types, is increasing daily with the deterioration of human eating and habits. The care processes for these types of cancers, whether in or after treatment, are costly and very difficult. Accordingly, it is essential always to conduct studies on the development of new active substances and new methods regarding cancer. It was revealed that both cell viability decreased significantly, and there was no proliferation effect in applying Alogliptin to cancer cells.

On the other hand, Alogliptin was also found to reduce DNA damage caused by cancer. Based on these findings, it was reported that Alogliptin showed a therapeutic and supportive effect on cancer recovery. The

results of this study will contribute to the literature as new information and shed light on future scientific and clinical studies.

Acknowledgments

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THE EFFECT OF PROSTATE BIOPSY AND PERIPROSTATIC NERVE BLOCK ON ERECTILE FUNCTION

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Introduction

Prostate cancer is the most diagnosed solid cancer in the male population [1]. Prostate biopsy is the gold standard diagnostic method. More than 2 million prostate biopsies are performed annually in Europe and the Americas [2]. It is reported that at least one complication is observed in 64–78% of patients, but mortality is quite low [3]. Although the prostate biopsy procedure is invasive, periprostatic nerve block significantly increases patient comfort by reducing the patients' pain [4]. This study aimed to evaluate erectile functions of cases where a prostate biopsy was performed by applying a periprostatic nerve block.

Method: Our study included 106 patients who underwent prostate biopsy between December 2021 and September 2022. Prophylactic antibiotics were administered to all patients the day before the procedure, and rectum cleaning was performed with routine enemas. Then, periprostatic nerve block was performed by injecting 10 ml of 2% prilocaine hydrochloride into the angle between the prostate tissue and seminal vesicles (5 ml each) using an 18-gauge needle under ultrasound guidance in the left lateral decubitus position. Then, a 12-quadrant prostate biopsy was carried out. Cases with chronic systemic diseases, mental health problems, malignancy, or prostate biopsy history were excluded from the study. We statistically analyzed the patients' answers to the international erectile function form-5 (IIEF-5) immediately before the procedure and in the first and sixth months after it.

Results: The average age of the patients was 62.2±3.01 year. Sixty-one (59.22%) cases had abnormal digital rectal examination findings. The patients' mean total PSA value was 9.7±2.14 ng/ml, and the IIEF score was 21.89±2.37 before the procedure. We observed a statistical decrease in the mean IIEF score of 18.84±1.6 in the cases who came for control in the first month (p:0.035). In the late follow-up, the average IIEF score in the 6th month was 20.01±1.07, similar to the pre-procedure results (p>0.05).

Conclusion: Although erectile dysfunction is not life-threatening, it can cause major psychosocial trauma. Anxiety due to prostate biopsy and temporary edema or hematoma in the neurovascular bundles during nerve blockade may negatively affect erection physiology [5]. The data in our study showed that although prostate biopsy caused a decline in erectile functions in the early period, it did not cause permanent sexual dysfunction.

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EMERGENCY DEPARTMENT VISITS DUE TO COMPLICATIONS AFTER TRANSRECTAL ULTRASOUND-GUIDED PROSTATE BIOPSIES: A FOUR-YEAR RETROSPECTIVE SINGLE-CENTER STUDY

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[1] *Tokat Gaziosmanpaşa University, Department of Urology*

Introduction

In the aging world population, prostate cancer draws attention as a significant health problem in males. Prostate cancer ranks second in cancer-related deaths after lung cancer. Approximately 288,300 new cases of prostate cancer are expected in the United States in 2023, of which 34,700 will result in death [1]. Transrectal ultrasound-guided prostate needle biopsy is the gold standard for prostate cancer diagnosis [2]. It can be tolerated in outpatient clinic conditions and easily applied with low levels of undesirable side effects. However, this invasive procedure may lead to severe complications, albeit rarely [3]. This retrospective study aimed to evaluate patients who visited our emergency department after transrectal ultrasound-guided prostate needle biopsy.

Method

We retrospectively examined the data of 801 patients who underwent transrectal ultrasound-guided prostate biopsy at Tokat Gaziosmanpaşa University, Urology Clinic between April 2019 and May 2023. All prostate biopsies were taken under antibiotic prophylaxis. A third-generation cephalosporin was administered for five days, starting at least 24 hours before the biopsy [4]. Following the application of local tropical anesthetic and periprostatic nerve blockade, a 12-core prostate biopsy was taken. Patients who underwent repeated biopsies, those with more than 12 cores biopsies, and those with an immunosuppressive condition were excluded from the study. The study analyzed the patient's ages, presenting clinics at the emergency department, prostate volumes, prostate-specific antigen levels, and comorbidities.

Results

The average age of the patients was 64.4±9.21 years, and the total prostate-specific antigen level was 16.1±10.21 ng/mL. The average prostate volume of the patients was 61.13±14.18 cc. One hundred and forty-one (17.55%) cases were diagnosed with prostate malignant neoplasm.

A total of 43 (5.36%) patients were admitted to the emergency clinic after transrectal ultrasonography-guided prostate biopsy. A total of 30 (69.76%) of these patients had a comorbid condition. The most common comorbidity was diabetes mellitus (63.3%)

A total of 18 (2.24%) patients presented to the emergency clinic with gross hematuria. Fourteen (77.7%) of these patients had a history of anticoagulant or antiplatelet use. The patients were catheterized and underwent continuous bladder irrigation. None of the patients required blood transfusion or fulguration accompanied by cystoscopy.

Two (0.23%) patients presented to the emergency department with rectal bleeding. All patients were treated with rectal compression. There was no need for gastroenterological intervention.

Eleven (1.36%) patients presented with a febrile urinary tract infection. There was growth in the urine culture of seven (63.6%) patients. Escherichia coli was the most determined microorganism. Two patients

diagnosed with urosepsis were followed up in the intensive care unit with intravenous vasopressor and broad-spectrum antibiotics due to hemodynamic instability. No mortality occurred in any patient.

Conclusion

The occurrence of life-threatening pathologies after transrectal ultrasound-guided prostate biopsies is very low [5]. However, we think it is crucial to inform healthcare professionals in the emergency department, considering that there may be referrals to emergency clinics due to these invasive procedures.

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SARCOID-LIKE REACTIONS IN PATIENTS WITH PROSTATE CARCINOMA: CAN MIMIC METASTASIS ON ONCOLOGIC IMAGING

Gizem Issın

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ABSTRACT

Background

Sarcoid-like reaction (SLR) is a condition characterized by non-caseating epithelioid cell granulomas in lymph nodes [1,2]. SLR can arise as a result of an immunological response triggered by several factors including infection, inflammatory conditions, malignancies, immunotherapy, and the presence of foreign objects [1,2]. SLR are typically considered to be non-malignant and generally resolve with corticosteroid [3]. Nonetheless, it is important to note that SLRs can exhibit characteristics that resemble lymph node metastasis or cancer recurrence in individuals who have previously been diagnosed with cancer [4,5].

Several studies reported that SLRs can be encountered in the diagnosis, monitoring, or follow-up of various organ malignancies, especially hematologic malignancies, breast, lung, colon, etc [4,5]. The objective of this study was to identify clinical and histopathological characteristics of SLRs in patients with prostate carcinoma.

Material and methods

Electronic health records are examined and cases who underwent radical prostatectomy and lymph node resection between 2012-2016 were documented. The pathology reports of these cases were evaluated, and cases with SLR were detected. Demographic, clinical, and histopathological data of the cases were analyzed.

Results

Between 2012 and 2016, 40 cases underwent prostatectomy and lymph node excision. SLR was reported in 4 of them (10%). The ages of the cases were 56, 58, 60, and 61. In cases without SLR, the average age was 60.12. Two cases had a tumor with Gleason 3+3 pattern, while the other two had Gleason 4+3 and 4+5 patterns. All SLR involvements were seen in pelvic lymph nodes. The number of involved lymph nodes ranged from 1 to 4. The average diameter of the involved lymph nodes was 1.2 cm. Lymphovascular invasion was reported in all four cases. However, immunohistochemical examination did not show evidence of lymph node metastasis.

Discussion

The presence of SLRs among cancer patients, reported in 4% to 14% of cases, presents intriguing diagnostic and clinical challenges [4,5] SLRs manifest as lymph node enlargement with mass effect, typically appearing as diffusely enlarged lymph nodes on imaging, often with long axes measuring less than 1.5 cm [4]. While these reactions frequently involve locoregional lymph nodes, also can seen in mediastinal-hilar or head and neck regions [6,7]. Notably, SLRs exhibit varying levels of F-fluorodeoxyglucose (FDG) uptake, with reported cases demonstrating values ranging from 1.2 to 17.2 [4]. These imaging characteristics can sometimes mimic malignancy, underscoring the importance of considering lymph node involvement cautiously.

As such, clinicians and oncologists should remain vigilant regarding the potential occurrence of SLRs both in preoperative assessments and during postoperative follow-up. A critical step in their diagnosis involves

sampling and histopathological examination. Importantly, SLRs are often associated with a favorable prognosis, possibly linked to the immune system's role in their development [8].

Notably, SLRs have been reported in association with various organ malignancies, including hematologic malignancies, breast cancer, lung cancer, and colon cancer. Our study extends this association to prostate carcinomas. Given the potential for SLRs to masquerade as metastases, particularly in cases with lymphadenopathy in unexpected region, a biopsy becomes essential to differentiate between the SLRs and metastases.

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EXPLORATION IMAGING BIOMARKERS AND TISSUE VALIDATION IN TRANSLATIONAL NEURO-ONCOLOGY

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ABSTRACT

The most common malignant brain tumour is glioblastoma with poor overall survival. The main imaging modality is magnetic resonance imaging (MRI) for glioblastoma. However, MRI has some inherent shortcomings and novel studies are limited. For example, in clinical examination of patient with glioblastoma, only gadolinium (Gd) has been used as a contrast agent while manganese (Mn) may be an alternative to Gd. Mn as a contrast agent for brain diseases may has some advantages over Gd such as clearance rate, toxicity, blood brain barrier (BBB) permeability, cell specific binding.

Mice with G7 cell implants in their brains underwent MRI scans in three separate visits, after 13 weeks from the time of implantation. Gd and Mn were administered as a contrast agent in visit 1 and 2, respectively. Tumour regions were drawn manually for each visit. Lastly, the T1 relaxation time of the tumours were calculated, and the regions with shortened T1 values were delineated to assess the similarity in Mn and Gd accumulations.

In our study, Mn shortened T1 value was comparable with Gd. For both Mn and Gd T1 relaxation time shortened significantly. While there was no Gd effect on T1 after 2-3 days, Mn kept shortening the relaxation time for 3-5 days in the tumour. Additionally, the T1 shortened areas were different for both post-Gd, post-Mn and Mn delay images.

As a conclusion, human derived glioblastoma cells (G7) and clinically used contrast agents were utilized to be applicable for human studies. Our study, therefore, is a translational pre-clinical study. Mn-DPDP leak from BBB and penetrate glioblastoma, and the abundance of Mn shortens T1 map value. Hence, Mn can be an alternative contrast agent for glioblastoma. Besides, Mn abundance may be related to the tumour characteristic.

Keywords: *Neuroimaging, translational neuro-oncology, radiomics, imaging biomarkers, MRI*

Introduction

The most common primary malignant brain tumour is glioblastoma (GBM) with a mean 14.6-month overall survival [1], which is characterized by invasive tumour growth, neoangiogenesis and an immunosuppressive tumour microenvironment. The standard of care calls for maximum debulking surgery, radiation with concurrent temozolomide, and adjuvant temozolomide are not affective enough to improve the poor survival rate of patients with GBM [2].

For the initial diagnosis and treatment monitoring of a glioma, MRI is the most crucial imaging modality. However, MRI has inherent limitations in sensitivity and specificity due to the lack of specific contrast agents, mesoscopic resolution (1 mm isotropic resolution at clinical field strength), and MR sequences. Therefore, it is still difficult to characterise various areas of malignancy, define precise tumour borders, and distinguish tumour progression from treatment-related alterations like pseudoprogression by utilising existing multiparametric MRI techniques. Current research focuses on the possibility of novel advanced MRI techniques to enhance the neuroradiological workup of brain tumours, such as chemical exchange saturation transfer imaging [3] or MR elastography [4,5]. But we still do not fully comprehend the structural, cellular, and/or molecular underpinnings of these innovative MR signals.

Contrast agents are frequently used in the MR imaging of GBM to improve visibility of the bulk of the tumour. Lanthanides and other paramagnetic chemicals, which influence the T1 relaxation rate of the tissues in which they accumulate, are the most used class of contrast agents [6]. The first intravenous contrast agent authorised for clinical use was gadopentetate dimeglumine, also referred to as Magnevist, in 1988 [6]. However, questions about safety, quick excretion, and lack of specificity have come to light regarding the limitations of Gd based contrast agents (GBCAs) for cancer imaging. Manganese, a different paramagnetic metal, is a necessary trace mineral and is found naturally in a variety of foods, including nuts, legumes, and tea [7], along with can be consumed as oral supplements of 10 mg/day [8]. All bodily tissues contain manganese, which is necessary for numerous enzymatic processes such the metabolism of amino acids, lipids, and skeletal development [7].

Mn ions can efficiently reduce T1 relaxation time despite only having five unpaired electrons (as opposed to Gd's seven). Mn acts as an intracellular calcium analogue, entering cells via voltage-gated calcium channels and resulting in the positive enhancement of the tissues it accumulates within on T1W-MRI, where Gd accumulates extracellularly in areas of BBB breakdown [9, 10, 11]. Due to the constant correlation between higher mitotic activity and an increase in calcium absorption, Mn may be helpful at characterising tumour tissue on MRI [12,13].

In this study, Gd-DTPA and Mn-DPDP contrast agents has been administered to compare their robustness on T1 shortening on GBM. The all method has been designed to be applicable for human studies. The current study, therefore, is a translational neuro-oncology study. To understand the actual meaning of MRI signals, MRI and whole brain slices were directly comprised. In this context, a novel image analysis method was improved to do a voxel-based comparison between tissue and imaging modalities. By this method, we aimed to see relationship of various MRI signals and tissue characteristics. We, therefore, implanted human derived GBM and used the MRI sequences clinically utilizing. As a conclusion, the current study aimed to evaluate Mn-DPDP as a contrast agent, thus, explore new imaging biomarkers.

Method

A G7 patient-derived orthotopic xenograft nude mouse model has been found to be capable of producing the morphological traits of glioblastoma, such as heterogeneous progression and infiltration. Experiments were conducted on CD1 nude mice (Charles River Laboratories) in accordance with the suggestions of the local ethical review panel [14]. Prior to any experiment, mice (weighing 20–25 g) underwent at least one week of acclimation. G7 human glioma cells were grown in stem-like environments on Matrigel-coated plates with Advanced DMEM:F12, 20 M EGF/FGF, 1 % B27, 0.5 % N2, heparin, and 1 % L-Glut. Using stereotactic tools, G7 cells (105 cells per mouse) were intracranially injected into the subventricular zone of ten animals [15]. For reporting study outcomes, the ARRIVE recommendations are adhered to [16].

Eight mice got three sessions of MRI scans 13 weeks after GBM cell implantation (one mouse showed no tumour growth and one mouse died before 13 weeks). Figure 1 illustrates the scanning procedure and the MRI sequences that were used. Through tail vein cannulation, the animals received Gd-DTPA, 1 mol/mL (Magnevist®), and Mn-DPDP, 10 mol/L (Teslascan®), each at a dosage of 0.2 mol/g. Be warned that this Mn-DPDP dosage is significantly greater when calculated using the converted technique (the similar dosage ratio between mice and humans is approximately 12 times lower) even though it is significantly lower than the human dosage (5 mol/kg). Pre- and post-Gd-DTPA injection scanning was carried out in session 1 (preGd/postGd). Scanning was carried out before and immediately after a MnDPDP injection during session 2 two to three days later (preMn and postMn, respectively). Scanning was carried out in session 3 3-5 days later to assess the MnDPDP injection's delayed effect (MnDelay). After the last MRI, animals were promptly scarified, and their brains were removed and frozen for further histological study.

MRI Protocol

A 30-cm horizontal bore Bruker Biospec Avance 7T imaging equipment (Bruker Medical Systems, Ettlingen, Germany) was used to capture the images. Rapid Biomedical, Wurzburg, Germany's receiver coil was a 4-channel phased array receiver head coil.

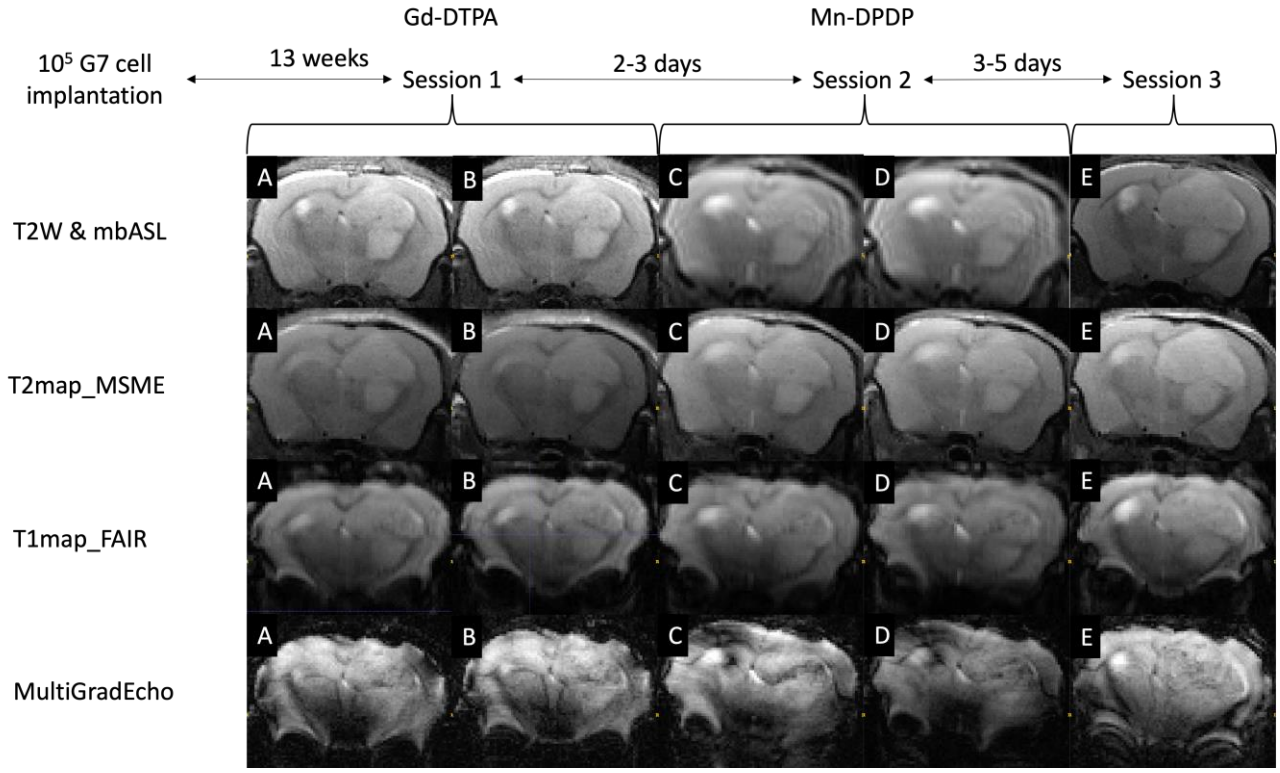

Figure 1. *100 days (13 weeks) following G7 cell implantation, T2W, mbASL, T2map MSME, T1mapFAIR, and Multi Gradient Echo MRI images were obtained. 3 sessions were used to acquire the images. Images A and B, C and D, and E are from Sessions 1, 2, and 3, respectively. In sessions 1 and 2, images A and C stand in for pre-contrast agent images while B and D stand in for post-contrast agent images. Additionally, session 3 images were captured to assess the Mn delay rate after 3-5 days of contrast agent injection: hence, images with label E show Mn delay image*

The mice were placed prone on an MRI mouse cradle after being given anaesthesia using an anaesthetic mask that delivered 1.5 to 2% isoflurane in a mixture of 30% O2 and 70% N2O. To maintain the physiological temperature (37-1 °C), hot air ventilation was used. To prevent movement and improve reproducibility of placement between visits, the conical ear bars and the teeth bar of the anaesthetic delivery mask were utilised to immobilise the head. To increase contact between the coil and the subject, dielectric pads were used.

T2-weighted, T1-weighted, T2 mapping, and T2*-weighted sequences were obtained at each MEMRI time point (see Figure 1) after two tripilot scans to make sure that each mouse's head was correctly positioned. With the following scanning parameters, a rapid acquisition with relaxation enhancement (RARE) sequence was used to perform T2-weighted imaging (14 coronal slices of 0.5mm slice thickness): 7.5 minutes, 176 × 176 matrix, 1.8 x 1.8 cm field of view, 46 msec echo time, 5,000 msec repetition time. Seven 1mm-thick coronal slices of a flow-sensitive alternating inversion recovery (FAIR) sequence were used for T1-weighted imaging, using the following scanning parameters: FOV: 1.8x1.8 cm, TE: 14.2 msec, TR: 10 s, 10 inversion recovery times, 30-5430 ms with 600 ms steps, matrix: 128 x 128, 13.5 minutes. T2 mapping was carried out utilising a multi-slice multi-echo spin-echo [MSME] procedure with seven coronal slices of 1 mm slice thickness and the ensuing scanning parameters: FOV = 1.8 × 1.8, TE = 10 ms, 30 spin echoes, TR = 4.5 sec, matrix = 128 x 128, and 9.5 min. Seven 1mm-thick coronal slices of T2*-weighted imaging were acquired utilising a multiple gradient-echo (multi GRE) process with the ensuing scanning parameters: 1.8 x 1.8 cm FOV, 6 ms TE, 14 gradient echoes, 3 sec TR, 144 x 144 matrix, 6.5 min.

Histology

After MRI, mice were put to death, their brains were taken, and they were immediately frozen. The OTF 5000 Bright cryostat was used for manually cutting the brain into pieces. T2W images used as a guide for sectioning. The location of the sectioning plane parallel to the MRI plane was made possible by the recognition of similar characteristics by an experienced neuroscience research technician (L. Gallagher). From the two central tumour slices visible on the last session T2W-MRI, interleaved 20m coronal sections were cut. The 20 m cryosections

were fixed in ice-cold acetone, cleaned in PBS, and then blocked for 30 minutes at room temperature with 3% BSA/TBS-tween. After that, the sections were stained with H&E (haematoxylin and eosin). x10 magnification Zeiss 710 upright confocal microscope was used to perform whole brain slice tile scans. Images of histology (13001000 pixels) were exported as .tiff files.

It should be emphasised that ROIs had to be chosen from these slices and did not necessarily reflect the peak contrast-enhancing regions because only the histology corresponding to the two central MR slices was available (due to Covid-related experiment delays). The study was unable to include some mice that only showed peripherally enhancing ROIs (Gd-enhancing [n=2], Mn-enhancing [n=2], and Mn-Delay [n=1]).

Additionally, quantitative laser ablation tandem ICP (LA-ICP)-mass spectrometry was incorporated into the process to investigate the distribution of metal ions (Mn, Zn, Cu, C, and Fe) and evaluate their spatial connection with cancer invasion. Finally, LA-ICP mass spectrometry images (MSIs) and H&E staining results have been obtained for each mouse.

Image processing

Raw images were imported into MATLAB 2019b (version 9.7; MathWorks Inc., Natick, MA) after image acquisition, where they were transformed into NIfTI format. T1 maps were created by using M0 and T1 as parameters to fit, for each voxel, the absolute value of the T1 relaxation equation to the experimental decay of the magnitude data recorded at various delays TAC. An internal MATLAB programme was used for fitting, and a mask was used to omit areas outside of the brain. Then, using ITK-SNAP (version 3.8; [17]), images were examined.

To prevent selection bias, all tumour volumes-of-interest (VOIs) and regions-of-interest (ROI) were manually segmented. This was done without having access to the histology data beforehand. The inclusion of nearby structures like the fluid-filled ventricles, which could impact T1 readings, was carefully avoided. T2-weighted images obtained at sessions 1 and 3 were manually segmented into volumes-of-interest (VOI). To measure tumour development and infiltration as a percentage change in tumour volume between these visits, tumour volumes (mm3) were extracted.

Following this, the final T2map MSME image was used as a base image for the co-registration of T1 maps from each acquisition time (preGd, postGd, preMn, postMn and MnDelay). This was selected as the final MSME image as it provided the largest whole tumour margins. Transformation matrixes have been created for between 3 sessions by an automatic rigid co-registration with ANTs (see Figure 2) [18]. The transformation matrixes have been utilized to warp images into visit 3's spatial orientation. The registration qualities have been checked by creating checkerboard images after each co-registration process as shown in the figure bellow. The checkerboard images have been created on terminal with a tool called ImageMagick [19].

Delta T1 map images were carried out by subtracting pre-contrast agent and post-contrast agent images as well as contrast agent persisting. The subtracting process has been performed for T1 map images as following; A-B, B-C, C-D, C-E and D-E.

A whole tumour region-of-interest (ROI) was then manually segmented on the baseline MSME image on the slice showing the most tumour in visit 3 and corresponding slices in visit 1 and 2. T1 relaxation values (ms) were then extracted for the MSME ROI across each T1 map to assess for change in T1 values in the whole tumour region preGd, postGd, preMn, postMn and at MnDelay. By this way, we had three regions for each image; tumour core (visit 1 tumour ROI), first tumour growth (tumour volume difference between visit 1 and visit 2) and second tumour growth (between visit 2 and visit 3) (figure 3). In such manner, we not only avoided measurement error because of tumour growth but also examined tumour growth areas, separately.

Statistical Design and Analysis

Statistical analyses were conducted using t-test (paired two sample for means) in excel. The t-tests were performed to evaluate differences in T1 relaxation time (ms) in the chosen tumour regions-of-interest (ROIs) at each acquisition point. Statistical significance was set at $p<.05$. Due to the exploratory nature of the work, no multi-test correction was applied. Boxplots show the median (black line), 25th/75th percentiles (boxes) and

minimum/maximum values (whiskers). Statistical significance flags: *p<.05. Box plots are created with a Python tool called seaborn [20].

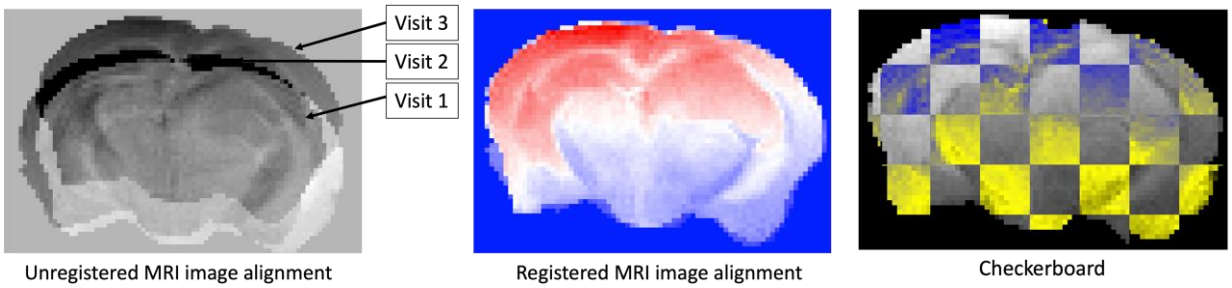

Figure 2. *Importance of co-registration for an accurate image analysis*

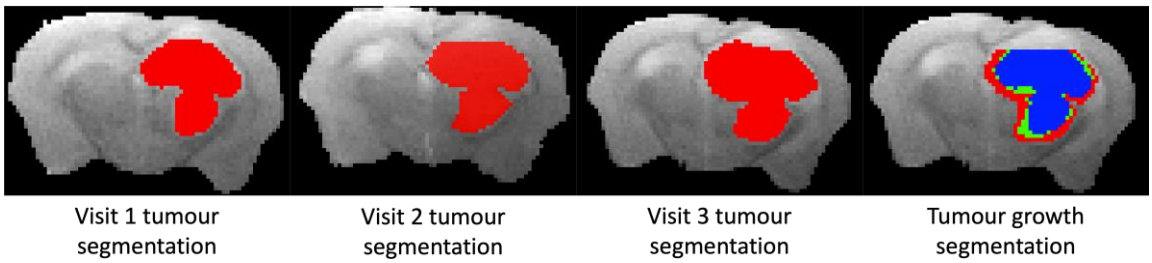

Figure 3. *Delineation of ROIs within sessions.*

Results and Discussion

In this section, effect of Gd-DTPA and Mn-DPDP was compared on T1 relaxation time. The box plots were created to compare their T1 shortening reactions. Since the different accumulations were observed among tumours in the LA-ICP-MS Mn, the relaxation times were separately investigated with different ROIs as shown in Figure 3. The cluster names are cluster 1, cluster 2 and cluster 3 represented with blue, green, red, respectively in Figure 3. Likewise, for all images, cluster 1 is tumour volume in visit 1, cluster 2 and 3 were tumour growth and infiltration between visit 1 & 2 and visit 2 & 3, correspondingly.

T1 Shortening in Whole Tumour

The whole tumour was evaluated in terms of T1 relaxation time change before and after contrast agent (Figure 4). The box labels are the same as images labels were described in the figure 1. The figure can be investigated into two categories as Gd and Mn related changes. To evaluate Gd dependant chances A, B and C boxes should be compered. It can be interpreted the mean relaxation time of dropped between A and B and it increased again among B and C (P=0.0024, P=0.0012, respectively). Thus, Gd have shortened the relaxation time, but it was cleared out after 3 days. On the other hand, for C D and E images relaxation time should be considered for evaluation of Mn. The mean value of relaxation time was 1957ms for image C while they were 1678ms for D and 1665ms for E.

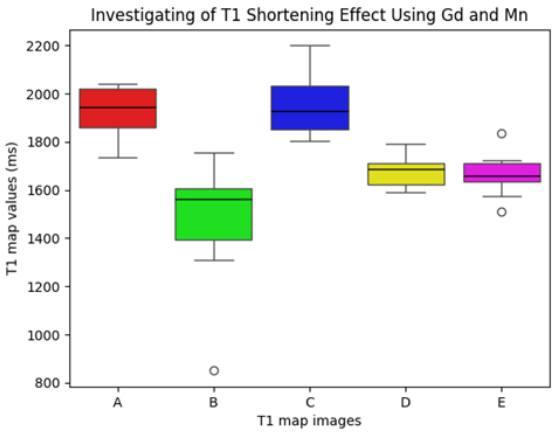

Figure 4. *T1 relaxation time between pre, post and persisting contrast agent images in whole tumour*

The relaxation time decrease was significant between both C&D and C&E (P=0.0001 and P=0.0023, respectively). Hence, Mn has effect on T1 relaxation time, and it stayed in the tumour after 3-5 days. Overall, Gd and Mn were shortening the relaxation time and Mn stayed in the tumour after 3-5 days while Gd did not persist after 2-3 days.

As mentioned in the method sections, T1 map images were subtracted as pre-contrast minus post-contrast and pre-contrast minus contrast persisting images to observe the T1 shortening areas. A box plot was created to illustrated delta T1 changes between visit (figure 5). The biggest change was between A and B as AB has higher delta T1 value while CD and CE was the same. Additionally, AB, CD and CE was significantly higher than AC (P=0.0012, P=0.0268, P=0.0299, respectively) Thus, it can be interpreted that Gd and Mn shortened the T1 values, but Gd did not persist after 2-3 days.

Gd vs Mn on T1 Shortening in Tumour

Effectiveness of Gd and Mn on T1 relaxation time was compared by subtracted images data as showed in figure 6. The bar named AC is created to show Gd clearance in 3 days (between visit 1 and Visit 2). It is observed that Gd and Mn shortened the T1 relaxation time in the tumour core area in figure 7 (Cluster 1). AB, CD and CE were higher than zero while AC and DE was zero centred. Gd has been cleared after 3 days as it can be seen in AC bar, as there was a significant difference between AB and AC (P=0.0408). Mn shortened the T1 relaxation time in visit 2 and 3 as CD and CE was higher than 0, which illustrates Mn stayed in the tumour core between visit 2 and 3 (3-5 days) as the statistical result above proved. However, there was no significant difference between AC and CE while there was a significant difference between AC and CD (P=0.0196) in cluster 1. Lastly, post-Mn more shortened the relaxation time than Mn persisting that can be seen on DE with being slightly under zero.

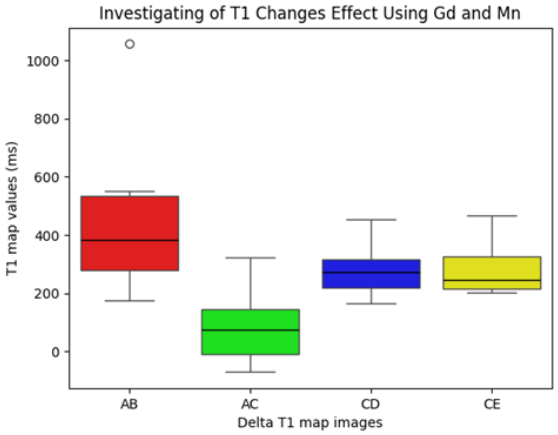

Figure 5. *Delta T1 map values between visits.*

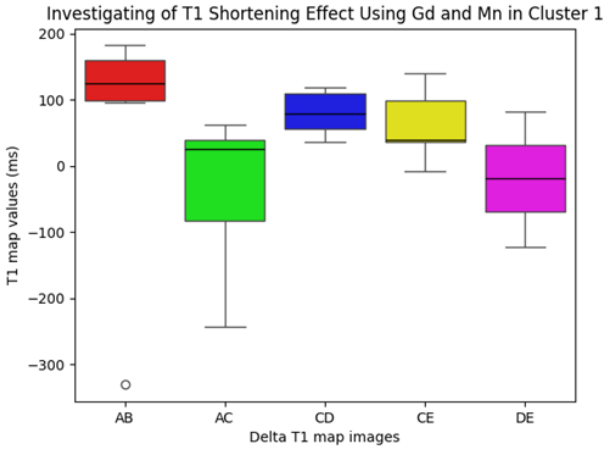

Figure 6. *Delta T1 relaxation time between pre, post and persisting contrast agent images in Cluster 1*

T1 shortening in Cluster 2

The T1 relaxation time effectiveness of Gd and Mn was examined in cluster 2 in figure 7. The outcomes were similar with cluster 1. The noticeable difference was that the change between CD and CE in cluster 2. The similarities and differences may be related tumour characteristic.

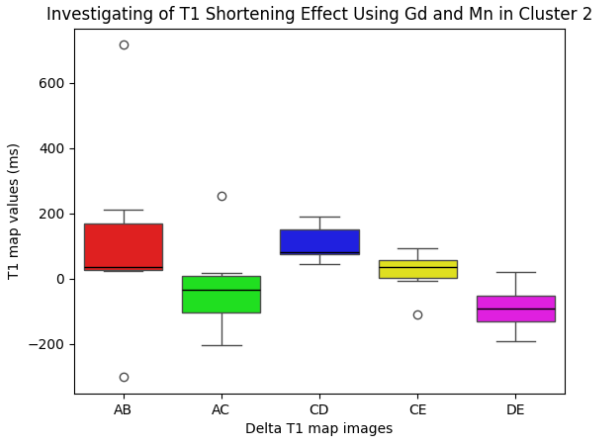

Figure 7. *Delta T1 relaxation time between pre, post and persisting contrast agent images in Cluster 2.*

T1 shortening in Cluster 3

The T1 relaxation times of tumour growth and infiltration regions between visit 2 and 3 (cluster 3) were compared in the figure 8. The plot created in the figure below is different since there was no visible tumour in MRI on visit 1 and visit 2 in cluster 3. While CD was above zero, AC, CE and DE were under zero, and AB was zero centred. As a main difference in this plot is relationship of CE and DE. CE was higher than DE for the other clusters, but they were similar in cluster 3. In other words, Mn persisting effect on T1 relaxation time shortening is different in the tumour growth and infiltration area. However, there was no significant chance between delta T1 map values in cluster 3. As it can be clearly seen Mn behave differently with different clusters.

Figure 8. *Delta T1 relaxation time between pre, post and persisting contrast agent images in Cluster 3.*

T1 Shortening in Healthy Regions

The Gd and Mn influence on T1 relaxation time in healthy regions were compared in figure 9. T1 shortening were not observed for post-contrast agent images both for Mn and Gd, with no statistically significant changes.

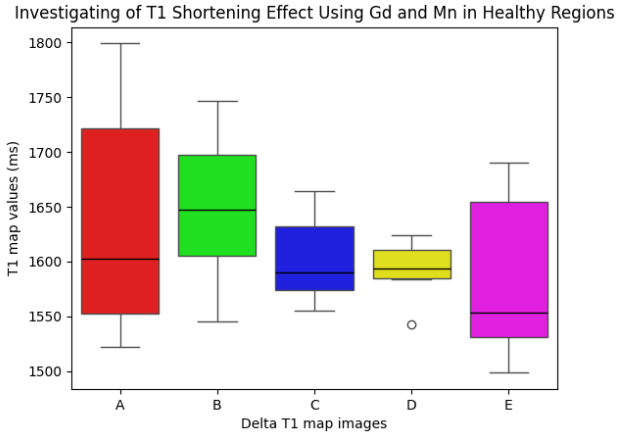

Figure 9. *T1 relaxation time between pre, post and persisting contrast agent images in healthy regions.*

Conclusion

In this study, not only Gd and Mn has been compared as a contrast agent for glioblastoma but also Mn behaviours were investigated with MRI tissue comparisons. Since Mn significantly shortens the T1 relaxation time, it can be a new contrast agent for glioblastoma evaluations. Additionally, it is possible that MEMRI may be used in conjunction with 5-ALA for intraoperative MRI, where it could provide visualisation of the contrast-enhancing tumour region for the duration of the procedure. Mn enhancement was also found to persist longer than Gd enhancement, with uptake visible up to 5 days after administration. As Mn behaved different among clusters, Mn abundance may vary related to tumour characteristic. Thus, to determine precisely how manganese uptake links to the features of the cancer cells, more research is required. As a next step of this study, voxel by voxel image analysis between whole slice of brain tissue and MRI sequences was planned.

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SYNTHESIS OF DIARYLUREA DERIVATIVE AND INVESTIGATION OF ITS ACTIVITY AGAINST INSULIN-LIKE GROWTH FACTOR (IGF) BY *IN SILICO* METHODS

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ABSTRACT

Cancer, one of the diseases whose cause and treatment have been investigated from past years to the present, is a group of diseases characterized by the uncontrolled proliferation of cells, invading normal tissues and organs, and spreading throughout the body, as a result of the disruption of the mechanisms that regulate the normal behaviour of the cell. Cancer develops from a single mutant cell that multiplies abnormally and, unlike normal cells, has the ability to multiply unlimitedly. At the cellular level, cancer occurs as a result of a multi-stage process that involves mutations and the selection of cells with increased proliferation, survival, invasion, and metastasis abilities. Many drug candidate studies have been conducted for the treatment of cancer, and it is clearly seen from the literature that more will be done in the future. In this study, we focused on the compound 1-(3-acetylphenyl)-3-(3-chlorophenyl)urea, which was synthesized for the first time. The synthesized compound was optimized at B3LYP-D3/6-31+G(d). The structural properties of the compound in question were revealed and its IR spectrum was calculated and compared with experimental results. Characterization of the compound to be synthesized was carried out experimentally using spectral methods such as IR and NMR. Finally, the activities of the compound, whose spectral characterization was completed, against target proteins were examined by the molecular docking method, and its pharmacological and pharmacokinetic properties were examined by ADME, MM-GBSA, and p450 analyses. As a result, it was determined that the synthesized compound was effective against the IGF protein and its pharmacokinetic and pharmacological properties were suitable.

IN-SILICO PREDICTION OF TOXICITY PARAMETERS OF SOME CONVENTIONAL AND NEW-GENERATION ANTICANCER DRUGS USED IN PROSTATE CANCER TREATMENT

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ABSTRACT

Prostate cancer is the second most common type of cancer in men after lung cancer. According to the data of the World Cancer Research Fund, its incidence among all cancers is around 15% [1]. There are many types of drugs used in the treatment of prostate cancer. Moreover, new potential anticancer agents and drug forms with higher efficacy are being increasingly investigated by researchers. On the other hand, since the experimental toxicity studies of the designed new anticancer agents require both high cost and time, in-silico toxicity predictions provide many advantages to scientists. In this study, the toxicity parameters of some conventional and new-generation prostate cancer drugs have been predicted in-silico. The predictions for the median lethal dose (LD50) of the drugs were determined in mg/kg body weight. The toxicity classes of the drugs were defined. While new-generation drugs had relatively lower toxicity parameters, old-generation drugs were found to have high carcinogenicity and hepatoxicity values. This result shows that the search for new-generation drugs with both lower toxicity and higher efficacy should continue for the treatment of prostate cancer. The results of the study also show that in silico predictions are in good agreement with experimental ones and that structure-activity-related computational studies can provide useful preliminary information to researchers.

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EVALUATION OF TREATMENT RESPONSE IN EARLY STAGE RENAL PELVIS TUMORS INTRODUCTION

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ABSTRACT

Background

Transitional cell tumor is mostly seen in the bladder, but is less common in the renal pelvis and ureter. Since tumors in this region are rare, there are not enough phase studies. Treatments are mostly based on inferences from studies conducted for bladder transitional cell cancer. In our study, we aimed to evaluate the effectiveness of treatment in patients with early stage renal pelvis transitional cancer.

Method

Cases from Sivas Numune Hospital and Afyonkarahisar State Hospital were included in the study. The patients were evaluated retrospectively. Pathologic data of a total of 326 cases diagnosed with kidney cancer were examined through hospital operating systems. Radiological data of 23 cases in which cancer originating from renal pelvis was evaluated and 2 of them were found to be denovo mestastic. These patients were excluded from the study, and 21 patients were included in the study.

Results

The average age of the patients included in the study was 65.4±13.2 years. Nine (23.9%) of the patients were male and 16 (76.1%) were female. When the tumor locations were examined, 13 (61.9%) were in the right renal pelvis; 8 (38.1%) originated from the left renal pelvis. Considering the histological subtypes, 12 (57.1%) were transitional cell carcinoma, 7 (33.3%) were papillary type uroepithelial carcinoma, and 2 (9.6%) were squamous cell carcinoma. When the T stage of the patients was evaluated, 7 (33.3%) were T2, 12 (57.1%) were T3, 2 (9.6%) were T4. The lymph nodes of 18 (85.7%) were clinically and pathologically negative; 3 of them (14.3%) were found positive. The T stage of the patients with positive lymph nodes was T4 in 2 (66.7%) and T3 in 1 (33.3%) patient. Seven (33.3%) patients received neoadjuvant chemotherapy; 14(66.7%) received adjuvant therapy. 16(76.1%) patients received cisplatin-gemcitabine treatment, and 6(23.9%) patients received carboplatin-gemcitabine treatment. On the date of completion of the study, 01.05.2023, it was observed that only 4 (19.1%) patients developed recurrence The progression-free survival of these patients were 8.6, 5.6, 25.5 and 34.4 months. Disease recurrence occurred in 3 (25%) of 12 patients with transitional cell renal pelvis cancer. All 3 patients had T3N0 disease and all received adjuvant chemotherapy. 2 of them (66.7%) received cisplatin-gemcitabine treatment; 1 of them (33.3%) received carboplatin-gemcitabine treatment. The fourth patient who relapsed was of the SCC histological subtype. The patient with T3N0 disease received adjuvant cisplatin-gemcitabine chemotherapy treatment. Neoadjuvant chemotherapy was administered to 7 patients. All of them received cisplatin-gemcitabine treatment. It was determined that only 5 patients had died until the end of the study. When all patients were evaluated, the average overall survival was found to be 28.7±24.0 months.

Conclusion

Cisplatin-gemcitabine treatment can be used in neoadjuvant or adjuvant treatment in renal pelvis tumors. Its use in the neoadjuvant period reduces the risk of recurrence more than in the adjuvant period.

THE MOST COMMON CAUSES OF ACUTE KIDNEY INJURY IN ONCOLOGICAL PATIENTS ADMITTED TO THE NEPHROLOGY CLINIC

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ABSTRACT

Acute kidney injury is a common complication in cancer patients. It may be caused by the cancer itself or by the treatment of the disease. It may also develop due to additional etiologies. Whatever the reason for consisting, it is very important issue because of mortality rate is about 50% and it remains constant. In fact, AKI-associated multiorgan failure and sepsis increase the risk of mortality by almost 100%. In this study, we evaluated 1155 patients referred to the nephrology outpatient clinic due to acute kidney injury in terms of etiology. At the end of the study, we identified that the top three causes of acute kidney injury are NSAID use, conventional chemotherapy, and pre-renal reasons. Therefore, we would like to emphasize that rational drug use is important for chronic pain management.

Keywords: *Acute kidney injury, oncological patients, rational drug use*

Introduction

The consensus criteria for acute kidney injury (AKI) developed by the Acute Dialysis Quality Initiative (ADQI) group, first published in 2004 [1] and named with the acronym RIFLE (risk, injury, failure, loss of kidney function, and end-stage renal failure). More recently, a modified version was proposed by the Acute Kidney injury Network (AKIN) [2] When we evaluate the differences between both definitions, we can notice that in RIFLE criteria, the diagnosis is based on serum creatinine (sCr) ≥1.5-fold increase or estimated glomerular filtration rate (eGFR) >25% decrease compared to baseline within seven days. But in AKIN, it is on sCr ≥1.5-fold increase or ≥ 0,3 mg/dl within 48 hours and eGFR criteria is not included at all. Urinary output criteria are the same in both definitions as <0.5 mL/kg/h for at least 6 consecutive hours. Oncology patients are a risk population for developing acute kidney injury (AKI), and the prevalence rate of AKI in oncology populations is 7.5%-9.3% in worldwide. [3,4] There is no large-scale study conducted in Türkiye. But in a study of 208 cancer patients conducted by Dr. Elif Güngör and her colleagues at Trakya University in 2018, the acute kidney injury rate was found 10.5%. The likelihood of developing AKI depends especially on the type of cancer and anti-cancer therapy. In a study the top three primary carcinomas were bladder cancer, leukemia, and lymphom [5].

In another study, the top three cancers with AKI were myeloma (26%), bladder cancer (19.0%), and leukemia (15.4%) [6].

In intensive care unit, the rate of AKI in patients with solid tumors was less than in patients with hematological malignances and the incidence of AKI was 59% in solid tumors primarily related to sepsis (80%), hypovolemia (40%), and outflow tract obstruction (17%) [7].

Intrinsic renal injury is the major reason for AKI in oncology patients and acute tubular necrosis (ATN) and acute tubular interstitial nephritis (ATIN) are the most frequently observed forms of this category. ATN caused by nephrotoxic drugs is more common. Antibiotics (especially amphotericin, vancomycin, aminoglycosides, and polymyxins), acyclovir, ganciclovir, bisphosphonates, calcineurin inhibitors (CNIs), contrast materials, ifosfamide, pemetrexed, methotrexate, and tyrosine kinase inhibitors (axitinib, pazopanib, sorafenib, regorafenib, and sunitinib) are best known. In some patients, acute tubular interstitial nephritis (ATIN) may appear after using CTLA-4 inhibitors and programmed death (PD)-1 inhibitors (nivolumab, pembrolizumab).

But pre-renal AKI can also occur often because of gastrointestinal symptoms associated with oncology, such as nausea, vomiting, and diarrhea that promote low renal perfusion.

The post-renal AKI, the third category of AKI, arise especially from the urinary tract obstruction (UTO) caused by blood clots produced from neoplastic tissues or hemorrhagic cystitis induced by drugs.

So, the key points in preventing AKI in oncology patients are avoiding infections and maintaining proper blood volume and hemodynamic stability. Maintaining adequate hydration is the most important and relatively easy intervention, both for pre-renal AKI and ATN. Adjusting patients' cancer care, such as chemotherapy options, is another main part of the treatment.

Material and Methods

In this present study, 1155 patients who were referred to the nephrology outpatient clinic due to acute kidney injury between January 2022 and July 2023 were evaluated in terms of the etiology. The patients who had previous chronic kidney disease were excluded. While evaluating the findings obtained in the study, NCSS (Number Cruncher Statistical System) 2020 Statistical Software (NCSS LLC, Kaysville, Utah, USA) program was used for statistical analysis. While evaluating the study data, qualitative variables were shown with descriptive statistical methods such as frequency and percentage. Student's t-test was used for quantitative evaluations of two normally distributed groups. Chi-Square test and Fisher's exact test were used to compare qualitative data. The results were evaluated at the 95% confidence interval and the significance level was $p<0.05$.

Results

640 of 1155 patients were men and 515 were women. 10.4% (n=120) of cases were intrinsic AKI secondary to non-steroidal inflammatory drugs and 9.1% (n=105) were secondary to antibiotic induced nephrotoxicity, 9.2% (n=106) were prerenal and 7.4% (n=86) were postrenal.

9.2% (n=106) of cancer patients had a conventional chemotherapy or 7.3% (n=84) 5 FU, treatment before, 9.1% (n=105) of them had hyperuricemia, 6.9% (n=80) had tumor lysis syndrome, and 4.8% (n=55) had hypercalcemia related chemotherapy treatment or the cancer itself. 7.6% (n=88) had urinary tract infection, 4.5% (n=52) had myeloma light chain, 4.2% (n=48) had ileostomy. 3.6% (n=42) of the patients had mild to severe proteinuria with a slight increase of sCr have treated with sunitinib, pazopanib. 2.4% (n=28) had nephrotic syndrome because of cancer related glomerular nephritis which are associated with hematological tumors such as chronic lymphocytic leukemia (CLL). the most frequently reported are membrane proliferation glomerular nephritis (MPGN, 36%) and membrane nephropathy (19%) [8].

2.1% (n=24) of patients had AKI secondary to ileus, 2.1% (n=24) secondary to nephrectomy.

It is seen that 0.2% (n=2) of the patients had Covid infection history (Thrombotic microangiopathy (TMA) or sepsis related).

Conclusion

As a result of the study, we saw that the majority of oncological patients referred to the nephrology clinic due to acute kidney injury have intrinsic acute kidney injury triggered by long-term and frequent NSAID use. For this reason, we emphasize that pain care of oncological patients should manage seriously with necessary and absolute coordination of the algology unit.

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TWIN PREGNANCY AFTER JUVENILE TYPE GRANULOSA CELL TUMOR

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Introduction

Abdominal masses in the pediatric population most commonly arise from the ovaries [1]. Ovarian masses, including both non-neoplastic lesions and neoplastic tumors, can occur in all age groups. The incidence, clinical presentation and histological distribution of such lesions in children and adolescents differ from those in adults and require a special therapeutic approach [2]. Ovarian masses range from simple functional cysts to malignant neoplasms. Ovarian malignancy is reported in 3-8% of children and adolescents with adnexal masses and accounts for 1-2% of all childhood cancers. Granulosa cell tumors are divided into adult and juvenile types according to their clinical and histopathological features. Juvenile granulosa cell tumor is a malignant, pure sex cord tumor composed of primitive-looking granulosa cells that grow in solid and follicular patterns [3]. It accounts for 5% of granulosa cell tumors and 70% of all sex-cord stromal tumors in patients under 20 years of age. It occurs mainly in patients under 30 years of age, and the average age at diagnosis is 13 years. Genc et al. studied 125 patients with juvenile granulosa cell tumors and reported that 44% of cases occurred in the first decade of life and 34% in the second decade. Patients with juvenile granulosa cell tumors may present with symptoms related to pelvic mass and hormonal disorders. Acute complications such as torsion and rapture are more common in children than in adults [4]. Juvenile granulosa cell tumors typically secrete estrogen [3]. As a result, premenarchal patients often present with clinical signs of isosexual peripheral precocious puberty, including breast enlargement, vaginal bleeding, axillary and pubic hair growth, and somatic growth(16) The imaging features of this neoplasm are heterogeneous and nonspecific [3]. Juvenile granulosa cell tumors are typically large and most contain both solid and cystic components, but they can be completely solid or completely cystic. The prognosis of juvenile granulosa cell tumor is good and late recurrences are rare. The majority of patients present with early-stage disease confined to the ovary and have an excellent prognosis with a survival rate of over 90% with surgery alone. However, rare cases with advanced disease have a worse prognosis and may require chemotherapy [4].Pediatric patients with ovarian masses have a long life expectancy after treatment; Preserving gonadal function is of great importance not only for the maintenance of fertility but also for the natural progression of puberty.

Case

Our patient was evaluated with ultrasonography at an external center when he was 17 years old due to right groin pain. In the USG, a solid mass with a diameter of approximately 10 cm was observed in the right adnexal area. In the lower abdominal MRI, a mass image of 9x10 cm with solid and cystic components was observed in the right adnexal area. Laboratory ; AFP:293 BHCG <1 LDH:153 other tumor markers were normal. After excision of the mass, the frozen section revealed a granulosa cell tumor and bilateral parapelvic paraaortic lymph node dissection and total omentectomy were performed. The final pathology result was juvenile type granulosa cell tumor. Our patient is now 27 years old and was admitted to our emergency department due to pain in her 35 w 4 d ivf twin pregnancy. The patient underwent laparotomy with a median incision above the umbilicus. Apgar 5/7 female and 6/8 male babies were delivered. Our patient was discharged with full recovery.

Discussion

Since granulosa cell tumors, especially the juvenile type, are very rare tumors, more comprehensive studies are needed to better manage their treatment. Granosa cell tumors of the ovary have a good prognosis

because they are usually diagnosed at an early stage, but patients need to be followed up regularly due to the possibility of recurrence.

Anti-mullerian hormone (AMH) and inhibin B can be used in the diagnosis and follow-up of patients. In fact, it has been shown that the combined use of AMH and inhibin B is more useful in detecting recurrences and is directly proportional to the tumor diameter (5). Unfortunately, in our study, these two tumor markers were not studied in patient serum.

Sampling of the endometrium in the preoperative evaluation of patients is important in diagnosing synchronous endometrial cancer and managing the patient accordingly.

Preservation of gonadal tissue in children and adolescents is of great importance not only for the maintenance of fertility but also for the natural progression of puberty. Treatment of pediatric ovarian cancer masses should be therapeutic and, if possible, function-preserving and minimally invasive. Children and adolescents with ovarian masses should be treated by multidisciplinary teams in specialized centers that can provide optimal physical and psychological support, avoid unnecessary oophorectomies, and ensure the best possible therapeutic outcome.

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COLON METASTASIS OF BREAST CANCER

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Introduction

Metastases of breast cancer to the colorectal region are quite rare. Approximately 3-10% of breast cancers present with distant organ metastasis at the time of diagnosis. In breast cancer, the initial site of metastasis commonly involves the axillary lymph nodes, with distant organ metastases occurring in the following order of frequency: bone, lungs, central nervous system, and liver. Metastasis of breast cancer to the gastrointestinal system (GIS) is a seldom-seen occurrence. Autopsy series indicate that this incidence is around 3-4%, with the most frequently affected organs being the stomach and small intestine.

Limited cases of rectal metastasis from breast cancer have been reported in the medical literature. The majority of these cases involve patients with multiple metastases and late-stage metastasis of previously diagnosed and treated breast cancer.

Case

A 68-year-old female patient underwent Modified Radical Mastectomy for left breast carcinoma at an external center in 2003. Following the surgery, she received 6 cycles of chemotherapy. Her oncological follow-ups were conducted at an external center, and during these follow-ups, no evidence of metastasis was detected.

Approximately twenty years later, on April 28, 2023, she presented to the emergency department with symptoms of ileus and a obstructive mass in the colon. A loop transversostomy was performed initially for palliative purposes. Subsequently, she underwent curative surgery, during which a tumor was identified in the sigmoid colon and splenic flexure, leading to an extended left hemicolectomy.

The pathology report, obtained when the patient sought further evaluation, indicated "ADENOCARCINOMA INFILTRATION OF THE BOWEL WALL." Additionally, sixteen lymph nodes that were excised were reported as showing "REACTIVE LYMPH NODE HYPERPLASIA." Immunohistochemical staining results revealed the following: GATA-3: Diffusely strong positive, ER: 90-95% strongly nuclear positive, PR: 90-95% strongly nuclear positive, Synaptophysin: Negative, Chromogranin: Negative, Sox-10: Negative, E-Cadherin: Positive, cerbB2: Negative.

Based on the patient's clinical history and these findings, the pathologist concluded that the observations were consistent with invasive carcinoma metastasis from the breast.

Discussion

Metastases from the breast to the gastrointestinal system (GIS) typically involve the stomach and small intestine, with less frequent occurrences in the colon and rectum. Notably, lobular carcinoma, particularly the morphological subtype known as signet ring cell carcinoma, is commonly associated with breast metastasis to the rectum. Prior reports have indicated a time gap of 5-6 years between the diagnosis of breast cancer and GIS metastasis. Colonoscopy and biopsy are crucial tools for determining whether a colon mass is of primary origin.

In this case, the patient's presentation with acute colon obstruction necessitated initial intervention with loop transversostomy. Subsequently, considering the possibility of a primary colon tumor due to the elapsed time, she underwent a second surgery for resection, which revealed the pathological diagnosis of metastatic

breast tumor within the extended left hemicolectomy specimen. Such a delayed metastasis, occurring 20 years after the initial breast cancer diagnosis, is exceptionally rare.

Breast cancer metastases to the colorectal region may mimic features of linitis plastica, presenting with a diffuse and rigid appearance. Immunohistochemical markers, such as Gross cystic disease fluid protein-15 (GCDFP-15), estrogen and progesterone receptors, play a pivotal role in distinguishing these metastases. While GCDFP-15 is typically negative in primary colorectal tumors, it can be positive in breast cancer metastases to the colon. The average survival time for GIS metastases from breast cancer is approximately 2 years, although some patients have survived up to 9 years. Treatment options and outcomes for colon metastasis of breast cancer remain diverse, with various approaches involving surgical, hormonal, or chemotherapy regimens.

In conclusion, breast cancer patients should have gastrointestinal symptoms investigated for potential metastasis. It is crucial to remember that colorectal tumors with challenging histopathological diagnoses may indeed represent metastatic foci, and occasionally, the unexpected presence of the primary tumor in the breast should be considered. Immunohistochemical studies, including the evaluation of estrogen, progesterone receptors, and GCDFP-15, are essential in such cases.

DELAYED DIAGNOSIS IN A MENTALLY MOTOR-RETARDED GIRL: A RARE CASE OF GIANT MUCINOUS CYSTADENOMA

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ABSTRACT

Objective: This presentation discusses the challenging case of a 15-year-old mentally motor-retarded (MMR) girl with a delayed diagnosis due to a misdiagnosis. Additionally, we highlight the rarity of mucinous cystadenomas in childhood, with only ten reported cases in the literature.

Case Report: We present a 15-year-old MMR girl who has been bedridden since birth. She visited the emergency department three times within two days with complaints of severe vomiting, restlessness, and abdominal swelling. Initially, she was misdiagnosed with constipation and sent home with incorrect treatment. An emergency abdominal CT scan revealed a 13x7x7 cm cystic lesion in the left ovary, filling the abdominal cavity (Figure 1a-e). Left salpingo-oophorectomy was performed, confirming a mucinous cystadenoma (Figure 2,3).

Conclusion: This complex case underscores the importance of considering ovarian masses in children with abdominal symptoms and the significance of timely imaging. Careful evaluation and early surgical intervention, ideally at centers equipped for frozen section examinations, are crucial when dealing with medically complex patients like those with MMR.

Keywords: *Mucinous cystadenoma, mental motor retardation, abdominal pain, ovarian mass, pelvic mass.*

Introduction

Individuals with mental motor retardation may have difficulty in receiving a diagnosis and consequently obtaining appropriate treatment due to factors such as speech difficulties, masking of symptoms, and accompanying neurological or genetic problems. Being disabled affects not only the individual but also their family. This places the clinician at risk of not obtaining accurate medical history from a stressed family, potentially leading to misdiagnosis. On the other hand, adnexal masses account for 1-2% of childhood masses. Approximately 60-70% of these are of ovarian origin, and most of them are benign [1,2].

Case Report

This case presentation discusses a 15-year-old girl with mental motor retardation who has been bedridden since birth. The reason for the patient's admission was severe vomiting, restlessness, and abdominal distension, which had been ongoing for 3 days. What is particularly noteworthy is that the patient had presented to the pediatric emergency department with similar complaints one and two days before the current admission and had been mistakenly treated for constipation and subsequently discharged.

During the physical examination, the patient exhibited advanced scoliosis. In addition, spastic paralysis was observed in all extremities, and tenderness with guarding was noted in the abdominal region. The patient was highly agitated. When these findings and the patient's ongoing condition were considered together, making a diagnosis became exceedingly challenging.

According to laboratory results, the patient had a high white blood cell count (21,960/mm^3), elevated CRP levels (5.46 mg/L), normal hemoglobin levels (14.0 g/dL), adequate platelet count (296,000/mm^3), and normal creatinine (0.85 mg/dL) levels. Tumor markers could not be assessed due to the urgency of the patient's condition.

The patient initially underwent an abdominal ultrasound; however, the origin of the mass filling the abdomen could not be determined. To identify the origin of the mass and any associated pathologies, if present, an abdominal computed tomography (CT) scan was performed before the operation. During emergency computed tomography scanning, a cystic lesion with a diameter of approximately 12 cm and multiple septa was detected in the left lower quadrant of the abdomen, along the midline (Figure 1a-d). This lesion was suspected to be of ovarian origin. The patient had scoliosis (Figure 1e). The patient was taken to emergency surgery due to the presentation of acute abdominal symptoms. During the operation, a cyst originating from the left ovary was removed, and since frozen section examination could not be performed under hospital conditions and the macroscopic appearance of the cyst raised suspicion of malignancy, the right ovary was of normal size and appearance (Figure 2). Left unilateral salpingo-oophorectomy was performed (Figure 3). No ascitic fluid was observed. Pathological examination reported the lesion as a mucinous cystadenoma.

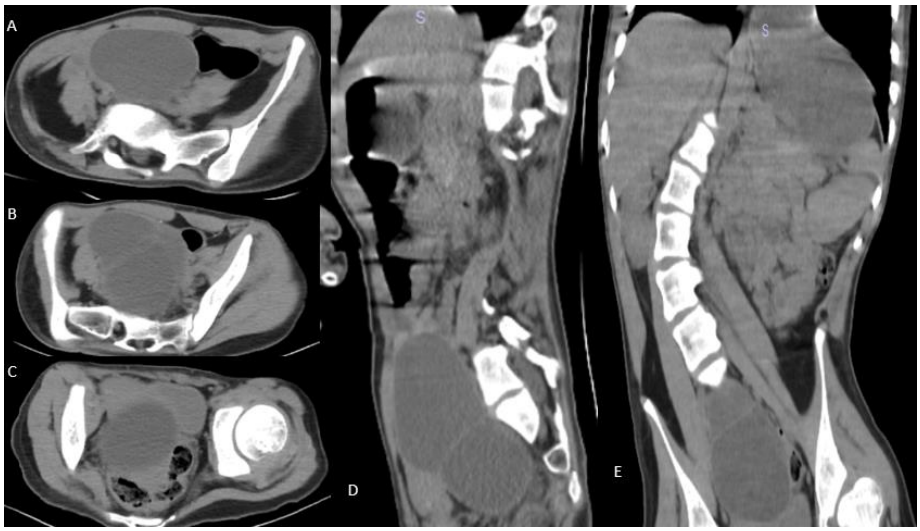

Figure 1. *Abdominopelvic Computed Tomography Examination.*

Figure 1A, 1B, 1C: In the axial section, in the lower quadrants of the abdominal midline, a 12 cm in diameter cystic lesion originating from the left ovary with multiple septations.

Figure 1D: In the sagittal section, the mass fills the abdomen.

Figure 1E: In the coronal section, a scoliotic appearance.

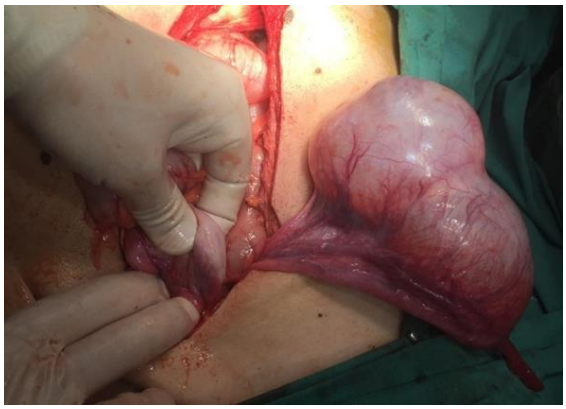

Figure 2. *Intraoperative View of the Cyst of Left Ovarian Origin, Normal Appearance of the Right Ovary.*

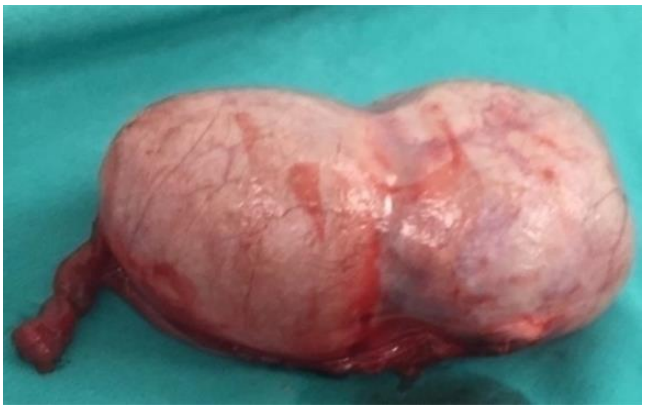

Figure 3. *Left Salpingo-Oophorectomy Specimen Measuring 13x7x7 cm.*

Discussion

The evaluation of individuals with mental motor retardation is much more challenging compared to other patients. Apart from the difficulty of clinical examination and the lack of understandable expressions, the families of these individuals also experience certain psychological effects. These families often experience

increased levels of stress and burnout syndrome due to the demanding physical and emotional aspects of caring for a disabled individual [3]. This, in turn, places a significant burden on the clinician, who often has no choice but to communicate with the family to obtain medical history.

The majority of adnexal masses in adolescents is ovarian cysts. Ovarian pathologies are observed in 2.6 out of 100,000 children, and malignant ovarian tumors constitute only 1% of all childhood cancers [4]. More than half of ovarian tumors in children originate from germ cells, with most being benign teratomas. Mucinous cystadenomas are rare but require pathological evaluation for diagnosis.

Symptoms and signs may not always be present, but when they do occur, the most common ones are nausea, vomiting, and bloating. Additionally, ovarian masses can cause torsion, leading to an acute abdominal presentation.

In the differential diagnosis of adnexal masses in adolescents, ovarian cysts, ovarian torsion, ovarian tumors, lymphoma, leukemia, and metastatic diseases should be considered.

There are very few reported cases of mucinous cystadenomas in childhood. In a study where Yazıcı et al. presented a mucinous cystadenoma in a 13-year-old girl, their review found that only 8 out of 623 ovarian masses in patients under 17 years of age were reported as mucinous cystadenomas [5].

The accepted approach for treatment is cystectomy, oophorectomy, or salpingo-oophorectomy if the mass appears benign [6]. Recurrence is rare in borderline cases. Furthermore, even in cases of malignant pathology, fertility-preserving surgery is often sufficient [7].

Conclusion

This presentation aims to increase clinical awareness for the recognition and management of such rare cases and similar cases. The limited expressiveness of individuals with mental motor retardation can complicate clinical diagnosis. Therefore, clinicians should not hesitate to use imaging methods. Moreover, the potential of large ovarian cysts to lead to an acute abdominal syndrome should not be underestimated, especially when patients present to the emergency department with acute abdominal pain. Abdominal ultrasound (USG) and computed tomography (CT) scans can detect large cysts, and the presence of giant ovarian cysts should always be kept in mind as they may require emergency surgical intervention.

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RADIOLOGICAL ANALYSIS OF BENIGN LESIONS MIMICKING RENAL TUMOURS

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ABSTRACT

Background

The incidence of incidental renal tumours is increasing with advances in radiological imaging modalities and their accessibility. However, imaging modalities do not provide sufficient information on histological subtype and are sometimes insufficient to differentiate between malignant and benign lesions. The aim of this study was to highlight the frequency of benign lesions in patients undergoing surgical treatment for renal masses and their radiological features, which are similar to those of renal tumours.

Methods

A total of 376 patients who underwent radical nephrectomy and nephron-sparing partial nephrectomy at Ankara City Hospital between March 2019 and April 2023 were retrospectively analysed. Pathology results of 228 patients who underwent nephrectomy with a prediagnosis of malignant renal mass were evaluated. The radiological features of benign lesions that were not found to be malignant in the differential diagnosis were evaluated.

Results

Of the 228 patients, 75 were female and 153 were male, with a mean age of 59 years. Radical nephrectomy was performed in 87.7% and partial nephrectomy in 12.3% of patients. 11.8% of the lesions were benign, 88.2% were malignant and 2.6% were in the unclassified group. Oncocytoma was the most common type of benign lesion.

Conclusion

Oncocytoma, fat-poor angiomyolipoma and xanthogranulomatous pyelonephritis are the most common radiologically confused lesions in the differential diagnosis of malignant renal masses [1]. There are radiological clues that can help in the differential diagnosis of fat-poor angiomyolipoma and xanthogranulomatous pyelonephritis. However, as oncocytomas arise from the same origin as chromophobe RCC, the histological and imaging findings are similar [2]. Oncocytomas are very difficult to identify preoperatively because they have non-specific imaging findings that are variable and overlap with renal cell carcinoma.

Keywords: *Renal masses, benign lesions, oncocytoma*

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EVALUATION OF PEOPLE WHO DIED OF PROSTATE CANCER IN TERMS OF RISK FACTORS IN EXCAVATIONS FROM THE ROMAN AGE

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Introduction

Ancient Rome was founded on the Palatinus hill on the Italian peninsula as a location today. While the traditional foundation date is 753 BC, it has been dated to the 8th century BC as a result of archaeological researchers and the emergence of city-state settlements [1] (Figure 1).

Figure 1. *The Antique Rome Empire Map (History Atlas, Karatay Publications: s.11)*

Figure 2. *Cancer Cell (URL-1)*

The achievements of the Romans in the socio-cultural field were mostly in architecture, military and public buildings. They did not attach importance to medical science. When they were sick, they asked for help from gods and spirits.

It is a complex disease that occurs as a result of uncontrolled proliferation of cancer cells in a tissue or organ. (Figure 2). Prostate cancer is among the top five deaths due to cancer.

Figure 3. *Bronze Statue of Imhotep (Wilkinson 2016: 112)*

It is known that Imhotep wrote the first written documents about cancer between 3500 and 2500 BC. Imhotep was the god of medicine in Ancient Egypt and was also an architect (Figure 3).

Risk Factors Of Prostate Cancer

It is known that age, family history, ethnicity and genetic predisposition are the leading risk factors for prostate cancer.

Prostate Cancer Cases Uncovered In Archaeological Excavations Of The Roman Empire Period

The table of people who died of prostate cancer in archaeological excavations from the Roman Empire is given below. In the archaeological site of West Amara, located in Sudan, it was determined that an individual aged 25-35 died of prostate cancer in bone scans. Again, in the table, it was understood that an individual between the ages of 40 and 50 died of prostate cancer in the Arzhan archaeological site, according to bone scans. Additionally, it was understood from the findings obtained from the grave of this individual that he was a Scythian king.

Table 1. *Cases of possible prostate cancer reported in the paleopathological literature (Minozzi, Lunardini, Caldarini, Caramella, Fornaciari, Catalano, Giuffra 2018: 2)*

Location	Archaeological site	Historical period	Specimen	Age, years
Laguardia, Alava, Spain	San Juan Ante Portam Latinam	3120±150 BC 3070±140 BC	Skeleton	Adult
Khartoum, Sudan	Amara West	1187–1064 BC	Skeleton	25–35
Siberia, Russia	Arzhan	700 BC	Skeleton	40–50
Egypt	Unknown	285–230 BC	Mummy	51–60
Peru	Huaca Las Ventanas Sican	900–1100 AD	Skeleton	20+
London, England	St. Bride's Lower Churchyard	1770–1849 AD	Skeleton	36–45

In this table, when the risk factors of people who died of prostate cancer obtained as a result of archaeological excavations from the Roman imperial period are examined, it is understood that these individuals died at an earlier age in terms of age. In terms of ethnicity, it has been seen that they do not come from a single ethnic origin and that prostate cancer cases are encountered all over the world.

Conclusion

We think that the risk factors of people who died due to prostate cancer during the Roman Empire are different from the risk factors of today.

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THE IMPORTANCE OF DIRECT LARYNGOSCOPY IN LARYNGEAL DISEASES

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ABSTRACT

Objective

This study highlights the critical role of direct laryngoscopy in identifying and treating laryngeal pathologies by analysing patients' medical data.

Methods

We retrospectively reviewed the records of patients who underwent direct laryngoscopy for laryngeal complaints between 2018 and 2023. We evaluated demographic data, lifestyle habits, clinical symptoms and histopathological results and compared them with hematologic inflammatory variables.

Results

Dysphonia was the main symptom in 210 patients. Most laryngeal lesions were in the glottic region, and saccular-cystic formations were the most common findings (56.7%). Significant associations existed between histopathologic results and factors such as gender, tobacco use and chronic diseases. Histologic types were closely associated with neoplastic progression. In particular, while 90 patients had benign features, low-grade dysplasia was the most important precancerous finding, and squamous cell carcinoma was the leading malignancy. Advanced age was correlated with malignant laryngeal tumours. There was no significant difference between the levels of inflammatory hematologic markers in benign, precancerous and malignant lesions.

Conclusions

More than half of the patients (57.14%) had precancerous and malignant laryngeal tumours. Our observations reaffirm the important role of direct laryngoscopy in laryngeal diagnosis and treatment.

Keywords: *Direct laryngoscopy, larynx, precancerous lesion, malignant, benign*

Introduction

Laryngeal disorders are frequently encountered in otolaryngology practice [1-3]. Chronic irritation, trauma, trauma due to intubation, infections, allergic diseases, reflux, smoking, alcohol, and occupational chemical exposures can lead to inflammation in the laryngeal mucosa. This can result in the development of benign, precancerous, or malignant lesions at various locations at the glottic level [2,4,5]. Factors such as reflux, allergic diseases, exposure to smoke, trauma from intubation, and voice misuse can lead to benign lesions at the glottic level, including nodules, polyps, cysts, and granulomas [6,7]. Lesions in the laryngeal area, whether benign or malignant, can impair voice and swallowing functions, thus diminishing the quality of life. Some treatments involve non-invasive modalities like voice therapy, voice hygiene, and medical treatments. However, for those unresponsive to these treatments, and in cases where the primary initial treatment is surgical, a critical first step in distinguishing between benign and malignant is the direct laryngoscopy (DL, micro laryngoscopy) performed under general anaesthesia [2,8,9]. This procedure can achieve both treatment and early diagnosis of potential premalignant or malignant lesions. Given this, it's crucial for otolaryngologists to fully understand the intricacies of the commonly performed DL procedure when intervening in lesions of the laryngeal and hypopharyngeal regions [10].

We aim to evaluate the clinical and histopathological data of patients undergoing direct laryngoscopy due to laryngeal lesions, highlighting its significance.

Methods

Patients

Patients who presented to the Otolaryngology Clinic of Sivas Cumhuriyet University Medical Faculty Hospital between 2018 and 2023 with laryngeal symptoms and were diagnosed with laryngeal lesions underwent the direct laryngoscopy (DL) procedure for diagnosis and treatment. Following the ethical approval (protocol number: 2023-06/25) granted by the Ethics Committee of Sivas Cumhuriyet University Medical Faculty on June 22, 2023, the medical, demographic data, habits (smoking, alcohol consumption), clinical information, and histopathological outcomes of these patients were retrospectively examined. Moreover, relationships were established between the average haemoglobin (Hb) values, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and platelet distribution width (PDW) values and the histopathological results of the laryngeal lesions. All medical data for the patients were sourced from file records. Patients of all ages and genders were included in the study. Direct laryngoscopy procedures performed due to foreign body aspiration were excluded from the study.

Statistical Analysis

The data obtained from our study will be analysed using the IBM SPSS 23 software package (Chicago, USA). Descriptive statistical parameters were examined. Descriptive statistics will be presented as counts and percentages for categorical variables and median values (minimum-maximum) for numerical variables. Nominal variables were assessed with the chi-square test analysis and the Likelihood Ratio. The Kruskal-Wallis H test was conducted to detect differences in patients' medical and demographic data, haematological parameters, and variables informing us about inflammation relative to the types of laryngeal lesions. A p-value of <0.05 will be considered statistically significant. For variables found to be statistically significant, the Mann-Whitney U test was used to identify which group they differed in. The Bonferroni correction was applied to reduce the margin of error at the significance level, and a p-value of 0.016 was adopted.

Results

Among the 210 patients included in the study, the mean age was 53.14 ±13.96 years (range: 10-83 years). The female-to-male ratio was 51:159, with mean ages of 48.39±11.38 and 55.06±14.36. The most common symptom for patients with laryngeal lesions was dysphonia at 87.62%, followed by dysphagia, sore throat, tickling and lump sensation in the throat, otalgia, odynophagia, and neck swelling. The predominant area of laryngeal lesions was the glottic region (81.9%, n=172), with others found in the supraglottic region (14.8%, n=31), subglottic (1%, n=2), transglottic (1%, n=2), and hypopharynx (1.4%, n=3). Pre-surgical outpatient endoscopic examination of the laryngeal region at 70° revealed the most frequent saccular and cystic lesions (nodules, polyps, Reinke's oedema, granulomatous, and cystic lesions at 56.7%, n=119). Both premalignant (leukoplakia) and malignant (vegetating and ulcerated lesions) were observed. The mean symptom duration for patients was 20.87 months (range: 1-240 months). Direct laryngoscopy (DL) for diagnosing laryngeal lesions was performed once for 157 patients, while 53 had it done multiple times, with one patient undergoing the procedure up to 6 times. A minority reported alcohol consumption; 128 (60.95%, F/M: 21/107) were smokers, and 82 (39.05%, F/M: 30/52) were non-smokers. Of the patients, 123 (58.57%, F/M: 30/93) had a history of chronic illnesses, while 87 (41.43%, F/M: 21/66) did not. The evaluation of patients after DL based on neoplasm types and medical, demographic data is presented in Table 1. Gender, smoking habits, and the presence of chronic illnesses were significant variables in terms of the obtained histopathological data ($p=0.001$, $p<0.001$, and $p=0.047$, respectively). The association between histopathological subtypes of laryngeal lesions and neoplasm type was significant ($p<0.001$). Overall, 90 patients were reported to have benign lesions (F/M: 31/59). Laryngeal nodules and polyps were the most common benign lesions (49/22). Low-grade dysplasia was the most frequent diagnosis among premalignant

lesions (26/66). Squamous cell carcinoma (SCC) was the most reported malignant lesion (52/54). Descriptive statistics of patients' medical, demographic data and haematological parameters, along with their average distribution results, are shown in Table 2. Additionally, as the average age increased among benign, premalignant, and malignant laryngeal lesions, age was observed as the most significant parameter in the diagnosis of malignancy (44y, 57y, and 64y, respectively, p<0.001). Among the haematological parameters, Hb and the NLR, PLR, and PDW averages, which increase with the degree of inflammation or severity of the disease, showed no significant difference among laryngeal benign-premalignant-malignant histopathologies. Although there was a slight increase towards malignancy when comparing NLR between benign and malignant laryngeal lesions, this was not statistically significant (a rise from 1.87 to 1.99, p=0.177). No meaningful relationship was observed with other PLR and PDW values (Table 3).

Table 1*. Evaluation of medical and demographic data of patients with laryngeal lesions and histopathological results of specimens obtained during direct laryngoscopy*

		Types of laryngeal histopathology			Test/p
		Benignn (%)	Premalignant (precancerous)	Malign	
Results of the laryngeal histopathological subtypes following direct laryngoscopy	Laryngeal nodule	**49(23,3)**	0 (0,0)	0 (0,0)	LR=451,975/ <0,001*
	Laryngeal polyp	**22 (10,5)**	0 (0,0)	0 (0,0)	
	Laryngeal cyst	9 (4,3)	0 (0,0)	0 (0,0)	
	Hemangioma	1 (0,5)	0 (0,0)	0 (0,0)	
	Chronic inflammation	9 (4,3)	0 (0,0)	0 (0,0)	
	Squamous epithelial hyperplasia	0 (0,0)	8 (3,8)	0 (0,0)	
	Verrucous hyperplasia	0 (0,0)	1 (0,5)	0 (0,0)	
	Pseudoepitheliomatous hyperplasia	0 (0,0)	8 (3,8)	0 (0,0)	
	SCC	0 (0,0)	0 (0,0)	**52(24,8)**	
	Verrucous carcinoma	0 (0,0)	0 (0,0)	2 (1,0)	
	Low-grade dysplasia	0 (0,0)	**26 (12,4)**	0 (0,0)	
	Moderate dysplasia	0 (0,0)	4 (1,9)	0 (0,0)	
	High-grade dysplasia	0 (0,0)	12 (5,7)	0 (0,0)	
	Carcinoma in situ	0 (0,0)	7 (3,3)	0 (0,0)	
Gender	Male	**59 (28,1)**	50 (23,8)	50(23,8)	X^2=13,417/ 0,001*
	Female	31 (14,8)	16 (7,6)	4 (1,9)	
Presence of smoking	Yes	37 (17,6)	43 (20,5)	48(22,9)	X^2=33,083/ <0,001*
	No	**53 (25,2)**	23 (11,0)	6 (2,9)	
Chronic disease	Present	44 (21,0)	44 (21,0)	35(16,7)	X^2=6,127/ 0,047*
	Absent	46 (21,9)	22 (10,4)	19 (9,0)	

**p<0,05*

Table 2. *An overview of the descriptive statistics and assessments of normality for the medical demographic and haematological parameters of the patients*

	K-S	**p**	**Min**	**Max**	$\bar{X}$	**S.S**	**Med.**	**Skewness**	**Kurtosis**
Age	,074	,008	10	83	53,44	13,96	54,00	-,163	-,595
Hb (g/dl)	,091	,000	9,5	18,3	15,05	1,64	15,30	-,743	,596
Neutrophil/Lymphocyte ratio	,216	,000	,66	15,02	2,32	1,82	1,88	4,313	22,946
Platelet/Lymphocyte ratio	,158	,000	11,86	370,83	116,52	52,64	104,24	2,003	5,820
PDW fL (10,1-16,1)	,176	,000	7,9	17,2	13,08	2,64	12,55	,061	-1,467

**Upon examining the measurements' descriptive statistics and regular distribution analyses, it was determined that they did not follow a normal distribution (p<0.05).*

Table 3. *Association between the histopathological results of laryngeal lesions, medical, demographic data, and haematological parameters.*

	Benign	Premalign	Malign	Test/p
Age	44,00 (36,75-56,25)	57,0 (45,0-65,0)	64,0 (55,0-70,25)	54,765/ **<0,001***
Hb (g/dl)	15,10 (13,77-16,00)	15,4 (14,27-16,30)	15,5 (14,57-16,5)	3,044/ ,218
Neutrophil/Lymphocyte ratio	1,87 (1,39-2,49)	1,78 (1,44-2,20)	1,99 (1,51-2,87)	3,466/ ,177
Platelet/ Lymphocyte ratio	109,82 (88,21-155,67)	95,64 (78,96-116,77)	103,93 (83,47-134,27)	5,910/ ,052
PDW fL (10,1-16,1)	13,35 (10,97-16,12)	11,95 (10,45-15,92)	12,2 (10,8-16,12)	1,455/ ,483

** p<0.05. Due to the measurements not originating from a normal distribution, the Kruskal-Wallis H test was conducted. Only the age variable yielded significant results (p<0.05), while the other measurements were observed to be statistically insignificant.*

Discussion

Direct laryngoscopy is an essential diagnostic procedure in the evaluation of laryngeal diseases. It allows for visualisation of the larynx and assessment of its mucosal extent, aiding in the staging and mapping of laryngeal cancers [11]. Also, it plays a crucial role in diagnosing and treating benign laryngeal lesions. It allows for a comprehensive evaluation of the larynx, identifying and characterising different lesions [12]. In addition, direct laryngoscopy can be used to sample and diagnose laryngeal neoplasms through biopsy [13]. It offers a high success rate in obtaining adequate surgical views, making it an effective tool for managing laryngeal lesions [9]. It is a standard technique for obtaining tissue samples and determining the nature of laryngeal lesions. Furthermore, direct laryngoscopy helps diagnose laryngeal hypersensitivity syndromes, such as chronic cough and vocal cord dysfunction [14]. It provides immediate feedback on laryngeal movement during respiration and phonation, enhancing treatment planning and diagnostic accuracy. Direct laryngoscopy is crucial in diagnosing and managing laryngeal diseases, allowing for accurate assessment, biopsy, and treatment planning [15,16].

Lesions of the laryngeal epithelium predominantly arise from the glottis. Before ascertaining the potential for malignant transformation of these laryngeal mucosal abnormalities, a histological assessment through biopsy is imperative. High-grade dysplasia necessitates heightened vigilance owing to its propensity for malignancy, and post-treatment surveillance is crucial for both dysplasia and carcinoma in situ, given the potential for disease recurrence or progression [17]. Smoking has been shown to significantly impact laryngeal lesions, with a higher prevalence of laryngeal tumours in smokers than those with benign or precancerous lesions [18]. Gender also plays a role, with specific benign mucosal lesions strongly associated with gender, such as pseudocysts and bilateral midfold lesions, occurring predominantly in young females. In contrast, polyps, contact lesions, leukoplakia, and sulcus are found chiefly in men [19].

Age is another factor, as older age is associated with more significant numbers of CD4+ T cells in the laryngeal mucosa, both in the epithelium and lamina propria [20]. These findings suggest that smoking, gender, and age can all influence the development and characteristics of laryngeal lesions. Chronic diseases such as lupus, rheumatoid arthritis, and amyloidosis can lead to laryngeal lesions. Additionally, studies suggest a potential association between depression and diabetes and increased head and neck cancer risk. Considering these findings, chronic conditions, including persistent infections and irritations, may play a significant role in developing laryngeal lesions [21-23]. Cikojević et al. examined the impact of smoking on laryngeal lesions, noting that 82.92% of their patients had a smoking history. When considering benign, precancerous, and malignant rates, they reported 72.13%, 81.48%, and 97.17%, respectively. They determined smoking increased in patients with malignant laryngeal lesions[20]. In our study, the smoking rate among patients with laryngeal lesions was 61%, with an observed increase from benign to malignant lesions (28.9% vs. 37.5%). Additionally, we

observed a higher risk of developing precancerous and malignant diseases in patients with chronic conditions, with no significant difference in benign lesions. Ince et al. reported that 82.1% (333) of patients undergoing DL were male, and 17.9% were female[24]. Similarly, in our study, a higher proportion of males was noted (M/F: 75.7%/24.3%). Özkırış et al. reported that out of 126 patients who underwent DL, 39 (30.9%) were female, and 87 (69.1%) were male. Among the 126 patients, 87 had laryngeal polyps, 24 had laryngeal nodules, 12 had SCC, two developed granulomas after intubation, and 1 had laryngeal tuberculosis[1]. The most commonly observed symptoms were dysphonia (88%), sore throat (35%), dyspnea (18%), and neck swelling (8%). Benign laryngeal lesions (nodule, polyp, Reinke's oedema, trauma, or intubation granuloma) are commonly observed in patients with voice hoarseness. Malignant tumours are rarer. They may arise due to functional trauma to the vocal cords, chronic inflammation, or a combination of both. Conservative treatments like voice therapy, smoking cessation, or antireflux have been reported to yield positive outcomes in benign laryngeal lesions, with surgery required when these interventions fail. DL under general anaesthesia is the most frequently applied surgical technique [2]. In a DL procedure performed by Cukic on 318 patients with benign laryngeal pathologies, the most common diagnosis was laryngeal polyp (n=159), followed by Reinke's oedema in 145 patients, with nodule (n=5), cyst (5), and granuloma (3) being less frequent[2]. Precancerous laryngeal lesions are described as a process that can be both hyperplastic and dysplastic of epithelial lesions; they may or may not progress to invasive carcinoma. With advancements in diagnostics, treatment, and surgical interventions in laryngology, all kinds of laryngeal pathologies can now be confidently and swiftly diagnosed. Avila et al. identified premalignant lesions in 59 (10.57%) of 558 patients they examined with DL for precancerous laryngeal lesions, noting a male predominance (69.9%)[4]. In our study, the incidence of benign lesions was 42.9% (nodules at 23.3% and polyps at 10.5%), with 31.4% having precancerous lesions and 25.8% having malignant ones. The most common symptom we identified was dysphonia (87.62%). The definitive diagnosis of many precancerous lesions has been reported to be achieved through DL after lesions were initially identified during endoscopic examination in clinics[4]. During the clinic visits of 210 patients, 119 were diagnosed with benign lesions based on endoscopic review; this number changed upon histopathological examination after DL (90 patients with benign lesions, 120 with precancerous and malignant ones). Thus, it has been reported that the most reliable technique for laryngeal lesions remains DL and suspension laryngoscopy where appropriate. Additionally, about 90% of laryngeal malignancies originate from precancerous lesions. Early diagnosis and treatment of precancerous lesions with DL prevent their transformation into invasive carcinomas and future indications for more radical surgeries[5].

Research has reported that inflammation, a significant component of tumour progression, is associated with poor prognoses of various malignancies and precancerous conditions attributed to mutations induced in oncogenes. An elevated neutrophil level, observed during inflammatory states, has been implicated in the angiogenesis phase, in the progression and metastasis of malignant conditions. Emphasis has been placed on the potential role of platelets in modulating adhesion molecules, augmenting angiogenesis, and fostering an increase in metastasis. Studies have proposed inflammation markers such as NLR, PLR, and PDW as prognostic indicators in various cancers [25-29]. The NLR, PLR and PDW have been studied in laryngeal lesions. Bulgurcu et al. found that NLR and PLR values significantly differed between patients with precancerous laryngeal lesions or laryngeal squamous cell carcinoma [25]. Kara et al. observed that PLR was considerably higher in patients with laryngeal squamous cell carcinoma, and both PLR and RDW were more elevated in patients who did not survive [26]. Pujani et al. reported that RDW, NLR, and PLR significantly differed between psoriasis patients and healthy controls, and these markers correlated with the severity of psoriasis [27]. Lu et al. found that NLR and PLR were associated with clinicopathological features and overall survival in nasopharyngeal carcinoma patients [28]. Ari et al. compared NLR and PLR in patients with thyroiditis and papillary cancer and found that both markers were higher than healthy controls [29]. In our evaluation of patients' inflammatory parameters and Hb levels, we found no anaemic individuals in any group. While benign laryngeal lesions exhibited lower average NLR than malignant lesions, we identified no significant differences among the groups when including PLR and PDW parameters. We observed that the mean age was notably higher in patients with malignant lesions, a statistically significant difference ($p<0.001$).

Conclusion

-Through DL, it's feasible to distinguish between benign, precancerous, and malignant laryngeal lesions. Furthermore, it is a reliable technique that aids in treating precancerous lesions and early-stage cancers before they advance to invasive carcinomas that might necessitate radical surgeries.

-This study has reaffirmed that numerous benign lesions have the potential to become precancerous. As observed in previous research, we identified a male predominance in the overall occurrence of laryngeal lesions, specifically within the malignant/precancerous group.

-Moreover, in cases of recurrence and in patients where new lesions developed on top of pre-existing ones, we observed that the DL procedure can be repeatedly executed to conclusively diagnose laryngeal lesions and carry out curative treatments until resolution.

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INVESTIGATION OF THE EFFECTS OF MELATONIN ON BRAIN TISSUE IN EAC TUMOUR MODEL BY IMMUNOSTAINING VIA TNF-α, NF-kB, IL-6

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ABSTRACT

Melatonin is the most important product of the pineal gland (pineal gland) and its secretion shows a circadian rhythm. The effect of various antioxidants on tumour models has been the subject of many studies. In this study, we aimed to demonstrate the antitumoural effect of different doses of melatonin on Tnf-α, NF-kB and IL-6 by immunohistochemical method in solid EAC tumour model. EAC cells were injected subcutaneously into the experimental groups. 50 and 100 mg/kg melatonin were injected intraperitoneally into solid tumour animals for 14 days. Histological evaluation showed that tissue integrity was disrupted in the control (tumour) group. As a result of the comparison of the melatonin-50-treated groups with the other groups, we determined that the increase of NF-kB expression in the cortex region was statistically significant ($p = 0.05$). However, no statistically significant difference was found between the groups with the variables (Tnf-α, NF-kB and IL-6). In our study, it was shown that melatonin may have an anti-tumour effect on the development of solid tumours formed by EAC cells.

Keywords *Melatonin, Ehrlich ascites carcinoma, Tnf-α, NF-kB, IL-6*

Introduction

Ehrlich ascites tumour (EAT), one of the experimental animal tumours that has been the subject of many studies, first appeared as a spontaneous mammary adenocarcinoma in a female mouse [1] and was transformed into an experimental tumour by Ehrlich & Apolant (1905) by transplanting tumour pieces under the skin from mouse to mouse. In 1932, Loewenthal and Jahn succeeded in obtaining a liquid form of this tumour growing in the peritoneum of mice, and the tumour was named Ehrlich Ascites Tumour because acid fluid was formed in the peritoneum as well as cells [2]. EAT is an undifferentiated tumour and with the availability of liquid and solid forms of EAT, liquid and solid tumours have been used extensively in studies. The reason for the intensive use is that the liquid form is in the form of a suspension containing free tumour cells, as a result of which the desired number of cells can be transplanted into another animal. Therefore, both the number of transplanted tumour cells and the size of the tumour can be easily determined by conventional simple counting methods [3].

Melatonin is a small, lipophilic molecule and, as the most important product of the pineal gland (pineal gland), its secretion shows a circadian rhythm. The release of melatonin, which is sensitive to ambient lighting, is 7-10 times higher at night than during the day. Melatonin is a powerful antioxidant [4] and is lipophilic [5]. In this way, all organelles of the cell and the cell nucleus can be reached and the blood-brain barrier can be crossed. Protective properties against tissue damage have been proven [6]. The pineal gland is known to inhibit tumour growth. The anti-cancer effect of the pineal gland is largely due to Melatonin. Molis et al. showed that melatonin dramatically decreased the expression of estrogen receptor in human breast cancer cells [7]. In addition, the effect of melatonin on neuron damage and spinal cord injury has been shown by various studies [8-10]. In addition, it has also been reported that melatonin may act as a proteasome inhibitor. In this direction, there are many studies showing that melatonin inhibits NF-κB activity [11, 12].

In our study, we aimed to immunohistochemically determine the Tnf-α, NF-kB and IL-6 expression intensity of melatonin administered at doses of 50, 100 mg/kg/day in the brain tissue of Ehrlich Ascites Carcinoma (EAC) solid tumour model developed in Balb/c mice originated from mouse mammary adenocarcinoma.

Method

The study was carried out with the permission and decision of Erciyes University Experimental Animals Ethics Committee numbered 23/181. For our study, 40 male mice of Balb/C strain 8-10 weeks old and 25-30 g were obtained from ERU Experimental Research Application and Research Centre (DEKAM). Mice were housed in automatically air-conditioned rooms with a constant temperature of 21 C and 12 hours light/dark periods. Four groups of 10 mice in each group were formed as follows;

Group 1: Control (-) = Mice without cancer and normal diet were administered saline subcutaneously (s.c.) for 15 days.

Group 2: Control (+) (tumour) = Mice were injected with 0.1 mL ascites fluid containing $1x10^6$ EAT cells s.c. from the nape area on day 0. Starting from day 0, 0.5 mL of saline was injected s.c. to the mice for 15 days.

Group 3: (Tumour + 50 mg Melatonin) = Mice were administered 0.1 mL ascites fluid containing $1x10^6$ EAT cells s.c. from the nape area on day 0. Starting from day 0, 50 mg/kg/day Melatonin was injected intraperitoneally for 15 days.

Group 4: (Tumour + 100 mg Melatonin) = Mice were administered 0.1 mL ascites fluid containing $1x10^6$ EAT cells s.c. from the nape area on the 0th day. Starting from day 0, 100 mg/kg/day Melatonin was injected intraperitoneally for 15 days.

After all procedures, mice in the groups were sacrificed on day 16 under general anaesthesia with ketamine-xylosine (60 mg/kg, 10 mg/kg).

Creation of stock mice

In order to create a solid tumour for EAT, a stock model was first created. In order to create stock mice, cells stored at -80 °C were thawed at room temperature when they were to be used and injected intraperitoneally into the stock mouse at the junction of the left hind leg and abdomen as 0.1 cc. The whole procedure was performed according to the study by Yilmaz et al. [13]. The cell counting procedure and follow-up of tumour development were also performed according to this study.

Histological and Immunohistochemical Analysis

After the brain tissues were removed, they were placed in formaldehyde and fixed for two days parallel to the tissue size, and after fixation, the tissues were kept under running water overnight [14]. The 5 µm thick sections taken from the paraffin blocks were stained with Haematoxylin-Eosin (H-E) stain and histopathological changes (in terms of cell shape, morphology, number, oedema etc.) were determined under light microscope (Olympus BX53). For immunohistochemical examination; brain tissues in paraffin blocks were cut into 5 µm thick deparaffinised sections and the procedure in the study by Doganyigit et al. [14]. Tnf-α (Elabscience, E-AB-22159, 1:100), NF-kB (Bioassay, 1:50) and IL-6 (Elabscience, 1:200) primary antibodies were applied to brain tissue. Sections were examined by Olympus BX53 light microscope and immunoreactivity levels were evaluated by Image J programme.

Statistical Analysis

In our study, data analysis was performed in IBM SPPS 15.0 ((SPSS Inc., Chicago, IL, USA) package program. Kruskal-Wallis test was applied for comparison between independent groups and Mann-Whitney U test was applied for descriptive statistics of variables between groups. $p < 0.05$ was considered statistically significant.

Results and Disscussion

Histological Results

When the haemotoxylin and eosin stained brain sections were examined under light microscope (Fig. 1), tissue integrity could not be preserved in the Ehrlich ascites carcinoma control (tumour) group. It was also observed that vascularisation increased in this group (Fig 1).

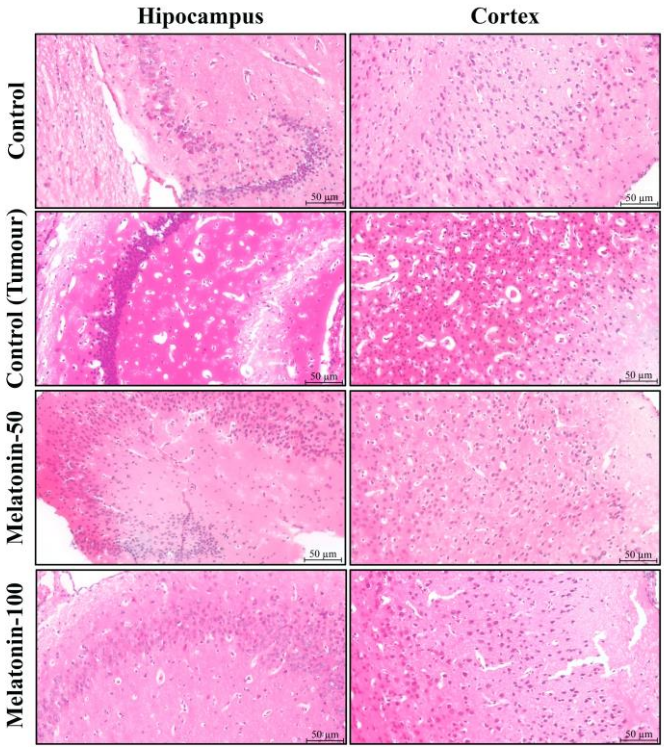

Figure 1. *Hematoxylin-eosin staining images of brain sections. Magnification: x20, bar= 50 μm*

Immunohistochemical Analysis Results

In the melatonin-50 group, Tnf-a expression was found to be increased and expressed in the neuron cell body, especially in the cortex. No significant difference was found between the groups (Fig. 2A, Fig. 2B, Fig. 3A, Fig. 3B). Furthermore, when inter-regional variables (Tnf-a, NF-kB and IL-6) were evaluated in all groups, we determined that NF-kB expression was intensely expressed in the cortex region (Fig. 3B) and there was a statistically significant difference (p=0.50). However, no statistically significant difference was found between the groups for the NF-kB variable. It was observed that NF-kB was expressed in both hippocampus and cortex in the control (tumour) group and its expression was increased in the Melatonin-50 group (Fig. 2B). Intense expression of IL-6 in the cortex is observed in the Melatonin-100 group (Fig. 3A, Fig. 3B).

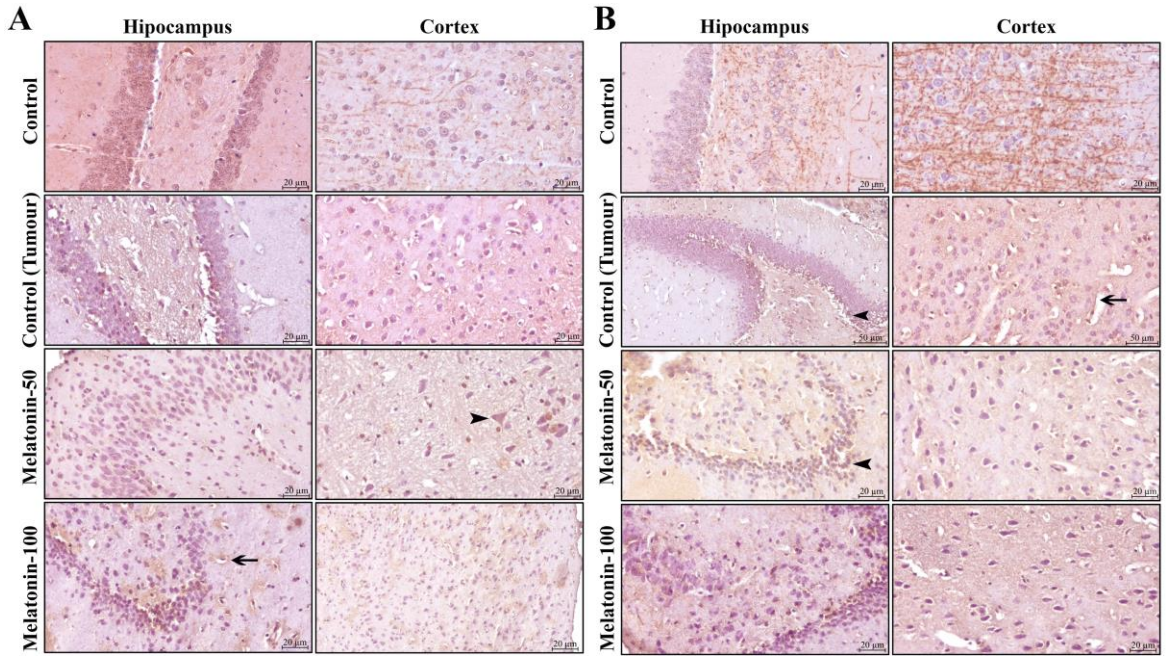

Figure 2. A: *Tnf-α immunohistochemical images in brain tissue.* ***B:*** *NF-kB immunohistochemical staining images in brain tissue. Arrowhead: Expression in the neuron cell body. Arrow: Expression around the vessel. Magnification: x20, bar= 50 μm*

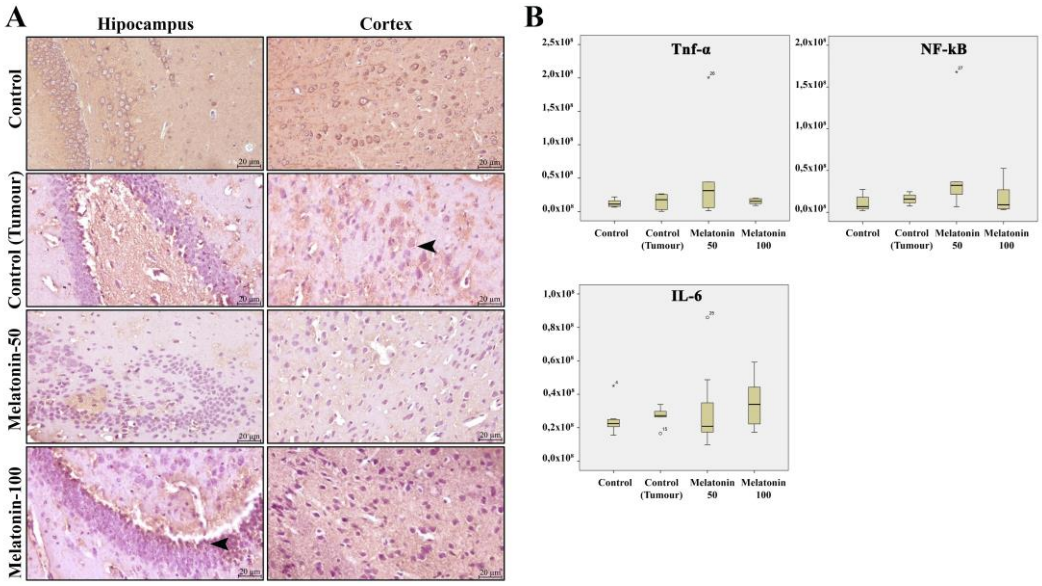

Figure 3. A: *IL-6 immunohistochemical images in brain tissue.* ***B:*** *Statistical analysis results for Tnf-α, NF-kB, and IL-6. Arrowhead: Expression in the neuron cell body. Magnification: x20, bar= 50 μm.*

Discussion

Cancer is a major problem of our global age and many studies are still being carried out for its treatment. One of the methods used in cancer studies; Ehrlich's acid carcinoma is a tumour model that can be used to study cancer both qualitatively and quantitatively [15]. For cancer treatment, studies are also carried out on various antioxidative reagents [16, 17]. Melatonin, which mainly regulates the circadian rhythm, has many studies showing its antiapoptotic effect [18-20]. In this study, we established a tumour cell model of EAC in an experimental mouse model and determined the antioxidant property of melatonin on tumour cells via Tnf-α, NF-kB and IL-6. In our study, in accordance with the literature [13], we found that the integrity of brain tissues was not preserved in the tumour-formed experimental group.

NF- kB signalling is a central regulator of inflammatory cytokines [21]. It has been reported that proinflammatory cytokines stimulate IL-6 and Tnf-α expression and thus activate the NF-kB pathway [22]. In our study, Tnf-α expression was increased throughout the brain tissue of the control (tumour) group, but no significant difference was found between the regions (p=0.401). In brain tissue, Tnf-α expression increased in the Melatonin-50 group, whereas it decreased in the Melatonin-100 group. However, there was no significant difference in the variables between regions and groups.

When inter-regional variables (Tnf-α, NF-kB and IL-6) were evaluated, we determined that NF-kB expression was intensely expressed in the cortex region and there was a statistically significant difference (p=0.50). However, no statistically significant difference was found in terms of variables in all groups. Existing studies have found that inhibition of NF-κB in malignancies significantly reduces tumour initiation and development [23]. Consistent with our results, NF-κB expression decreased in the Melatonin-100 group. We also found that NF-kB and IL-6 expression increased in Melatonin-50 groups, while their expression decreased in Melatonin-100 group. We have thought that 0,50 mg/kg/day melatonin dose may not be sufficient for adequate cytosine release in the EAC tumour model.

Conclusion

In conclusion, melatonin seems to play a dual role in NF-kB expression depending on the cell type and site of expression. In the EAC tumour model, the role of melatonin on Tnf-α, NF-kB and IL-6 was evaluated over groups and regions. Further studies are needed to better elucidate the effect of melatonin on NF-kB and various cytokines, as this transcription factor may act on different signalling pathways that are essential for the tumour model. Such studies may reveal the effect of activation or inhibition of various cytokines and NF-kB depending on the tissue type as well as the tumour model.

Acknowledgments

The study was carried out with the permission and decision of Erciyes University Experimental Animals Ethics Committee numbered 23/181.

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RARE ENDOMETRIAL TUMOR WITH MALIGNANT POTENTIAL: PAPILLARY ADENOFIBROMA

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ABSTRACT

Introduction

Uterine adenofibroma is a rare, benign neoplasm classified as a mixed epithelial and mesenchymal tumor group. It typically affects the endometrium, but can also develop in the cervix or in an extrauterine location. Preoperative diagnosis of this tumor is often difficult (1,2). Although the lesions appear benign histologically, local invasion and transformation into adenocarcinoma and numerous recurrences have been reported (1).

Case

Our case is a 39-year-old virgo patient. Hysteroscopy was previously performed after hymenotomy due to irregular menstruation. The endometrial biopsy result was reported as endometrial polyp. Due to the persistence of her complaints and the addition of foul-smelling discharge, the patient returned to our polyclinic and during the pelvic examination, a biopsy was taken from the lesion covering the cervix. The pathology result was reported as endometrial papillary adenofibroma. First of all, hysteroscopy was performed. However, hysteroscopic resection could not be performed due to the hard, adherent tumor tissue that could not be separated from the myometrial tissue by hysteroscopy, and the patient underwent hysterectomy with her consent.

Discussion

Mixed mesodermal tumors constitute a rare group of uterine lesions. It contains epithelial and mesenchymal cells together, and the clinical and pathological features of the lesions are not clearly defined. Histological differential diagnosis ranges from benign endometrial polyps to malignant carcinosarcoma and endometrial stromal sarcoma(1).

Since patients diagnosed with adenofibroma are mostly in the perimenopausal period, the definitive treatment is hysterectomy, because it may recur if the neoplasm is not completely removed by curetting or excising (3,4). Additionally, cases have been reported showing that adenofibromas can develop into adenosarcomas (3).

In this case, we performed a hysterectomy in a patient under the age of 40 who had not been pregnant due to local myometrial invasion caused by a benign tumor. Our aim in this case report is to share our selection of a rare case and discuss it in the light of the literature.

Keywords: *Mixed mesodermal tumor, adenofibroma, adenosarcoma of the uterus*

Introduction

Uterine adenofibroma was first described by Ober in 1959 as a mixed mesodermal benign tumor form with epithelial and stromal components [1].

Uterine cysts can be cystic degeneration of uterine leiomyoma, cystic adenomyosis, congenital uterine cysts and echinococcal cysts [5]. Uterine adenofibroma is an extremely rare mixed, benign biphasic neoplasm of müllerian origin, classified in the epithelial and mesenchymal tumor group [6,7]. Consists of glandular and fibrous tissues [8,9].

Tumors may consist of papillary prominences, clefts, and cysts into which papillae protrude[4,10]. The epithelial component of the tumors is of stratified squamous and mucinous and non-mucinous columnar types. The stroma may consist of small fibroblasts resembling ovarian and breast adenofibroma(4). These papillae may be occupied by adenocarcinoma in a focally infiltrating manner. Only one of 15 cases of uterine adenofibroma reported in the literature was focally involved by adenocarcinoma [10].

These tumors tend to occur in the pre-postmenopausal period and with abnormal genital bleeding [1,11]. Typically affects the endometrium but can also occur in the cervix or somewhere outside the uterus [1,8]. Cervical adenofibroma is a rare 10% of uterine adenofibromas [1]. Preoperative diagnosis of this tumor is often difficult. It can be seen as a cervical mass containing multiple combined cysts on transvaginal ultrasound. These lesions appear clinically and histologically benign, but their differential diagnosis from malignant lesions of the uterus, especially adenosarcoma, which may be suggestive of adenofibroma, allows appropriate counseling of patients [2,7,12].

Case

Our case is a 39-year-old virgo patient. He has a medical history of Neuromyelitis optica. She had previously applied to our center in 2017 due to irregular menstruation. When there was no response to medical treatment, hymenotomy was performed with the patient's consent and endometrial sampling was performed and an endometrial polyp was detected. When office hysteroscopy (HS) was performed, fibrotic bands were observed in the endometrial cavity. Asherman syndrome was considered. Fibrotic bands were dissected. It was observed that the patient's complaint of irregular menstruation continued despite the operation. In 2022, the patient applied to our clinic again with persistent foul-smelling vaginal discharge and secondary amenorrhea. On examination with a speculum, an amorphous mass was observed covering the cervical os, and a biopsy was taken from this structure (Figure 1). The pathology result showed a papillary adenofibroma protruding into the vagina, originating in the endometrium. A literature search was conducted on this rare report. A contrast-enhanced pelvic MRI was performed. "It is a light and heterogeneous type of contrast that fills the endometrial cavity almost completely, extends towards the vaginal cuff through the cervix-uteri, and expands the vaginal cuff to a large extent, does not show any signs of erosion or invasion, has a heterogeneous appearance, and occasionally contains septations and solid-like components." There is a mass lesion showing involvement. It is thought that it may be significant in terms of endometrial malignancy. Tissue diagnosis is recommended. "No lymph nodes were detected." reported as.

Operative HS was recommended to the patient again, but it was explained that this tumor could recur and even turn into adenocarcinoma, although rare. Hysterectomy was offered as an option to the patient, who was not married, did not want to become pregnant, and whose examinations showed that she was in the perimenopausal period.

Hormone and tumor marker results; FSH:21, LH: 9,96, E2: 51,7, PRL: 28,1, TSH: 3,75, CA 15-3: 13,6, CA 19-9: 13,3, CA 125: 37,9, CEA: 0,77 recorded as.

On 14.11.2022, under general anesthesia, cystic lesions in the vagina were first removed with an ovarian clamp (Figures 2-3). The cavity was entered with operative HS. During the observation, the inside of the cavity was observed to have an irregular structure, and the fundus and tubal ostia could not be evaluated. An attempt was made to correct the cavity with cautery and a sharp curette, but since the extremely adherent and hard tissue could not be removed sufficiently, HS was terminated and laparotomy was performed. During the observation, the uterus was observed to be smaller than normal in size, multiple cystic structures were observed in the left ovary, Douglas, bilateral tubas, right ovary and bilateral paracolic areas were observed to be normal. A sagittal incision was made in the uterus and the uterine cavity was entered. The lesions in the endometrium could not be separated from the myometrium, the tissue was very hard and adherent. Since the patient was discussed and her consent was obtained before the surgery, the decision for hysterectomy was made.

Pathology result: "The endometrium was gray-brown in irregular appearance and contained papillary areas in some places. Reported as "papillary adenofibroma, endometrium".

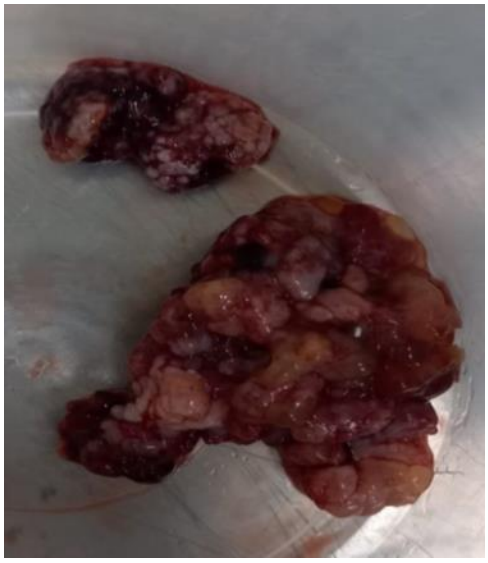

Figure 1. *Papillary adenofibroma (biopsy sample taken during speculum examination)*

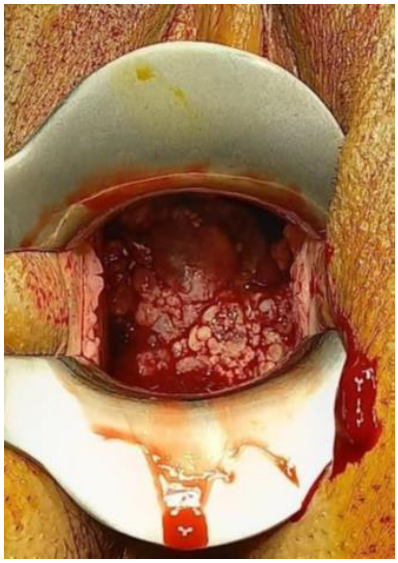

Figure 2. *Before HS is done*

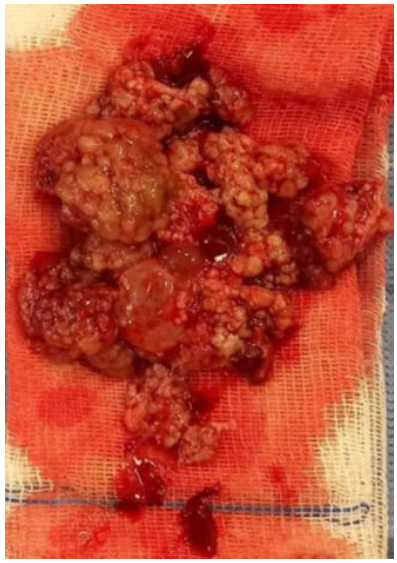

Figure 3. *The mass removed after HS was performed*

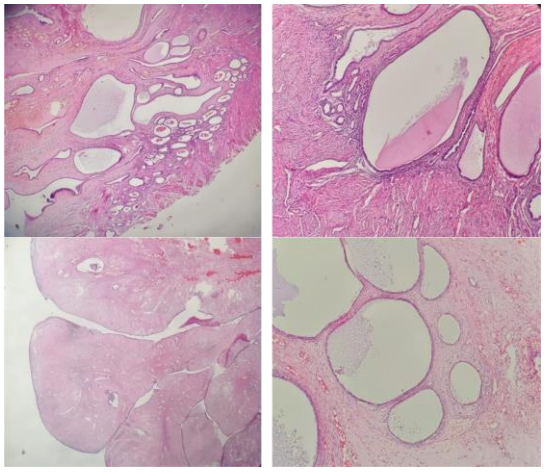

Figure 4. *Microscopy images*

Discussion

Mixed mesodermal tumors are a rare group of uterine lesions that also contain epithelial and mesenchymal cell components. Defining the clinical and pathological features of the lesions is still not clearly established. They are divided into two groups: benign and malignant lesions. It is common in the pre-postmenopausal period and patients present with vaginal bleeding(4). Our case was in the premenopausal period and had foul-smelling and occasionally bloody discharge.

While adenofibroma and adenomyoma are in the benign group, adenosarcoma, carcinosarcoma and carcinofibroma are in the malignant group. Although adenofibromas often arise from the endometrium, they may also arise from the cervix at a rate of approximately 10% [13]. They usually occur as polypoid masses They generally have cystic spaces surrounded by hard tissue and broad-based villous and spongy cut surfaces. Adenofibromas can occur in women of all ages, most commonly peri- or postmenopausal women [2]. Abnormal vaginal bleeding is the most common complaint. Some patients with a previous history of polypectomy or tamoxifen treatment have been reported in the literature [14]. Our case also had a history of polypectomy. Although the mass originated from the endometrium, it had spread outside the cervix. It was hard and cystic.

It is important to clinically differentiate adenofibromas from adenosarcomas [2]. Clement and Scully suggested that adenosarcoma should be diagnosed if one or more of the criteria of significant stromal cellularity, stromal HPF count ≥2, and more than mild stromal nuclear atypia are present [13].

On the other hand, Zaloudek et al. they suggested that adenosarcomas should be diagnosed when there are more than 4 cell mitoses per 10 HPF [15]. The frequency of mitotic figures in the stroma is the most important

factor in distinguishing adenofibroma from adenosarcoma. Adenofibromas had fewer than four mitotic figures per 10 HPF in the most active areas; Four or more have been seen in adenosarcomas. Malignant heterologous mesenchymal elements and marked atypia in stromal cells, which are only found in adenosarcomas, are histological features. The only morphological feature associated with the aggressive behavior of adenosarcoma is deep myometrial invasion. Adenofibroma and adenosarcoma belong to the family of mixed mesodermal tumor [15].

The treatment of choice for adenofibroma is hysterectomy, as patients are mostly in the perimenopausal period because the neoplasm can recur if not completely curetted or excised [3,4]. Additionally, there is a report that adenofibromas can develop into adenosarcomas [3].

When hysterectomy specimens were examined, the presence of endometrial polypoid tumors that invaded the deep myometrium was found to be associated with increased recurrence [13]. On histological examination, a mixed structure can be seen consisting of benign endometrial type glands and a moderately cellular stroma containing fibroblasts with benign nuclear features and very low HPF (less than one mitotic figure in 10 high power fields) [16]. It can infiltrate the myometrium almost to the serosa and growth into the lumens of large myometrial veins can be observed. During follow-up of patients, it has been observed that rarely, typical uterine adenofibromas may exhibit invasive features and have malignant potential [16).

In this case, we performed a hysterectomy in a patient under the age of 40 who had not been pregnant due to local myometrial invasion caused by a benign tumor. Our aim in this case report was to share our selection of a rare case and discuss it in the light of the literature.

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DIAGNOSIS AND SURGICAL MANAGEMENT OF SYNCHRONOUS COLORECTAL CANCERS: A CASE PRESENTATION AND DISCUSSION

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ABSTRACT

Cancer is a leading cause of global and national mortality, second to cardiovascular diseases. Colorectal cancer ranks third in both incidence and cancer-related mortality. Synchronous multiple colorectal cancers are rare, occurring in 1.1% to 8.1% of cases. They simultaneously involve numerous primary colorectal tumors, often sharing genetic or environmental factors. Risk factors include hereditary syndromes, inflammatory bowel diseases, and lifestyle choices. Early detection of synchronous cancers is crucial, as overlooking the second tumor can lead to advanced-stage disease. This case presentation underscores the importance of prompt diagnosis and timely surgical intervention.

Introduction

Cancer ranks among the most common causes of mortality worldwide and in our country, following cardiovascular diseases [1].

Colorectal cancers are the third most common cancer type in both men and women. They also rank as the third leading cause of cancer-related deaths. Synchronous multiple colorectal cancers are a rare clinical condition compared to solitary tumors, with an incidence ranging from 1.1% to 8.1% among all colorectal cancers [2]. Cunliffe et al. defined synchronous colorectal cancers as the presence of multiple primary colorectal cancers detected simultaneously, with a minimum distance of 5 cm between the two primary tumors, and the second primary tumor diagnosed within six months after the detection of the first primary tumor [3]. Synchronous colorectal cancers develop on a shared etiological background, which can be either genetic or environmental. Studies in the field of molecular colorectal carcinogenesis have shown that chromosomal instability, microsatellite instability (MSI), and gene methylation have been detected in many predisposing factors for synchronous cancers [4]. MSI rates have been found to be higher in synchronous colorectal cancers, especially when compared to solitary cases [5]. Predisposing conditions include hereditary colorectal cancer syndromes (FAP, Lynch syndrome), inflammatory bowel diseases, and serrated polyposis. In these predisposing conditions, the incidence of synchronous colorectal cancer can rise to 10-20% [6]. Ariba et al. suggested that environmental factors are more influential than genetic factors in the development of synchronous colorectal cancers, while Pajares stated that familial etiopathogenic factors play a more significant role in the development of metachronous colorectal cancers, with personal factors being more relevant to synchronous cases [4], [7], [8]. Personal factors that contribute to tumorigenesis, particularly through DNA methylation, include alcohol consumption, smoking, and a body mass index greater than 21 [8], [9]. Detecting synchronous colorectal cancers is crucial; if overlooked, the second tumor can present as an advanced-stage metachronous cancer, while its preoperative detection can influence the extent and type of surgical resection. In this context, we aim to present a case of a synchronous colon tumor that was admitted to our clinic and underwent emergency surgery.

Case Report

A 66-year-old male patient presented to our clinic with a history of diarrhea and indigestion, persisting for approximately six months. Physical examination of the patient revealed no abnormalities, and there was no palpable mass during rectal examination. Laboratory findings for the patient were as follows: Hgb: 11.4 g/dl, Hct:

33.5, albumin: 2.99 g/dl, Na: 135 mmol/L, K: 3.06 mmol/L, and Cl: 99 mmol/L. Other biochemical values were within normal limits. The patient was scheduled for elective endoscopy and colonoscopy, and bowel preparation was initiated. On the second day of bowel preparation, the patient presented with abdominal pain and distension to the emergency department. Further investigations revealed a colonic level air-fluid level on the abdominal X-ray, leading to the diagnosis of ileus. Bowel preparation was halted. Although the patient had gas passage, there was no bowel movement. Rectosigmoidoscopy identified two fragile, ulcerative masses in the sigmoid colon that narrowed the lumen and prevented the passage of the colonoscope. The patient underwent emergency surgery. Exploration revealed two tumoral masses in the left colon and sigmoid colon. There was slight dilatation in the colon segments proximal to the tumors. No other pathology was detected during additional exploration. The patient underwent extended left hemicolectomy with an end-to-end anastomosis. Following the surgery, the patient was admitted to the ward without any complications. Pathological examination of the specimens revealed grade 2 moderately differentiated adenocarcinoma in the sigmoid colon lesion and grade 1 well-differentiated adenocarcinoma in the left colon lesion. All 21 removed lymph nodes were determined to be reactive lymph node hyperplasia. The patient was referred to the medical oncology clinic based on the pathology results. At the 1-month follow-up, the patient had no active complaints.

Discussion

Detecting synchronous colorectal cancers is important in terms of prognosis and surgical treatment decisions [10]. It is noted that synchronous tumors have a worse prognosis compared to solitary tumors, making timely detection crucial to prevent further deterioration of the prognosis [9]. The most important factor influencing surgical technique, resection extent, and, consequently, postoperative quality of life for synchronous colorectal cancers is the localization of the tumors. Some studies suggest a higher prevalence of synchronous colorectal cancers in the right colon, while others indicate a more frequent occurrence in the left colon or different segments [11], [12]. Surgical treatment varies, with some advocating extensive resection for synchronous colorectal cancers to prevent potential recurrent surgeries due to missed tumors, while others argue that multiple colon resections are more physiologic [13]. Recent studies indicate that for solitary synchronous colorectal cancers, multiple colon resections yield similar results to extensive resections in terms of postoperative complications, length of hospital stay, and survival [14][15]. You et al. reported that patients who underwent multiple segmental colon resections had fewer daily defecations and a significantly better quality of life than those with extensive resections [16]. In hereditary colorectal cancer syndromes cases, extensive resection is necessary [17].

Additionally, a detailed clinical and molecular evaluation is essential in patients with synchronous colorectal cancers diagnosed at a young age. Berg et al. recommended screening for Lynch syndrome in all newly diagnosed cases. One complicating factor in detecting synchronous colon tumors is the development of mechanical bowel obstruction due to a distally located tumor [18]. Especially when there is no involvement of the serosa/subserosa, identifying a second primary tumor can be challenging. Intraoperative colonoscopy or three-contrast computed tomography is recommended [19].

Conclusion

The diagnosis and treatment scope and content will vary if a synchronous colon cancer is detected, and if it is caught early, it will positively affect the prognosis and survival. Therefore, early diagnosis's importance in emergency and elective cases cannot be overstated. In conclusion, these studies highlight the importance of screening high-risk patient groups for gastrointestinal conditions, whether in emergency or elective cases. All patients diagnosed with primary tumors must undergo screening for synchronous, metachronous tumors and metastases.

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EFFECTS OF LACOSAMIDE ON CELL VIABILITY IN VARIOUS CANCER CELL LINES

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ABSTRACT

The repurposing of existing drugs, such as anti-epileptic drugs (AED), could yield potent new agents in the treatment of cancer. Lacosamide is a 3rd generation AED that is proposed to increase the slow inactivation of voltage-gated sodium channels without affecting the rapid inactivation, a distinct new mechanism from AEDs targeting sodium channels. In previous studies, it has been reported that lacosamide shows anticancer properties in some glioblastoma cell lines. The aim of the study is to investigate the potential anti-cancer effect of lacosamide on C6 glioma, Sh-sy5y, and HT-29 cell lines. Cell viability was examined by the XTT method 24 hours after the application of lacosamide. It was evaluated that lacosamide has no toxic effect on C6 glioma, Sh-sy5y, and HT-29 cells. Although AEDs such as lacosamide may be a possible choice for adjuvant cancer therapy, their effectiveness in different cancer cell lines requires further investigation.

Keywords: *Cancer, lacosamide, voltage-gated sodium channel, XTT assay*

Introduction

Cancer is one of the leading causes of death worldwide. The development of drug resistance, one of the main challenges in cancer treatment, is the primary cause of this high mortality. Drug resistance is thought to cause more than 90% of cancer-related deaths. Multidrug resistance (MDR) in cancer cells receiving chemotherapeutic treatment can be explained by several mechanisms, in particular genetic variables, increased DNA repair capacity and growth factors, and increased xenobiotic metabolism. These mechanisms make it more difficult to treat tumors because they decrease the efficacy of drugs. This approach is critical to success in the fight against cancer, which is a diverse and multi-targeted disease.

The majority of innovative drugs/molecules have been unable to demonstrate safety and efficacy in clinical trials and, as a consequence, have not entered the clinical arena: The success rate is < 10%. Numerous organizations are re-analyzing commercially licensed drugs from a drug repurposing perspective as a novel strategy to overcome these limitations. Drug repositioning ("creative innovations for old medications") is a management strategy to develop new applications for marketed or exploratory drugs that extend beyond the original medical indication. The main advantages of this technique are that the pharmacodynamic, pharmacokinetic, and toxicity profiles of medications have been extensively documented in preclinical and Phase-1 trials.

AEDs are versatile drugs that have the capability to be used in functional drug preparations by means of drug repurposing strategies. Valproic acid, oxcarbazepine, lacosamide, lamotrigine and levetiracetam are the drugs that have demonstrated potentially helpful results for different types of cancer. Lacosamide is a third-generation AED that enhances the delayed inactivation of voltage-gated Na+ channels. Histone deacetylase inhibition is also an effect of lacosamide. This effect may indicate that antitumor effects should be studied. In addition, the inhibition of cell cycle migration in glioma cells has been hypothesized to be explained by this mechanism. Previous researchers hypothesized that by modifying the transcription of other miRNAs (such as miR-107), lacosamide could reduce cell proliferation, enhance apoptotic events, and inhibit cell movement and invasion. One research group has shown that phosphorylation of collapsin response mediator protein (CRMP2) (S522) is an important indicator of

glioblastoma cell proliferation. To investigate the effect of CRMP2 phosphorylation at S522 on tumor growth, they used the CRMP2 phosphorylation inhibitor (S)-lacosamide and discovered that inhibiting of CRMP2 phosphorylation with (S)-lacosamide decreased glioblastoma cell outgrowth in all glioblastoma cell lines and also demonstrated that (S)-lacosamide prevents glioblastoma growth in vivo models.

Although the anticancer effect of lacosamide has been demonstrated in a number of glioblastoma cell lines, its anti-proliferative effects on human colon cancer cells and other glial tumor cells have not yet been investigated. Therefore, in this study, we investigated whether lacosamide has potential anti-proliferative effects on HT-29, a human colon cancer cell line, and C6 and Sh-sy5y glioma cell lines.

Material & Methods

Lacosamide (Benvida) was purchased from a pharmaceutical company (Adeka Corp., Samsun, Türkiye). The final concentration of the drug is 10 mg/mL, and the final dilutions were made just before use. C6 glioma, Sh-sy5y, and HT-29 cell lines were purchased from ATTC (American Type Culture Collection, USA) and maintained in DMEM medium. The cytotoxicity activity of lacosamide against these cell lines was evaluated by XTT assay (Roche Diagnostic, MA, USA). HT-29 cells were cultured in 96-well plates at (10^4 cells/well) in a DMEM medium containing 10% fetal bovine serum (FBS), 1% L-glutamine, and 1% penicillin-streptomycin. Then, different concentrations of Lacosamide (400 µg/mL, 200 µg/mL, 100 µg/mL, 50 µg/mL, and 25 µg/mL) were added to the wells. Cells were maintained in a humidified atmosphere with 5% CO_2 at 37°C and incubated for 24 h. After incubation, the culture medium was removed and a fresh medium was added with 50 µL of XTT solution, the cells were further incubated for 4h at 37°C. ELISA microplate reader (Thermo Fisher Scientific, Altrincham, UK) was employed to record the absorbance at 450 nm. Cell viability was then calculated using the following formula:

Cell viability (%) = absorbance of sample / absorbance of control * 100

Results & Discussion

The cytotoxicity activity of lacosamide was studied against C6 glioma, Sh-sy5y, and HT-29, at different concentrations such as 400 µg/mL, 200 µg/mL, 100 µg/mL, 50 µg/mL, and 25 µg/mL. No significant effect of any dose of lacosamide on cytotoxicity activity was observed in these cancer lines. The cell viability % of the lacosamide-treated cells at different concentrations is shown in Fig 1-3.

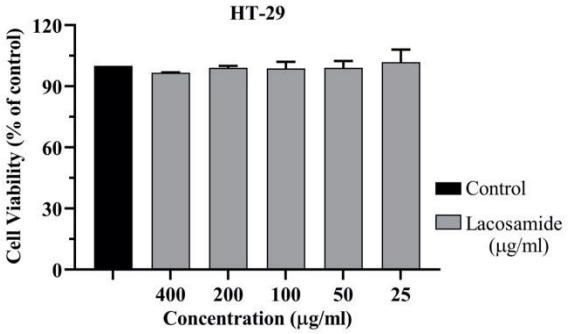

Figure. 1. *Percentage of HT-29 cell viability using XTT assay*

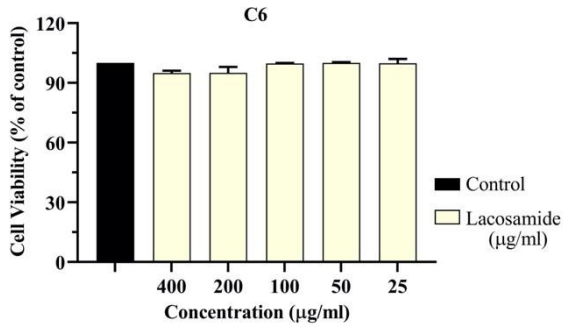

Figure. 2. *Percentage of C6 glioma cell viability using XTT assay*

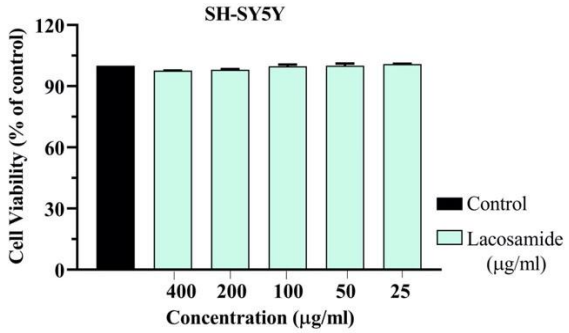

Figure. 3. *Percentage of Sh-sy5y cell viability using XTT assay*

In our study, the anticancer effect of AED lacosamide on human colon cancer and glioma cell lines was investigated and it was determined that the drug did not have a concentration-dependent cytotoxic effect on these cancer cell lines. AEDs such as lacosamide might be a good option for adjuvant cancer therapy, but there is a need to investigate further their efficacy in different cancer cell lines.

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TEN YEAR ANALYSIS OF OVARIAN CANCER IN SIVAS CUMHURIYET UNIVERSITY HOSPITAL GYNECOLOGY AND OBSTETRICS CLINIC

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ABSTRACT: Gynecological cancers, including ovarian carcinoma, contribute significantly to women's morbidity and mortality rates, ranking second only to breast cancer. The global incidence of gynecological cancers varies, with these cancers comprising 11.2% of all female cancer cases in our country. Notably, endometrial, ovarian, and cervical cancers are prevalent, with respective rates of 5%, 3.7%, and 2.5% across all age groups. Ovarian carcinoma is the second most common gynecologic malignancy, leading to a substantial number of gynecologic cancer-related deaths each year.

The majority of ovarian malignancies originate from epithelial cells, with various subtypes. Symptoms of ovarian cancer, such as ascites, pleural effusion, bowel obstruction, and adnexal masses, are often nonspecific, leading to late-stage diagnoses. Genetic factors, such as BRCA mutations and Lynch syndrome, as well as exposure to gonadotropins and hormonal factors, contribute to ovarian cancer risk.

Early detection remains a challenge, but pelvic examinations, advanced radiological imaging, and tumor markers like CA 125 aid in diagnosis. Most ovarian cancer patients undergo surgical staging, while fertility-sparing surgical approaches are applicable in certain cases. A retrospective study at Sivas Cumhuriyet University Hospital between 2011 and 2021 included 94 ovarian cancer patients, with epithelial ovarian tumors being the most common (85.1%). Elevated CA 125 levels and lymph node positivity were observed in some cases.

In conclusion, gynecological cancers, especially ovarian cancer, have a significant impact on women's health. Early detection through regular examinations and monitoring of adnexal masses can substantially reduce morbidity and mortality.

Keywords: *Ovary cancer, CA-125*

Introduction

Gynecological cancers constitute a significant portion of morbidity and mortality after breast cancer in women. The incidence rates of gynecological cancers vary by country [1]. According to statistics in our country, gynecological cancers constitute 11.2% of all female cancers. In all age groups, endometrium, ovary and cervix uteri cancers are among the top 10 cancers with rates of 5%, 3.7% and 2.5%, respectively [2]. Ovarian carcinoma is the most common cause of gynecologic cancer death in the United States and other resource-abundant countries. Approximately 314,000 women are diagnosed with ovarian cancer in a year and more than 207,000 women die from this disease [3]. The majority of ovarian malignancies are derived from epithelial cells (subtypes include high-grade serous, low-grade serous, endometrioid, clear cell, and mucinous); the remainder arise from other ovarian cell types (germ cell tumors, sex cord-stromal tumors. Among all ovarian cancers; epithelial tumors (50-70%), germ cell tumors (20%), gonadal stromal tumors (10%), metastatic tumors (10%) and unclassifiable tumors (10%) [4], [5]. Symptoms (ascites, pleural effusion,bowel obstruction,adnexal mass etc.) of ovarian cancer are often non-specific and may result from other conditions (e.g. primary gastrointestinal or urological disease), so women with this disease are often diagnosed at an advanced stage [6]. It is known that approximately 10 percent of patients with ovarian cancer have a genetic predisposition. Primarily BRCA 1 mutation, BRCA-2 mutation and Lynch syndrome are the most important familial causes of ovarian cancer [7]. Exposure to gonadotropins, advanced age, reproductive and hormonal factors, early menarche or late

menopause, nulliparity, infertility, endometriosis, polycystic ovary syndrome, and postmenopausal hormone use are the risk factors for ovarian cancer [8]. First of all, following a good anamnesis and family history questioning, the most important element of ovarian cancer evaluation is the presence of an adnexal mass in pelvic examination and imaging. Advanced radiological imaging can also be used to understand the nature of the adnexal mass. Imaging studies can help assess for the presence of ascites and disease spread.The tumor marker used in EOC is CA 125.Up to 80 percent of patients with EOC will have an elevated CA 125, and posttreatment CA 125 testing is used to evaluate for response to treatment and recurrence [9]. Other tumor markers (eg, human epididymis protein 4, lactate dehydrogenase, alpha fetoprotein, carcinoembryonic antigen) should be ordered as clinically indicated [10]. Most patients with ovarian cancer undergo surgical staging according to the International Federation of Gynecology and Obstetrics (FIGO)/Tumour, Node, Metastasis (TNM) joint classification system . Total hysterectomy and bilateral salpingo-oophorectomy with pelvic and para-aortic lymph node dissection are the standard staging procedure. Cytoreduction, including intestinal or partial liver resection, is also performed when metastases are evident. However, one thing that should not be forgotten is that fertility-sparing surgical approaches can be applied to the appropriate patient group in non-epithelial (germ cell) ovarian cancer, which is seen especially in young women [11].

Method

The Type of Research: The research is a retrospective study. The Location of Research: The research was carried out in the Department of Obstetrics and Gynecology of Sivas Cumhuriyet Universty Health Services Research and Application Hospital. The Population and The Sample: Patients who were diagnosed and operated for ovarian cancer between 2011 and 2021 in the Department of Obstetrics and Gynecology, Sivas Cumhuriyet University Hospital were the target group of the study. The retrospective file data of the patients were obtained voluntarily;

-Preoperative and postoperative blood results (CA 125)

-Demographic data

-Pathology results were analyzed.

Data Collection Tools: File data were analyzed retrospectively. Data Analysis: Statistical analysis was performed using SPSS version 22 (IBM Corp., Armonk, NY, USA). Numerical variables will be expressed as median according to distribution (Kolmogorov-Smirnov/Shapiro-Wilk) and categorical variables will be expressed as percentages. Survival analysis for cases will be calculated using the Kaplan-Meier log-rank test.

Result

There were 94 patients who underwent surgery in our clinic between 2011 and 2021 with final pathology results as Ovarian Ca. 80 (85.1%) of the patients were Epithelial Ovarian Tumors, 9 (9.6%) were Sex Cord Stromal Tumors and 5 (5.3%) were Germ Cell Tumors. Of the epithelial ovarian tumors, 68 were serous type, 6 were endometroid type, 3 were mucinous type and 3 were clear cell type. Of the 9 patients with Sex Cord Stromal tumors, 7 were adult type and 2 were juvenile type. In germ cell tumors, 1 was endodermal sinus tumor and 1 was dysgerminoma. The mean age of the patients with epithelial ovarian tumor was 54.61 years (min:24 max:79). The mean duration of hospitalization was 7.86 (min:4 max:73) days. The mean Ca125 values were 718.37 (min:1.04 max:7406). Parapelvic and paraaortic lymph node dissection was performed in 74 patients. The mean number of collected lymph nodes was 25 (min:3 max:61) and 14 of these patients had positive pelvic lymph nodes and 13 had positive paraaortic lymph nodes. The mean age of the patients with sex cord stromal tumor was 44.66 (min: 19 max: 72). The mean duration of hospitalization was 5.88 (min:1 max:12) days. Pelvic lymph node dissection was performed in 8 and 7 of these patients and pelvic and paraaortic lymph node positivity was detected in 1 patient. The mean age of the patients with Germ Cell Tumor was 25.2 years (min:17 max:54). The mean duration of hospitalization was 6.8 (min:3 max:14) days. Parapelvic and paraaortic lymph node dissection was performed in 4 of these patients and lymph node positivity was detected.

Table 1.

	Number of patients	Average age	Duration of hospital stay	Pelvic lymph node positivity	Paraaortic lymph node positivity
Epithelial Tumor	80	54,6	7,86	14	13
Endometrioid type	6				
Serous type	68				
Mucinous type	3				
Clear cell	3				
Sex Cord Stromal Tumor	9	44,6	5,88	1	1
Adult type	7				
Juvenile type	2				
Germ Cell Tumors	5	25,2	6,80	-	-
Endodermal sinus tumor	1				
Dysgermioma	1				

Discussion

Ovarian cancer is the second most common gynecologic malignancy in our country as in developed countries. In this study in which 94 ovarian cancer cases treated in our hospital between 2011 and 2021 were evaluated, our data are generally compatible with the literature. Most of our patients underwent staging surgery and their adjuvant treatment was planned with a multidisciplinary approach according to the FIGO staging system. When the histologic classification of ovarian cancers and the average age of occurrence are examined; it has been reported that epithelial ovarian cancers are the most common and the average age of occurrence is 63 years. Other histological types are seen at younger ages and even germ cell ovarian tumors are reported to be the most common ovarian tumors in patients under 20 years of age. In our retrospective examination, 75% of patients with ovarian cancer were found to have epithelial ovarian cancer, while germ cell tumors were found more frequently in early age groups, again in accordance with the literature. Ca125 was used as a tumor marker and we found elevated Ca125 especially in epithelial ovarian tumors. In our clinic, we also use Ca125 level in the follow-up period after surgery. Most of the germ cell tumors were in young or reproductive age women and in this patient group we planned to treat the patients with fertility preserving approach.

Conclusion

In conclusion, women's awareness about gynecological cancers should be increased and they should be encouraged to attend routine gynecological examinations. It is important to pay attention to adnexal masses even if they are not accompanied by symptoms. Although ovarian cancer does not have a screening program, a possible tumor can be detected at an early stage by using examination, USG and, when necessary, tumor markers. Diagnosis at an early stage will have a significant impact on the morbidity and mortality of patients.

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PARTIAL HYDATIFORM MOLE AND COEXISTING ALIVE FETUS IN THE SECOND TRIMESTER CASE REPORTS AND REVIEW OF THE LITERATURE

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ABSTRACT

Introduction

Gestational trophoblastic diseases are a group of diseases that originate from the placenta and have the potential to locally invade the uterus and metastasize. This disease is a pathology of gestational tissue and of paternal origin. This group of diseases, also referred to as hydatiform mole and molar pregnancy, have two basic types as complete and partial, with a frequency of 23-1299/100000 [1-2]. Although molar pregnancies are generally benign, they are considered as a premalignant disease because they also carry malignancy potential.

Case

Twenty-four years old, first pregnancy, 16 weeks of gestation according to the last menstrual period, molar pregnancy was observed in ultrasonographic examination. The perinatology consultation was reported as "Complete mole hydatiform in the twin partner in twin pregnancy, fetal plans were normal as far as can be observed". In the perinatology council, the risks of pregnancy and its aftermath were explained to the patient and it was decided to offer the option of termination of pregnancy. Upon the patient's consent to termination, induction with misoprostol was started and pathology after abortion was reported as partial mole hydatiform and fetus.

Discussion

With the use of reproductive techniques, it is thought that the frequency of KMCFG and PHMCF may increase due to multiple pregnancies. Management is controversial. Since live births have been reported in some cases, a conservative approach may be considered. However, the risks of abortion, preterm delivery, thyrotoxicosis, preeclampsia, severe bleeding, postmolar neoplasia should be explained to the patient and termination should be offered as an option.

Keywords: *Twin pregnancy, hydatiform mole, alive fetus*

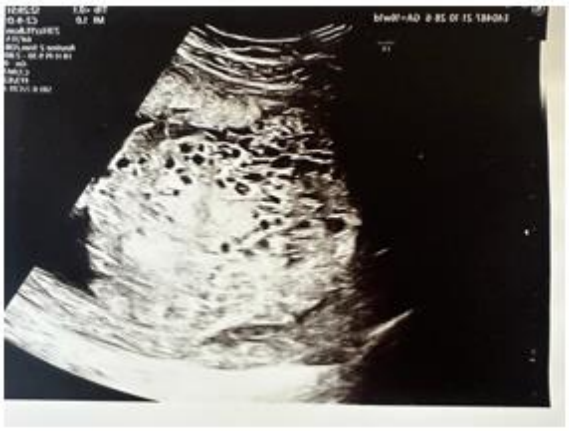
Introduction

Gestational trophoblastic diseases are a group of diseases that originate from the placenta and have the potential to locally invade the uterus and metastasize. This disease is a pathology of the gestational tissue. It is characterized by abnormal fetoplacental development and villous trophoblast hyperplasia resulting from a genetic disorder of paternal origin [1-3]. This group of diseases, also referred to as hydatiform mole and molar pregnancy, have two basic types as complete and partial, with a frequency of 23-1299/100,000 [2-4]. Although molar pregnancies are generally benign, they are considered as a premalignant disease because they also carry malignancy potential and are divided into subgroups according to malignancy potential [1].

Case

A 24-year-old patient, first pregnancy, 16 weeks gestation according to the last menstrual period date, was referred to us from an external center with a prediagnosis of mole pregnancy. The perinatology consultation was reported as; "In obstetric ultrasonography, the placenta was anteriorly located, the placenta dimensions

increased on the right lateral side, and multiple cystic appearances were remarkable (complete mole hydatiform in twin pregnancy?) Fetal plans were normal as far as they could be observed". The patient was informed about the ultrasound findings and the maternal and fetal risks of complete mole hydatidiform. Hemogram, beta-hCG, TFT, indirect coombs were ordered. Fetal karyotype evaluation was recommended. Emergencies were explained to the patient. It was decided to discuss in the perinatology council.



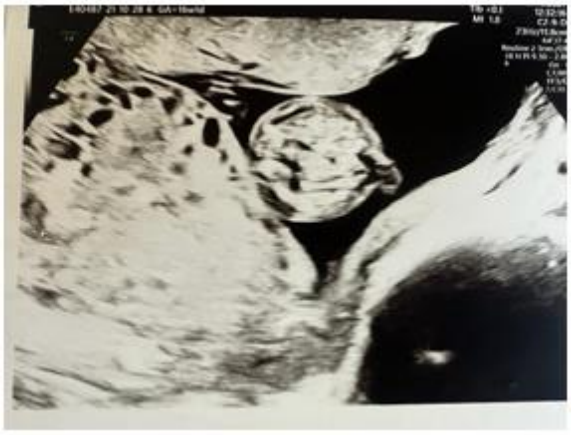


Figure 1. *Ultrasonographic image of molar pregnancy in the uterus.*
Figure 2. *Ultrasonographic image of molar hydatiform in the right lateral part of the uterus and viable fetus in the left lateral part.*

In our patient, beta-hCG value: 339.460, Hb: 10.5, Plt: 210.000, TSH: 0.956, T4: 1, T3: 2.99. The patient was discussed by the perinatology council and it was decided to offer the family the option of termination of pregnancy. The family was informed about the risks of the disease and treatment options and detailed consent was obtained. Upon the patient's request for termination of pregnancy, induction with misoprostol was started. The abortion material was sent to pathology. After the procedure, the diagnosis of molar pregnancy was confirmed by pathology. The patient was recommended beta-hCG follow-up after discharge.

Discussion

The reported incidence of complete hydatidiform mole and coexisting fetus is 1 in 22000-100000 pregnancies. However, partial hydatidiform mole and coexisting fetus (PHMCF) is a single pregnancy and the reported prevalence is 0.005%-0.01% of all pregnancies [2-4].

Today, it is thought that the actual prevalence may be higher due to the increase in multiple pregnancies as a result of early diagnosis with ultrasonography (USG) and the use of assisted reproductive techniques [8].

The management of such pregnancies creates a dilemma for both the physician and the parents, especially when PHMCF occurs in the second trimester of pregnancy. Unfortunately, in most patients, serious complications can occur leading to significant challenges and difficult choices for both the obstetrician and the patient.

In practice, cases with molar appearance and fetus association on USG examination can be encountered in three ways: twin pregnancy in which the first fetus is normal and the second fetus is BM, singleton PM accompanied by a triploid fetus, and twin pregnancies in which the other fetus is normal accompanied by PM [9]. The differential diagnosis of the disease should be made with these three conditions.

Complete (CM) and partial molar pregnancies (PM) have different pathologic mechanisms [10]. In PM, dispermic fertilization of a normal haploid oocyte results in a conceptus with triploid chromosomes and almost always the accompanying fetus has triploid chromosomes. KM, on the other hand, has diploid chromosomes, all of paternal origin. The fetus accompanying PM is usually triploid or tetraploid and these pregnancies tend to result in abortion in the first trimester [11]. However, the presence of fetal anomaly in ongoing pregnancies facilitates the decision for termination, whereas the most likely normal fetus in KMCFG creates confusion in clinical management [4-11].

Although the management of pregnancy after the diagnosis of twin pregnancy in which mole and viable fetus are present together is still a controversial issue, the fact that it is more frequently encountered in patients conceived with assisted reproductive techniques and live births have been reported in some cases where termination was not performed has led to the prominence of the conservative approach. However, the traditional approach is still in favor of termination especially because of maternal complications [2-4].

The coexistence of a live term baby and hydatiform mole pathologies is much rarer because of problems such as abortion, termination recommendations, preterm delivery, and preeclampsia [4-12). Although in our case, when the family was informed about the risks of the disease and treatment options as a result of the perinatology council, the family decided for termination, it has been reported in the literature that the chance of live birth is 21-50% and the risk of PTN is between 19-50% and the risk of preeclampsia is around 20% in expectant mothers who choose to continue the pregnancy [11,13,14]. When a conservative approach is preferred, although demonstration of the presence of a diploid fetus by amniocentesis is considered necessary in the literature, evaluation with USG every two weeks, MS-hCG (maternal serum human chorionic gonadotropin), and follow-up in a center with oncology and perinatology units in terms of maternal and fetal complications of molar pregnancy are recommended [4,9,11]. Continued elevated MS-hCG levels during follow-up have been associated with increased risk of maternal complications and PTN. Conversely, stable or declining MS-hCG levels are thought to reduce the risk of fetal death in the absence of lutein cysts. Due to the risk of preeclampsia, it is important to regularly monitor arterial blood pressure, to screen for proteinuria in urine, to be careful in terms of maternal anemia in small but continuous bleeding, and to monitor the signs of hyperthyroidism that may occur due to the thyrotropic effects of HCG molecules [11].

The clinical features of gestational trophoblastic diseases (GTDs) include vaginal bleeding, uterus larger than week, pelvic pressure sensation or pain, teka lutein cysts, hyperemesis, hypertrophy, preeclampsia starting before 20 weeks and postpartum persistent trophoblastic disease (PTH) [4-11].

Although there are many types of gestational trophoblastic diseases in terms of malignancy potential, they are diseases that respond well to chemotherapy and can be followed up easily because the beta-hCG level is correlated with the number of viable cells. Since mole hydatiform may develop after persistent trophoblastic disease in 1/5 of cases, beta-hCG level should be followed up with serial measurements after treatment [15].

Although the diagnosis of molar pregnancies can be made by USG, it should be kept in mind that the diagnosis may not be made in the first trimester. Caution should be exercised in terms of confusing partial molar pregnancies with twin paired complete molar pregnancies. In molar pregnancies, family counseling is very important in terms of maternal and fetal risks, and there are publications supporting a conservative approach, as live births have been reported in some cases as well as termination. Management is controversial. However, the risks of abortion, preterm delivery, thyrotoxicosis, preeclampsia, severe bleeding, postmolar neoplasia should be explained to the patient and termination should be offered as an option.

Table 1. *Previously reported cases of PHMCF in the second trimester in the literature [16]*

Time of termination of pregnancy	β-HCG before termination (IU/L)	Methods of termination of pregnancy	Live fetus	Persistent trophoblastic disease	Metastasis	IVF-ET
17 weeks	449078	Rivanol and aspiration curettage	No	Yes	Lung Metastasis	No
16 weeks	800842	Rivanol	No	Yes	Lung Metastasis	Yes
14 weeks	229000	Misoprostol	No	Yes	Lung Metastasis	Yes
15 weeks	270000	D&C	No	Yes	No	No
20 weeks	878000	D&C	No	No	No	No
27 weeks	-	Spontan abortus	No	Yes	Lung Metastasis	No
21 weeks	1100000	Spontan abortus	No	Yes	No	No
23 weeks	133100	Spontan abortus	No	No	No	No
15 weeks	600000	hysterectomy	No	Yes	No	No
27 weeks	-	caesarean section	No	No	No	No
23 weeks	76642	caesarean section	No	No	No	No
23 weeks	510427	caesarean section	No	No	No	Yes

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MENTAL STATUS AND LONELINESS IN CANCER PATIENTS

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ABSTRACT

Objective

Although cancer diagnosis affects a person's mental health in many aspects as well as their physical health, mental problems often lag behind physical problems during the treatment process. This leads to the emergence of secondary problems and an increase in psychosocial problems. Loneliness is an significant problem affecting approximately 50% of adult cancer patients. This study was conducted to determine the mental status and loneliness in patients diagnosed with cancer.

Methods

This descriptive study was conducted with 185 patients diagnosed with cancer who were followed up in the Palliative Care Application and Research Center, Internal-Surgery Clinics and Chemotherapy Unit of Tokat Gaziosmanpaşa University Research and Application Hospital. Research data were collected using with the descriptive characteristics information form, Brief Symptom Inventory and UCLA Loneliness Scale. The data were analyzed with Mann-Whitney U test, Kruskal Wallis test, correlation and path analysis using IBM SPSS 22.0 and IBM AMOS V24 programs. The significance level was accepted as $p<0.05$.

Results

The mean age of the patients was 58.26±13.83 years, 63.8% were male, 88.6% were married, 50.3% have 3-4 children, and 30.8% were being treated for respiratory system cancers. 83.8% of the patients stated that they were compliance with the treatment and 55.7% of them perceived cancer as a disease requiring long-term treatment. The patients' mean BSI total score is .52±.44, and the BSI subscales somatization (1.02±.74) and depression (.60±.65) scores are higher. It was determined that there was a statistically significant difference between the total score and subscale scores of the BSI according to patient's age, marital status, educational status, employment status, income status, duration of illness, duration of treatment, duration of hospitalization, presence of another disease, adaptation to the disease and perception of the disease ($p<0.05$). Those who were 65 years of age and older, illiterate, not working, and whose income was less than their expenses had higher somatization scores. Anxiety score was higher in those who were single, had high school education and above, treatment duration was 5 years or more, and hospitalization duration was 1-3 days. Hostility score is higher in those with primary education. Depression, negative self-concept, somatization and total BSI scores were higher in those with another comorbidity. Somatization, depression and hostility scores are higher in patients with a disease duration of more than one year. Depression, hostility and total BSI scores are high in those who cannot adapt to the disease. Depression scores are higher in outpatients with a disease duration of more than one year. Those with a treatment duration of 7 years or more have a high negative self-concept score. Those who do not work, those with a disease duration of more than 3 years, and those with a treatment duration of 7 years or more

have a higher total BSI score. Those who perceived cancer as an incurable disease had higher scores in all subscales and total BSI. It was found that there was a statistically significant difference between the UCLA loneliness scale score according to the patients' employment status, income status, duration of illness, presence of another disease, adaptation to the disease, and perception of the disease ($p<0.05$). The UCLA loneliness scale score was higher in patients who were not working, whose income was less than their expenses, whose disease duration was one year or more, who had another comorbidity, who had a problem of adaptation to the disease and who perceived cancer as an incurable disease. UCLA loneliness scale total score has a positive effect on BSI total score and a one-unit increase in the UCLA loneliness scale score increased the BSI score by 0.272 unit ($p<.001$).

Conclusion

In the study, it was determined that there was a significant relationship between loneliness and mental problems in patients diagnosed with cancer and that loneliness negatively affected mental status. In line with the results obtained, it is recommended that the treatment and care of patients diagnosed with cancer should be handled with a holistic approach, and arrangements should be made to maintain the mental health of patients and reduce loneliness.

Keywords: *Cancer, loneliness, mental state, anxiety, depression*

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FIVE-YEAR SURVIVAL AND RELATED FACTORS IN ELDERLY LUNG CANCER PATIENTS IN SİVAS PROVINCE

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ABSTRACT

Introduction and Purpose: Lung cancer is the most common cause of cancer deaths worldwide. It is more common in men receiving lung cancer treatment. The median age at lung cancer diagnosis is 70. The 5-year survival rate is 14-15% in lung cancers seen in the elderly. The purpose of this treatment is to examine the survival times of elderly patients with lung cancer.

Materials and Methods: This programming universe, which is a retrospective cohort type, consists of lung cancer cases aged 65 and over, starting from a known total follow-up period of five years, as provided by the Sivas Provincial Health Directorate Cancer Registry Unit. The dependent variable is the five-year survival rate; The survival rates of patients diagnosed with lung cancer between 2013 and 2017 were calculated on a five-year basis. Independent variables were socio-demographic; scheme age, gender, place of birth, socioeconomic development level of the districts where the patients live (the Socioeconomic Development Ranking Research Report (SEGE-2017) provided by the Ministry of Industry and Technology of the Republic of Türkiye was used to determine this level), diagnosis system, comorbid diseases, metastasis, treatment status, treatment is the type of situation. The data of the study were analyzed with the statistical program SPSS-22 (SPSS INC., Chicago, IL, USA). Data indicated by measurement are presented descriptively with mean and standard deviation (minimum - highest values), number of data indicated by count and percentage.

Results: 209 patients over the age of 65 were included in the study. 84.2% (n=176) of these patients were male. His age is 72.25±5.63 (minimum 65-maximum 87). 93.8% (n=196) of the patients were born in Sivas. 86.6% (n=181) of the patients were between the ages of 65-79, and 13.4% (n=28) were 80 and over. When the living spaces of the patients are evaluated, 50.2% (n=105) are in the 2nd category according to SEGE 2017, 29.7% (n=62) are in the 3rd and 4th categories, and 20.1% (n=42) are in the 2nd category according to SEGE 2017.) lives in the 5th category. When the lung cancers seen in the patients were evaluated, 31.1% (n = 65) were squamous cell carcinoma, 30.1% (n = 63) were adenocarcinoma, 16.7% (n = 35) were small cell carcinoma and % 22.0 of them (n=46) are different from other. 55.0% (n=115) of the patients had comorbid diseases. The rate of patients receiving treatment was 56.5% (n=118). The mortality rate within five years after the diagnosis is cleared is 84.7% (n=177). Median survival time was 8.6 (95% CI 6.9-10.3). Kaplan Meier, combining log rank test and 5-year survival analysis; men (median 7.8 months, p=0.005) and those aged 80 and over (median 3.6, p=0.002). Survival time was shorter in those who received treatment (median 6.2 months, p=0.455), those living in category 5 districts (median 7.3 months, p=0.282) and those in areas with small cell carcinoma features (median 7.8, p=0.085). There was no significant difference between them.When the data of the study were evaluated with Cox Regression analysis, the 5-year risk of death due to lung cancer was 3.2 times higher in men than in women (p<0.017). It is 2.07 times higher in young people aged 80 and over than in older people (p = 0.002). The risk of death is 1.31 times higher in those living in the least developed categories than in those living in central districts (p=0.160), and 1.84 times higher in those diagnosed with small cell carcinoma than in areas defined as independent adenocarcinoma (p=0.008).

DEPRESSION AND CAREGIVING BURDEN IN CAREGIVERS OF PATIENTS RECEIVING CHEMOTHERAPY TREATMENT

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ABSTRACT

Objective

This study was conducted to determine depression and care burden in caregivers of patients receiving chemotherapy treatment.

Methods

This descriptive study was conducted with 142 of patients who were caregivers of patients receiving outpatient chemotherapy in the Oncology service and center of Sivas Cumhuriyet University Application and Research Hospital. The data were collected using the Personal Information Form, Zarit Caregiver Burden Scale and Beck Depression Inventory. The data were analyzed with descriptive tests, student t test, one-way analysis of variance and correlation analysis using SPSS 22.0 program.

Results

The mean age of the caregivers was 50.21±12.71 years, 68.3% were female, 74.7% were married, 43.0% were high school graduates, 52.1% were not working, 48.6% had income equal to expenses, and 43.0% were spouses. The diagnosis of the patient receiving care was mostly breast cancer [23.2%] and respiratory system cancer [22.5%]. The rate of those with a disease diagnosis period of 0-2 years is 64.8%. 39.4% of the caregivers do not receive support from any other person and care for the patient only by themselves. The mean score of ZCBS was 32.65±15.44 and the mean score of BDI was 17.90±1.51. It was found that there was a statistically significant difference between caregiver burden scores according to the variables of gender, marital status, duration of disease diagnosis, duration of care given and presence of other caregivers, and depression scores according to the variables of marital status, educational status and presence of other caregivers [$p<0.05$]. In the study, it was determined that there was a moderate positive significant relationship between caregiver burden and depression scores [$r=.588$, $p=.000$] and depression increased as caregiver burden increased.

Conclusion

In the study, it was determined that there was a significant relationship between care burden and depression in caregivers of patients receiving chemotherapy treatment and that care burden increased depression. In line with the results obtained, it is recommended that healthcare team members working with patients diagnosed with cancer should make plans and practices to maintain the mental health of patients and caregivers and support them in disease management.

Keywords: *Cancer, chemotherapy, caregiver, care burden, depression*

Introduction

Cancer is a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020, or nearly one in six deaths [1]. A cancer diagnosis directly or indirectly changes the lives of not only patients but also their families [2]. More than 90% of individuals living with Cancer have a caregiver [a friend or family member] who can provide care throughout their disease and treatment [3].

Caregivers are involved in every stage of disease management including diagnosis, treatment and treatment of side effects [4]. Chemotherapy, which is one of the treatment modalities of cancer and is frequently used, aims to prolong the life span of patients and provide a better quality of life. However, cytotoxic drugs used in chemotherapy also damage normal cells and cause side effects such as pain, anorexia, cachexia, changes in taste, alopecia, dehydration, nausea and vomiting, fatigue, dyspnea, bone marrow suppression, depression and anxiety [5]. Because of these side effects, it is known that the daily life order of family members as well as the patient is disrupted and the stress of the family of the patient with cancer increases [6]. The ability of caregivers to provide optimal care is important in reducing their own distress, relieving the pressure on the healthcare system and improving treatment outcomes for patients [7]. In general, caregiver burden refers to the distress experienced by caregivers while providing care to patients, affecting their physical, emotional, social, financial and daily living areas [8]. Long-term caregiving has an impact on health, socio-financial and physical status and all of these together may lead to mental problems such as depression or anxiety in caregivers [9]. In meta-analysis studies, it was determined that depression in caregivers of cancer patients is around 42% [10] and two out of every five caregivers globally have a level of depression that required treatment [3].

Chemotherapy treatment is a process that affects human life both physically and psychologically, with the possibility of taking a long time, having side effects, having a systemic effect, the possibility of recurrence, or the treatment being completely ineffective [5]. Not only the patient but also the caregivers are directly affected by this process.

This study was conducted to determine the care burden and depression status of caregivers of patients receiving chemotherapy treatment.

Method

The sample of this descriptive study was conducted of the relatives of patients receiving outpatient chemotherapy in the Oncology services of Sivas Cumhuriyet University Application and Research Hospital between July 25 and September 15, 2023, who met the research criteria [over the age of 18, who agreed to participate in the study, whose patient received chemotherapy treatment, whose patient's cancer diagnosis has been at least 1 month, and who did not have any barriers to communicate].

Ethical Approval

Approval was obtained from Sivas Cumhuriyet University Application and Research Hospital [No: 2023-321874] and Sivas Cumhuriyet University Ethics Committee [No: 2023-07/43].

Data Collection Tools

The research data were collected with Personal Information Form, Zarit Caregiver Burden Scale and Beck Depression Inventory.

Personal Information Form

This form was developed by the researchers and consists of questions such as age, gender, marital status, educational status, employment status, disease diagnosis, duration, duration of caregiving and support status of the patients.

Zarit Caregiver Burden Scale

It was developed by Zarit, Reever and Bach-Peterson in 1980. It is a scale used to assess the distress experienced by caregivers of individuals in need of care. It is a 22-item, five-point Likert-type scale. A minimum score of 0 and a maximum score of 88 can be obtained from the scale. A high scale score indicates that the distress experienced is high. The scale was adapted to Turkish and validity and reliability studies were conducted and Cronbach's alpha coefficient was found to be .95 [11,12]. In this study, the Cronbach's alpha coefficient of the scale was found to be 0.86.

Beck Depression Scale [BDS]

Beck et al. [1961] and the Turkish validity and reliability study of the scale was conducted by Hisli [1989]. The scale consists of 21 items, each of which is scored between 0-3. Total depression score is determined by summing these scores. A maximum of 63 points can be obtained from the scale, and a score between 0-9 is considered as minimally depressive, 10-16 as mild, 17-29 as moderate, and 30 and above points as severe depressive symptoms. Cronbach's alpha coefficient of the scale is .80 [13, 14]. In this study, Cronbach's alpha coefficient was found to be.81.

Data Analysis

Research data were evaluated through the SPSS 22.0 package program. Demographic and descriptive information about the individuals were determined as numbers and percentages. Compliance with normal distribution was examined by means of Shapiro-Wilk and Kolmogorov-Smirnov tests, t test for two independent groups and one-way analysis of variance [ANOVA] for more than two groups were used since the data met the parametric test assumptions. The relationship between the two scales was examined by Pearson correlation analysis. The 95 % confidence interval was determined.

Results and Discussion

Table 1 displays the descriptive characteristics of the caregivers. 68.3% of the caregivers were female, mean age was 50.21±12.71 [min:20 max:72], 74.7% were married, 43.0% were high school graduates, 52.1% were not working, 48.6% had income equal to expenses, and 43.0% of the caregivers were spouses. The diagnosis of the patient receiving care was mostly breast cancer [23.2%] and respiratory system cancer [22.5%]. he rate of those diagnosed with the disease between 0-2 years is 64.8%. 39.4% of caregivers do not receive any help and only care for the patient themselves.

In this study, the mean score of the ZCBS was found to be 32.65±15.44 [min: 5.00, max: 82.00]. In the study of by Orak and Sezgin [2015], in which the burden of care was determined in family members caring for patients diagnosed with cancer in our country, the mean score of the ZCBS was 39.02±18.44 [15]; and in the study of by Özdemir et al. [2017], it was determined to be 36.68±7.64 [16]. It was observed that the study findings were similar to the literature.

The mean BDI score of the caregivers was 17.90±1.51 [min:1.00, max:50.00]. Moghaddam et al. [2023]'s study on caregivers of patients diagnosed with cancer found that the mean depression total score was 28.01±13.28.

In this study, according to the rating of depression scores, 39.1% of the caregivers' depression level was minimal [0-9 points], 23.2% [10-16 points] was mild, 24.6% [17-29 points] was moderate, 13.1% [30-63 points] was found to be severe. In the study by Götze et al. [2018], which determined the level of depression in caregivers of cancer patients receiving palliative care, it was determined that the level of severe depression was 29% [18]; in the systematic review by Geng et al. [2018], it was determined that the prevalence of depression was around 42%. It is seen that the depression status of caregivers shows a course ranging from mild to severe. Various factors such as the duration of caregiving and the presence of people who can help with care may be effective in this result.

Table 2 shows the comparison of the scale scores of caregivers. It was determined that there was a statistically significant difference between the caregiver burden scale scores of the caregivers according to gender, marital status, duration of disease diagnosis, duration of care and the presence of other caregivers [$p<0.05$]. It was determined that the caregiver burden scale score was higher in caregivers who were female, married, had a disease duration and treatment duration of six years or more, and did not have other family members taking care of the patient. In previous studies, it was found that female gender [19], long-term caregiving and undertaking care alone increased care burden in caregivers of patients diagnosed with cancer [17, 20]; in the study conducted by Mishra et al. [2021] with caregivers of patients diagnosed with cancer receiving chemotherapy, it was found that the level of care burden did not differ significantly according to marital status, education level, ageof the caregiver and type of relationship with the patient [21]. In this study, it

is thought that the caregiving burden of married people is higher because these caregivers have more other roles and responsibilities along with caregiving.

It was determined that there was a statistically significant difference in the depression scale scores of the caregivers according to their marital status, educational status and the presence of other caregivers [p<0.05]. It was determined that depression scores were higher in caregivers who were single, educated at university and above and who did not have other people to support care [Table 2]. In previous studies, it was found that caregivers' receiving help from their environment was associated with depression levels [22-24]. Our finding that the level of depression was lower in the presence of other people taking care of the patient is consistent with the literature. In this study, the higher depression level of people with university education or higher may be affected by the level of awareness of the disease and their ability to access many different sources of information.

It was determined that there was a moderate positive significant relationship between caregiver burden and depression scores of caregivers [r=.588, p=.000] and depression increased as caregiver burden increased [Table 3]. In the study conducted in China in which the relationship between caregiver burden and depression was determined, it was found that depression increased as caregiver burden increased [25]; in the study conducted by Seo et al. [2019] in caregivers of patients diagnosed with lung cancer, depression was the most effective factor on the increase in caregiver burden, as shown in this study, as well as in many previous studies [26].

Conclusion

Since the need for care increases due to the effects of chemotherapy on the patient's life, the care burden of caregivers also increases and this situation negatively affects mental health. In this study, it was observed that depression increased as the care burden of caregivers increased. It was determined that gender, marital status, duration of diagnosis, duration of care and the presence of other caregivers negatively affected care burden, while marital status, educational status and the presence of other caregivers negatively affected depression level. In line with the results obtained, it is recommended that healthcare team members working with patients diagnosed with cancer should make plans and practices to maintain the mental health of patients and caregivers and support them in disease management.

Table 1. *Descriptive Characteristics of Caregivers [n=142]*

Sex	**Number**	**Percentage**
Female	97	68.3
Male	45	31.7
Mean age [years]	[mean±Sd] 50.20±12.71	
Marital status		
Married	106	74.7
Single	36	25.3
Education Status		
Illiterate	15	10.6
Literate - Primary Education	34	23.9
High school	61	43.0
University and above	32	22.5
Working status		
Working	68	47.9
Not working	74	52.1
Income status		
Less than income	45	31.7
Income equal to expense	69	48.6
More than income	28	19.7

Relationship to patient		
Spouse	61	43.0
Child	44	31.0
Parents	16	11.2
Brother, sister, relative, friend	21	14.8
Physical disease		
Yes	58	40.9
No	84	59.1
Cancer type		
Breast cancer	33	23.2
Respiratory system cancer	32	22.5
Gastrointestinal system cancer	28	19.7
Hematologic cancer	24	16.9
Other	25	17.6
Disease diagnosis		
0-2 years	92	64.8
3-5 years	37	26.0
6 years and above	13	9.2
Duration of care		
0-2 years	96	67.6
3-5 years	36	25.4
6 years and above	10	7.0
Presence of other people caring for the patient		
Yes	86	60.6
None	56	39.4

Table 2. *Comparison of scale scores according to demographic variables of caregivers*

	ZCBS			**BDI**		
	Mean±SD	**Test**	**p**	**Mean±SD**	**Test**	**p**
Sex						
Female	35.32±15.51	**2.830**	**.005**	12.7±9.2	-.744	.457
Male	28.62±13.64			14.4±10.1		
Marital status						
Married	33.39±15.21	**2.594**	**.010**	11.05±9.40	1.03	**.009**
Single	27.43±14.47			14.79±8.95		
Education Status						
Illiterate	33.83±15.91	2.421	.721	13.4±9.51	-2.308	**.013**
Literate - Primary Education	31.66±16.21			11.8±8.32		
High school	31.04±11.90			12.2±8.90		
University and above	32.01±15.69			16.0±11.21		
Working status						
Working	32.31±14.23	-.238	.713	13.77±7.94	.912	.317
Not working	32.18±14.12			15.44±11.13		
Income status						
Less than income	35.13±13.91	4.180	.124	18.69±7.91	1.373	.134
Income equal to expense	30.51±15.91			13.59±8.24		
More than income	30.41±15.89			13.00±6.25		

Relationship to patient						
Spouse	36.29±15.73	1.909	.464	18.41±9.24	.184	.700
Child	35.76±12.11			17.00±9.89		
Parents	32.91±12.49			18.28±8.94		
Brother, sister, relative, friend	32.90±12.88			14.12±8.47		
Physical disease						
Yes	33.10±15.21	-.717	.474	15.21±9.83	-.891	.406
No	31.71±14.98			15.58±9.39		
Cancer type						
Breast cancer	28.52±16.82	1.951	.185	16.47±11.02	1.213	.226
Respiratory system cancer	27.14±16.25			13.77±7.74		
Gastrointestinal system cancer	25.64±17.51			18.00±9.32		
Hematologic cancer	28.51±16.52			17.23±9.91		
Other	25.58±17.27			18.22±8.90		
Disease diagnosis						
0-2 years	30.46±13.41	**3.606**	**.032**	13.77±8.27	.882	.606
3-5 years	33.91±10.61			14.39±8.86		
6 years and above	35.98±12.26			16.10±7.90		
Duration of care						
0-2 years	23.87±28.62	**4.521**	**.000**	12.73±6.68	5.941	0.051
3-5 years	23.50±3.61			18.27±8.93		
6 years and above	35.50±6.44			19.61±10.34		
Presence of other people caring for the patient						
Yes	25.51±17.21	**4.214**	**.000**	11.04±9.71	-2.308	**.031**
None	35.41±9.71			15.83±7.79		

Table 3. *The relationship between caregivers' care burden and depression scores*

	BDI	
ZCBS	r=.588	p=.000*

**p<.05*

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RARE VARIANT IN THE PTEN GENE CHARACTERIZED BY A VARIABLE PHENOTYPE WITHIN THE FAMILY

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ABSTRACT

Introduction: Bannayan-Riley-Ruvalcaba syndrome (BRRS) is a rare disease with childhood-onset and autosomal dominant inheritance, characterized by macrocephaly, intellectual disability, genital pigmentation, hamartomatous polyposis, lipoma, and vascular malformations [1]. Germline variants in the *PTEN* (protein tyrosine phosphatase and tensin homolog) gene have been detected in approximately 60% of BRRS cases [2]. *PTEN* is a tumor suppressor gene located at the q23 region of chromosome 10 and regulates several cellular functions such as cell growth, proliferation and migration [3]. BRRS is included in the *PTEN* hamartoma tumor syndromes and this group also includes Cowden syndrome (CS). The clinical findings of BRRS and CS may overlap. The same variant has been reported to cause clinical findings of both BRRS and CS in different individuals within the family. Therefore, BRRS/CS phenotypes are considered to be identical disorders with variable expressivity and age-related penetrance [1].

Case presentation: A 20-year-old case was referred to the medical genetics outpatient clinic due to a nodular mass in the right lumbar region, gynecomastia, widespread comedones at the face and upper body, and mental retardation. The parents of the case were not consanguineous, and the mother had signs of macrocephaly, facial comedones, and subcutaneous hemangioma. It was learned that the patient's motor development stages were on time, but he received special education. On physical examination, macrocephalic appearance, downslanting palpebral fissures, high palate, widow's peak, full lips, gynecomastia, widespread comedones on the face and body, facial papular lesions, pectus excavatum, nodular mass in the right lumbar region, multiple skin tag on the trunk, pigmented macular lesions on the glans penis were present. Based on these findings, conventional cytogenetics and *PTEN* gene sequence analyses were performed, considering BRRS in the preliminary diagnosis. The case's karyotype was normal. A heterozygous c.1027-1G>A variant was detected at intronic region of the PTEN gene. The variant was classified as a likely pathogenic according to ACMG (American College of Medical Genetics) criteria. Segregation analysis was performed and the same variant was detected in the mother. Maternal clinical characteristics are more compatible with the CS phenotype. Genetic counseling was given. The proband and his mother were referred to the relevant departments due to possible accompanying findings and increased risk of malignancies.

Conclusion: A rare variant in the *PTEN* gene was detected in this case. The same variant within a family may exhibit variable phenotypic features. Follow-up of these patients and their families is important for early diagnosis.

Keywords: *Bannayan-Riley-Ruvalcaba syndrome, PTEN, PTEN hamartoma tumor syndrome*

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REMISSION IN GALLBLADDER CANCER WITH OLAPARIB AND PEMBROLIZUMAB TREATMENT AFTER SURGERY: CASE REPORT

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ABSTRACT

Background

Gallbladder cancer, though rare, is a significant health concern, often diagnosed at advanced stages due to nonspecific symptoms. Risk factors include age, gender (more common in women), gallstones, race, and certain medical conditions. Diagnosis primarily relies on imaging techniques like ultrasound, CT, MRI, and angiography. Common clinical symptoms include abdominal pain, jaundice, fever, and weight loss.

Histopathologically, adenocarcinoma is the most common type, while other variants like undifferentiated carcinoma and sarcoma can also occur. Surgical resection remains the primary curative approach, but the long-term prognosis is challenging.

Chemotherapy, including drugs like 5-fluorouracil, mitomycin C, and cisplatin, is used for treatment. Recently, immunotherapy has shown promise, with drugs like pembrolizumab (PD-1 inhibitor) and olaparib (PARP inhibitor) offering new avenues for treatment.

Case

We present a case of a 62-year-old patient diagnosed with stage 4 gallbladder adenocarcinoma following cholecystectomy in 2019. After initial chemotherapy with FOLFIRINOX, genetic testing revealed mutations in genes like BRCA2 and TP53. The patient then participated in a clinical trial receiving olaparib and pembrolizumab, resulting in a remission period after two years.

Conclusion

Gallbladder cancer is challenging to diagnose and treat, but emerging therapies like immunotherapy hold promise for improved outcomes. This case highlights the potential benefits of targeted therapies based on genetic mutations.

Introduction

Gallbladder cancer is a rare type of cancer, accounting for only 0.6-3% of all cancers [1,2]. While it is the most common cancer of the hepatobiliary system [1,2], it ranks fifth in frequency (2-4%) among gastrointestinal system cancers and is the ninth leading cause of death due to gastrointestinal system cancers [3-9]. It is more commonly observed in women than men [10,11]. There are five main predisposing factors for the development of gallbladder cancer: age, female gender, gallstones, specific race/ethnicity/geographical distribution, and ulcerative colitis [7]. Gallbladder polypoid lesions, genetic predisposition, chemical carcinogens, anatomical variations in the pancreatic-biliary ductal system, porcelain gallbladder, primary sclerosing cholangitis, and carrier status for typhoid are other possible etiological factors [3,8]. Gallbladder cancer is usually seen in the elderly population, with over 75% of cases occurring in patients aged 65 and older [12].

Gallbladder cancers do not have specific symptoms. Hematological and biochemical parameters are not usually significant in diagnosis. The preoperative diagnosis of gallbladder cancer is typically made using imaging

techniques. Ultrasound (USG), endoscopic ultrasound (EUS), computed tomography (CT), magnetic resonance imaging (MRI), and selective/superselective angiographies are commonly used methods for diagnosis.

Clinical symptoms and findings include abdominal pain, jaundice, fever, and weight loss [13]. There is no typical symptom for early diagnosis. Despite advances in imaging techniques, the diagnosis is often made at advanced stages or during surgery.

Adenocarcinoma accounts for over 90% of cases [1,12]. Other histopathological types, in order of frequency, are undifferentiated carcinoma, adenosquamous carcinoma, sarcoma, carcinoid tumor, melanoma, lymphoma, and leiomyosarcoma [12]. Fibrous histiocytoma and myxoid tumors are seen very rarely [12]. In 3% of cases, a combination of these cell types is detected. In 70% of patients, the tumor is well-differentiated, approximately 50% produce mucus, and 40% are papillary in type.

In patients with a preoperative diagnosis of a benign disease who undergo cholecystectomy, the specimen should be opened in the operating room by the surgeon before awakening the patient and examined macroscopically. If any suspicious nodules or mucosal abnormalities are present, a "frozen section" should be requested, and if carcinoma is detected, the extent of invasion into the wall of the tumor must be investigated. If the lesion is limited to the mucosa, simple cholecystectomy is sufficient. If the tumor penetrates the gallbladder wall or beyond, and there are no signs of distant spread, a "wedge" resection of the neighboring liver tissue and regional lymph node dissection should be performed in addition to cholecystectomy. After determining the N level with the "frozen section," resection surgery is performed. In cases where resection is not possible, the decision to perform palliative drainage (bypass) to the biliary tract and stomach should be made based on intraoperative findings. The basic principle in the surgical treatment of gallbladder cancer is to remove all areas containing tumor as a whole, including infiltrated neighboring organs and regional lymph nodes (unblock resection). Radical resection should be a surgical method that leaves no macroscopic or microscopic residual tumor, has a low risk of morbidity, can be safely and easily applied, and provides a significant extension in survival.

Various drugs are used in chemotherapy for the treatment of gallbladder cancer. Fluoro-pyrimidines, including 5-fluorouracil (5-FU), 5'-fluoro-2'-deoxyuridine (FUdR), and deoxyfluridine (dFUR), are the most commonly used systemic chemotherapy (CT) agents [14]. Mitomycin C (MMC), cisplatin (CDDP), and anthracyclines such as adriamycin (ADM) and epirubicin (EPI) are other CT agents used [14-16].

Pembrolizumab, a programmed cell death protein 1 (PD-1) inhibitor, is being used as a new treatment option. Olaparib, a PARP inhibitor, has been approved by the United States for use.

Treatment with the anti-PD-1 antibody pembrolizumab has been shown to improve clinical outcomes in many previously treated advanced tumors. Olaparib, a poly (ADP-ribose) polymerase (PARP) inhibitor, has shown antitumor activity as monotherapy in previously treated advanced ovarian, breast, pancreatic, gallbladder, and prostate cancers with BRCA1/BRCA2 mutations (BRCAm).

Pembrolizumab and olaparib are referred to as immune checkpoint inhibitors (ICIs), and these treatments have fundamentally reshaped the treatment of many malignancies by providing significant improvements in survival outcomes.

Pembrolizumab has been approved to treat inoperable or metastatic tumors in patients who have progressed after prior treatment, regardless of histology.

In this report, we aim to describe the remission process of a patient who was diagnosed with stage 4 gallbladder adenocarcinoma after cholecystectomy in 2019 and underwent olaparib and pembrolizumab treatment.

Case Presentation

In 2019, a 62-year-old patient with no underlying diseases was admitted to the hospital due to abdominal pain and bloating. The patient was hospitalized for follow-up due to these complaints. During the follow-up period, it was observed that the gallbladder was edematous, and an MRI was performed due to suspected gallbladder perforation. Perforation was not observed. One year later, the patient was admitted to the hospital

again with a recurrence of cholecystitis. Investigations during this admission revealed two different opinions: one suggested the presence of a mass that could be a tumor, and the other suggested the possibility of an abscess. Biopsy was performed, and an abscess was aspirated. The patient was prepared for surgery. Intraoperatively, gallbladder cancer was detected. Cholecystectomy and removal of the invasive tumor tissue were performed. Liver metastasis was also observed. After postoperative treatment, the patient was referred to oncology with a diagnosis of stage 4 gallbladder adenocarcinoma.

As the initial chemotherapy protocol, the patient received FOLFIRINOX treatment.

Fol: Folinic acid F: Fluorouracil Irın: Irinotecan Ox: Oxaliplatin

The patient received a total of 12 cycles of FOLFIRINOX protocol with a 6+6 schedule. Oxaliplatin was later discontinued in the treatment. The patient continued with this treatment. Upon recurrence observed in the PET scan, the patient was switched back to FOLFIRINOX. Genetic testing was performed during the treatment, and mutations were identified.

MSI genes were intact as determined by immunohistochemical methods. PD-L1 Expression Information: No expression was detected.

PATHOGENIC AND POSSIBLE PATHOGENIC MUTATIONS RTEN: Variation present TP53: Variation present PTEN: Variation present BRCA2: Variation present CERBB2: Variation present

The patient was enrolled in a clinical trial based on these mutations. The patient received olaparib and pembrolizumab treatment for 2 years. After 2 years, the study concluded, and immunotherapy was discontinued. The patient continues to receive olaparib treatment. According to the latest imaging tests, the patient has entered a remission period.

Discussion

Gallbladder cancer is a rare, aggressive cancer, especially in older individuals, and it ranks fifth among gastrointestinal cancers. It often presents with right upper quadrant pain clinically, while weight loss and jaundice are less common symptoms [17]. The diagnosis of gallbladder cancer is often delayed because the disease's clinical course resembles benign gallbladder diseases. Only one-third of patients can receive a correct diagnosis during the preoperative period.

Currently, surgery remains the main curative approach for patients with gallbladder cancers, and surgical resection has been shown to improve short-term survival outcomes in these patients. However, the long-term prognosis after surgery remains insufficient.

The 5-year survival rate for all gallbladder cancers is less than 15%. In stage 4, the average survival is limited to only three months from the time of diagnosis [6].

In conclusion, gallbladder squamous cell carcinoma is a rare and more aggressive tumor compared to adenocarcinoma. In our case, the tumor was adenocarcinoma, and treatment included a Programmed cell death protein 1 (PD-1) inhibitor and a PARP inhibitor.

Programmed death-ligand 1 (PD-L1) is a protein encoded by the CD274 gene in humans. PD-L1 expression is one of the ways that tumor cells inhibit the cancer immunity cycle. T lymphocytes need to engage with PD-1 on their surface and PD-L1 extensions on the tumor surface to successfully eliminate cancer cells. However, when PD-L1 produced by tumor cells binds to the PD-1 receptor on the surface of T lymphocytes, the binding of lymphocytes to the tumor is prevented. In this way, cancer cells evade the immune system's defense. Our patient's treatment was initiated based on this principle.

Conclusion

In this case, we determined that remission was achieved with olaparib and pembrolizumab treatment after cholecystectomy in 2019 for stage 4 gallbladder adenocarcinoma. Pembrolizumab and olaparib are referred to as immune checkpoint inhibitors (ICIs), and we are hopeful that this treatment regimen will completely reshape the treatment of many malignancies by providing significant improvements in survival outcomes.

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INVESTIGATION OF THEORETICAL ACTIVITIES OF TRIAZOLE DERIVATIVE MOLECULES AGAINST PROSTATE CANCER PROTEINS

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ABSTRACT

Prostate cancer is the second most common cancer that causes death in men worldwide, after lung carcinoma. Although early treatment and preventive medicine practices come to the fore in the form of PSA monitoring.Although it became easier to detect tumor development in patients with the emergence of tumors and subsequent needle biopsies [1], we did not have much possibility other than reproductive risk scoring schemes in terms of determining the reproduction of the tumor before, during and after specific treatment [2]. Nowadays, the connection signature and biology that we can use to determine specific treatment models of the person and to predict the prognosis in general without advanced stage are important. In this regard, the pathogenesis and biological functioning of prostate cancer is a disease that will be guided by medical professionals [3].

In this study, the chemical and biological activities of triazol derived molecules will be compared. First, triazol derived molecules, Calculations were made on 6-31^{++}G(d,p) basis set at HF, M062X, and B3lyp levels. Afterwards, these molecules were characterized by IR, ^{1}H NMR, ^{13}C NMR and UV-Vis spectrum analysis. Additionally, molecular docking calculations of the studied molecules were performed for prostate cancer (PDB ID: 6XXP and 3RUK).

Keywords: *Computational, DFT, spectrum, Triazol, docking*

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ASSESMENT OF THE RELATIONSHIP BETWEEN ENDOMETRIAL CANCER AND SYSTEMIC INFLAMMATION

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ABSTRACT

Objective

The relationship between endometrial cancer and systemic inflammation has been evaluated in recent years, particularly in terms of pre-treatment assessment, lymph node metastasis, and prognosis prediction. However, a conclusive consensus on this topic has yet to be reached. This study is based on the retrospective data from a tertiary center study conducted on patients who underwent surgery for endometrial cancer in our clinic within the past 2 years. The aim of this research is to assess the potential effects of age, gravidity, parity, hemoglobin (Hb), platelet (PLT), white blood cell count (WBC), lymphocyte count (LYM), monocyte count (MONO), and calculated systemic inflammatory indexes (NLR, PLR, LMR, dNLR, SII, SIRI, PIV) on the diagnosis and prognosis of endometrial cancer.

Methods

This study is based on the analysis of retrospective data from endometrial cancer patients treated at a single center. Patient data including age, obstetric characteristics, and hematologic parameters were recorded. Systemic inflammatory indexes were calculated using the following formulas: NLR (Neutrophil-to-lymphocyte ratio), PLR (Platelet-to-lymphocyte ratio), LMR (Lymphocyte-to-monocyte ratio), dNLR (Derived NLR ratio - neutrophil count divided by the result of leucocyte count minus neutrophil count), SII (Systemic inflammatory index - neutrophil x platelet / lymphocyte), SIRI (Systemic inflammatory response index - neutrophil x monocyte / lymphocyte count), and PIV (Pan-immune inflammation value - neutrophil x platelet x monocyte / lymphocyte count).

Results

Our study includes 21 patients who underwent surgery for endometrial cancer in our clinic within the past 2 years. We examined the relationships between age, obstetric characteristics, and hematologic parameters in endometrial cancer patients. The results indicated that the mean age was 56.6 years, with an average gravidity of 3. The average hemoglobin level was within the normal range at 12.7. The mean values for the systemic inflammatory indexes were as follows: SII (694.6 ± 319.1) SIRI (1.4 ± 0.9) PIV (346.8 ± 137.2), NLR (2.9 ± 2.6), PLR (147.3 ± 51.7), LMR (4.1 ± 1.43), and dNLR (2.03 ± 1.6). In conclusion, the relationship between endometrial cancer and systemic inflammation is a significant focal point for future cancer research and treatments. Current research findings in this area may contribute to a better understanding of this relationship and improve the healthcare of patients.

Keywords: *Endometrial cancer, systemic inflammation, pan-immun inflammation value, systemic inflammatory index*

Introduction

The idea of assessing systemic inflammation in endometrial cancer, as in other cancers, is based on the hypothesis that chronic inflammation may play a role in cancer development. Chronic inflammation can lead to cellular damage, genetic mutations, and the formation of cancer cells.

Systemic inflammatory indexes are combinations of parameters measured through blood tests ((such as leucocyte, lymphocyte, monocyte, platelet count) and reflect the inflammatory response in the body. Among these indexes, there are well-known ones like SII (Systemic Inflammatory Index), NLR (Neutrophil-to-Lymphocyte Ratio), and PLR (Platelet-to-Lymphocyte Ratio), which have been studied in various cancer types. In recent years, studies examining the relationship between endometrial cancer and systemic inflammation have raised [1-3].

Several studies suggest that elevated SII, NLR, or PLR values may increase the risk of endometrial cancer and impact prognosis [2]. These indexes have also been linked to the ability of cancer cells to metastasize and grow [3]. The role of systemic inflammatory indexes in the treatment and monitoring processes of endometrial cancer patients is also under investigation. These indexes can assist in determining patients' response to treatment, lymph node metastasis and their risk of recurrence. Furthermore, in recent years, systemic inflammatory indexes have been used to predict the presence of lymph node metastasis in endometrial cancer [4]. The exact mechanisms underlying the relationship between endometrial cancer and systemic inflammation are still not clear, and further research is needed. Studies in this field can help us better understand this relationship and optimize the treatment processes for patients.

Method

This study is conducted based on the retrospective analysis of data from patients diagnosed with endometrial cancer who received treatment. The patients included in this study are those who underwent surgical intervention for endometrial cancer within the past two years at a single medical center. All of these patients have received a definitive diagnosis of endometrial cancer and conform to the FIGO 2009 stage I-III classification [5].

Exclusion and Inclusion Criteria

Specific exclusion and inclusion criteria were applied in the selection of participants for our study.

The inclusion criteria comprise patients who meet the following criteria:
Diagnosis of endometrial cancer.
Treatment at a single center.
Availability of complete records of hematologic parameters and obstetric characteristics.

The exclusion criteria encompass:
Presence of other cancer types or serious systemic illnesses.
Patients with missing data or incomplete records during the treatment process.

Data Collection

The necessary data for this study were retrospectively collected from the medical records of the patients. Demographic information including age and obstetric characteristics (gravida and parity) of the patients was recorded.

Hematologic Parameters

Hematologic parameters were obtained using the results of routine blood tests conducted on the patients. These parameters include hemoglobin levels, leucocyte, lymphocyte count, monocyte count, and platelet count. These data were utilized in the calculation of the patients' systemic inflammatory indexes.

Systemic Inflammatory Indexes

In this study, the prominent indexes used in the calculation of systemic inflammatory indexes are as follows: Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), Lymphocyte-to-Monocyte

Ratio (LMR), derived NLR (dNLR), Systemic Inflammatory Index (SII), Systemic Inflammatory Response Index (SIRI) and Pan-immune Inflammation Value (PIV).

The collected data were used for statistical analysis. The data analysis aimed to investigate potential relationship between the patients' cancer diagnosis and systemic inflammatory indexes. These analyses were conducted to assess the characteristics of patient groups and their outcomes. The study includes 21 endometrial cancer patients treated at the same center within the last two years. The obtained results provide a comprehensive analysis, including patients' age, obstetric characteristics, and hematologic parameters. Mean values for the systemic inflammatory indexes are separately reported.

Results and Discussion

The study includes 21 endometrial cancer patients treated at the same center within the last two years. The data were analyzed by means of IBM SPSS 22 statistical program for statistical analysis.. Whether the data showed normal distribution or not was determined by Kolmogorov-Smirnov test. Data are reported as Mean ± SD.

The results were calculated individually for each systemic inflammatory index, and the findings are presented in Table 1. In our study, the mean age of the patients was 56.6, and the average parity of the patients was 3,3.

In a study conducted by Aoyama and colleagues in 2019, aiming to determine whether pretreatment NLR (Neutrophil-to-Lymphocyte Ratio) and PLR (Platelet-to-Lymphocyte Ratio) serve as predictors of lymph node (LN) metastasis in 197 patients with endometrial cancer, a relationship was found between lymphovascular invasion and NLR. The study identified a cutoff value of 2.18 for NLR [2]. In our study, the average NLR was found to be 2.91, which is higher.

In a study conducted by Holub and colleagues, which included 155 patients and aimed to assess the effects of systemic inflammatory factors on survival outcomes, NLR, SII, and lymphopenia were associated with decreased survival. Similarly, in our study, NLR was found to be high (2.9) and lymphopenia was observed (2.1), which is consistent with this study [3].

In a study conducted in 2021 involving 392 cases of endometrial cancer to predict lymph node metastasis by assessing systemic inflammation, those with lymph node metastasis had an SII of 636.74 or higher. In our study, the average SII was 694.62, which is in line with this study, indicating a high SII [4].

Table 1.

Parameters	Endometrial Cancer (n=21) Mean ±SD
Age (years)	56..6 ± 8.4
Gravida	3.3 ± 1.8
Parity	2.7 ± 1.3
Hemoglobin (g/dl)	12.7 ± 1.5
Neutrophil (10^9/L)	4.7 ± 1.4
Lymphocyte (10^9/L)	2.1 ± 0.7
Platelet (10^9/L)	283.2 ± 88.1
NLR	2.91 ± 1.6
PLR	147.3 ± 51.7
SII	694.6 ± 319.1
SIRI	1.4 ± 0.9
PIV	346.8 ± 137.2
LMR	4.1 ± 1.43
dNLR	2.0 ± 1.6

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, dNLR: Derived NLR ratio (neutrophil count divided by the result of leucocyte count minusneutrophil count), SII: Systemic inflammatory index (neutrophil x platelet / lymphocyte), SIRI: Systemic inflammatory response

index (neutrophil x monocyte / lymphocyte count) and PIV: Pan-immune inflammation value (neutrophil x platelet x monocyte / lymphocyte count).

Conclusion

Increased SII, NLR and PLR, as well as decreased lymphocytes, are observed in endometrial cancer in this paper. This study highlights the potential role of systemic inflammatory indexes in patients with endometrial cancer. Further research into the clinical application of these indexes may contribute to better guiding the diagnosis and treatment processes for patients. Larger sample sizes and long-term follow-up studies will be beneficial in providing further insights into these findings.

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INVESTIGATION OF THEORETICAL ACTIVITIES OF AMINOPHENYL DERIVATIVE MOLECULES AGAINST ENDOMETRIAL CANCER PROTEINS

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ABSTRACT

Endometrial cancer is the most common gynecological cancer in women and its incidence is increasing worldwide. Although an aging population and fewer benign hysterectomies have contributed to this trend, the main underlying cause is the increasing prevalence of obesity. The early onset of postmenopausal bleeding allows most endometrial cancers to be treated with hysterectomy, but those with advanced disease have a poor prognosis [1]. Minimally invasive surgical staging and sentinel lymph node biopsy provide a low-morbidity alternative to historical surgical treatment without compromising oncological outcomes [2]. The cornerstone of endometrial cancer treatment is surgery; This is not only important for staging, but also enables appropriate tailoring of adjuvant treatment methods that will benefit only high-risk patients.

In this study, the chemical and biological activities of aminophenyl derived molecules will be compared. First, aminophenyl derived molecules, Calculations were made on 6-31^{++}G(d,p) basis set at HF, M062X, and B3lyp levels. Afterwards, these molecules were characterized by IR, ^{1}H NMR, ^{13}C NMR and UV-Vis spectrum analysis [3]. Additionally, molecular docking calculations of the studied molecules were performed for endometrial cancer (PDB ID: 3UUD and 5F6E).

Keywords: *Computational, DFT, spectrum, Aminophenyl , docking*

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INVESTIGATION OF THE THEORETICAL ACTIVITIES OF PHENYLMETHAMINE DERIVED MOLECULES AGAINST BREAST CANCER PROTEINS

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ABSTRACT

Breast cancer is one of the most common types of cancer worldwide. This type of cancer occurs when cells in the breast tissues grow and multiply abnormally and usually affects women [1]. BRCA1 gene is a gene that plays an important role in repairing damage to DNA and regulating the healthy growth of cells. Mutations in the BRCA1 gene in breast cancer increase the risk of breast cancer. Breast cancer is more common in people carrying such mutations [2]. Estrogen is a hormone that plays an important role in breast cancer. Estrogen is a hormone that contributes to the controlled proliferation of breast cancer cells and the normal development of breast tissue [3]. Long-term exposure to estrogen may increase the risk of breast cancer [4].

Molecules designed from phenylmethanemine derivatives have been studied for their effects on breast cancer. For this purpose, calculations were first made on the 6-31++g(d,p) basis set at B3LYP, HF, and M062X levels using the Gaussian package program. IR, NMR and UV spectrum analyzes were performed for the characterization of the molecules using the optimized structures obtained from these calculations. Afterwards, in order to examine the activities of the studied molecules against breast cancer, their activities against the estrogen receptor and BRCT repeat region receptors, which are breast cancer receptors, were compared. Afterwards, ADME/T analysis was performed to examine the drug properties of the studied molecules [5].

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INVESTIGATION OF THEORETICAL ACTIVITIES OF PHENYLMETHAMINE DERIVATIVE MOLECULES AGAINST GASTRIC CANCER PROTEINS

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ABSTRACT

The stomach is an important organ where food is digested, and gastric juice and enzymes are produced [1]. Stomach cancer is the fourth most common type of cancer in the world. It is a type of cancer that occurs as a result of uncontrolled growth of cells on the surface of the stomach. This uncontrolled growth causes tumorization [2]. Environmental and genetic factors play a role in this type of cancer. Helicobacter pylori is the environmental factor that causes this type of cancer [3]. Molecules such as E-cadherin gene mutations and EGF oncogenes play a role in genetic factors. Mutations of the E-cadherin gene may facilitate the invasion of cancer cells by reducing cell adhesion [4]. Excessive activation of EGFR can support tumor growth.

The effects of molecules designed from phenylmethanamine derivatives on stomach cancer have been investigated. For this purpose, first of all, calculations were made on the basis of 6-31++g(d,p) determined at B3LYP, HF and M062X levels using the Gaussian package program. Using the optimized structures obtained from these calculations, IR, NMR and UV spectrum analyzes were performed for the characterization of the molecules. Then, in order to examine the activities of the examined molecules against stomach cancer, receptors such as HDAC (Histone Deacetylase) (PDB ID: 4BKX) and mTOR (PDB ID: 4JR6) (Mammalian Target of Rapamycin), which are thought to be effective on stomach cancer, were examined. ADME/T analysis was performed to examine the drug properties of the studied molecules [5].

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INVESTIGATION OF THE ANTIPROLIFERATIVE EFFECT OF N-(P-AMYLCINNAMOYL) ANTHRANILIC ACID ON THE AGS AND SNU-1 CELL LINES

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ABSTRACT

Gastric cancer is a highly prevalent malignancy globally and is a major contributor to cancer-related mortality. According to statistics from the GLOBOCAN database, in the year 2020, there were over one million reported new cases of GC, leading to documented fatalities surpassing 768,793 [1]. While contemporary treatment options can induce remission in cancer patients, the significant concern lies in the adverse effects associated with current medications, which restrict physicians' ability to employ existing treatment approaches [2]. Within this context, it is imperative to conduct further research aimed at creating novel pharmaceutical drugs characterized by reduced side effects. The aim of this study was to investigate the antiproliferative effect of N-(p-amylcinnamoyl) anthranilic acid, a TRPM2 antagonist, on the AGS and SNU-1 cells. Using XTT test, the effect of the drug on the survival of AGS and SNU-1 cell lines was investigated. These cells were cultivated at a concentration of 1×10^4 cells per well and incubated overnight before the addition of the drug. After that, the different concentrations of the drug (from 6.25 to 400 µM) were applied. Cells that were not subjected to treatment were used as a control group. Following the incubation period, 50 µL of an XTT solution was introduced into each well. After an additional 4-hour incubation, the cells were gently stirred, and their absorbance was measured at 450 nm using a microplate reader. Cell viability was determined as the percentage of live cells relative to untreated cells, and each experiment was replicated three times [3,4]. Statistical analysis of the data was conducted using One Way ANOVA, and significance was established at a threshold of $p<0.05$. It was observed that N-(p-amylcinnamoyl) anthranilic acid did not exert any antiproliferative effect on the two cells when compared to the control ($p > 0.05$). N-(p-amylcinnamoyl) anthranilic acid cannot cause anticancer effect against gastric cancer.

Keywords: *N-(p-amylcinnamoyl) anthranilic acid, gastric cancer, AGS cell line, SNU-1 cell line, antiproliferative effect*

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COLONOSCOPY-BASED EARLY DIAGNOSIS OF COLORECTAL CANCER: A SINGLE-CENTER RETROSPECTIVE STUDY AND LITERATURE REVIEW

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ABSTRACT

Introduction

This study explores the application of fiber optic and video technologies in healthcare, particularly in colonoscopy, a critical method for colorectal disease diagnosis and treatment. Colorectal cancer is a prevalent global malignancy, making early detection vital. Despite its benefits, colonoscopy can lead to complications. This article presents a retrospective analysis of 1078 colonoscopies conducted between June 2021 and June 2023 at Cumhuriyet University's Department of General Surgery. The study examines patient demographics, presenting complaints, and outcomes, alongside a comprehensive literature review.

Methods

Patients underwent pre-colonoscopy preparation involving dietary restrictions, sodium phosphate intake, and enemas. Procedures were performed using Fujinon equipment. Data analysis utilized SPSS 24.0 for statistical examination.

Results: Among 1078 patients [560 women, 518 men], average age 58.7, 49.6% had no pathology, 9.55% had colorectal cancer, 15.2% had polyps, 17.1% had diverticula, 8.2% had colitis, and 20.8% had benign proctological diseases. One patient experienced colon perforation, necessitating surgical intervention, while three patients developed post-polypectomy bleeding, which resolved without blood transfusion.

Discussion

Colonoscopy is essential for diagnosing rectal and colon diseases. Detecting conditions like hemorrhoids, fissures, and cancer emphasizes its importance in elderly patients. Complications like bleeding and perforation are known, with our perforation rate [0.9%] aligning with literature. Polyp detection [15.2%] and cecal intubation [92%] rates were also consistent with previous studies.

Conclusion

This study underscores colonoscopy's efficacy in early colorectal disease detection, affirming its potential to enhance patients' quality of life and survival. Widespread access to colorectal cancer screening and colonoscopy is imperative.

Introduction

Today, developments in fiber optic and video technologies are used in many places in the healthcare field. Colonoscopy is a standard method used for both imaging and treatment [1]. Apart from detecting cancer, colonoscopy is also used to diagnose inflammatory bowel diseases, stop lower gastrointestinal bleeding, and treat volvulus. Colorectal cancer is one of the most common types of cancer worldwide, and detecting the disease in the early stages is of critical importance to increase treatment success and improve patients' quality of life [2]. Since it is an invasive procedure, complications such as 0.24%-0.33% bleeding and 0.08%-0.19% perforation have been reported [3]. In this article, we aimed to present a retrospective analysis of the results of

colonoscopies performed in the endoscopy unit of the Department of General Surgery at Cumhuriyet University and, at the same time, to present a comprehensive literature review to support these results and deepen the existing knowledge.

Method

This retrospective analysis examined data from colonoscopies performed between June 2021 and June 2023 in the endoscopy unit of Cumhuriyet University's general surgery department. A total of 1078 patients were evaluated in detail in terms of colonoscopy results and histopathological evaluations, along with demographic information such as age, gender, and family history. The patients' presenting complaints are defecation problems, occult blood positivity in the stool, iron deficiency anemia, rectal bleeding, and colon-related abnormalities detected during radiological imaging. In preparation for the colonoscopy procedure, patients were placed on liquid food 2 days before the procedure. One day before the procedure, two 45 cc sodium phosphate bottles were given to the patients with plenty of water and enemas were applied to the patients the night before and the morning of the procedure. All procedures were performed with a Fujinon brand device. The analysis involved statistical examination of these data. SPSS 24.0 program was used for statistical analysis.

Results

In the sample of 1078 patients in our clinic, 560 of the patients were women, and 518 were men. Their ages range from 19 to 92. The average age is 58.7. No pathology was detected in 535 [49.6%] of the patients. Colorectal cancer was detected in 103 [9.55%] patients. Polyp was detected in 164 [15.2%] patients, diverticula in 185 [17.1%] patients, colitis [ulcerative colitis, Crohn's, infectious colitis] in 89 [8.2%] patients, and benign proctological diseases were detected in 225 [20.8%] patients. Colon perforation developed in one patient after the procedures. Since the patient's mass appeared malignant, the patient underwent left hemicolectomy + colocolonic anastomosis. Bleeding was observed in 3 patients after polypectomy. The patients were followed for 24 hours. None of them required a blood transfusion.

Discussion

Colonoscopy is a very commonly used method in the diagnosis and treatment of rectum and colon diseases [3]. The fact that some of the patients were diagnosed with diseases such as hemorrhoids and fissures, as well as cancer resulting from colonoscopy, shows the importance of colonoscopic screening, especially in elderly patients. Complications of colonoscopy encountered in the literature are bleeding and perforation. Bleeding usually occurs after polyp excision and biopsy with forceps. Bleeding occurred after polyp excision in all 3 of our patients who developed bleeding. Perforation usually occurs by straining the sigmoid colon as a result of looping. Mortality after perforation is as high as 15%[4]. In our patient, perforation developed while passing the mass, narrowing the lumen. Our perforation rate [0.9%] is similar to the literature. In previous studies conducted in Türkiye, the frequency of polyp detection in colonoscopy was reported as 11.1%, 13.3%, 14.4%, and 22%. In these studies, it was determined that most of the polyps were in the left colon. Depending on gender, the incidence rate in men has been reported to be between 59.3% and 76.4% [5,6,7,8]. Our polyp detection rate was found to be close to the literature at 15.2%. Another issue regarding the colonoscopy procedure is that it can proceed as far as the cecum, and even the terminal ileum can be visualized in patients where necessary. It has been reported in the literature that cecal intubation is generally performed in over 90% of cases in experienced centers. Our rate of reaching the cecum is 92%. Contrast-enhanced tomography was requested in 83 patients for whom we could not reach the cecum.

This study shows that colonoscopy has high success rates and low complications for early detection and screening of colorectal cancer. The effectiveness of colonoscopy once again emphasizes the fact that early diagnosis can improve a patient's quality of life and improve survival. Therefore, it is of great importance to disseminate and make accessible colorectal cancer screening and colonoscopy practices.

Conclusion

This study shows that colonoscopy has high success rates and low complications for early detection and screening of colorectal cancer. The effectiveness of colonoscopy once again emphasizes the fact that early diagnosis can improve a patient's quality of life and improve survival. Therefore, it is important to disseminate and make accessible colorectal cancer screening and colonoscopy practices.

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SMALL CELL NEUROENDOCRINE CARCINOMA OF THE CERVIX, SINGLE-CENTER EXPERIENCE

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ABSTRACT

Cervical neuroendocrine tumors, mainly small cell variants, constitute a mere 2 percent of all cervical malignancies. Characterized by its increased likelihood of metastasis and recurrence in comparison to squamous cell carcinoma and adenocarcinoma subtypes, small cell neuroendocrine carcinoma of the cervix (SCNEC) is a distinctive malignancy. It is susceptible to early distant metastasis and carries an adverse prognosis [1]. The preferred approach among most clinicians involves employing combined modality therapy for limited-stage potentially resectable disease, which includes surgery followed by chemotherapy or combined chemoradiotherapy. For locoregionally advanced unresectable but nonmetastatic disease, definitive chemoradiotherapy is favored. For patients with metastatic disease, the standard practice is to administer palliative chemotherapy alone, typically utilizing chemotherapy regimens commonly employed for small cell lung cancer [2].

At our institution, we conducted a retrospective analysis of patients diagnosed with cervical small cell neuroendocrine carcinoma. Between January 2010 and May 2023, records of patients diagnosed with cervical cancer were retrospectively reviewed. Among the 439 patients; 360 had squamous cell carcinoma, 51 had adenocarcinoma, 18 had adenosquamous carcinoma, 4 had SCNEC, 5 had epithelial carcinoma, and 1 had carcinosarcoma. The average age at diagnosis was 44.5 years (ranging from 33 to 65). Three patients had metastatic disease at diagnosis, one patient had locally advanced disease. All patients received platin based regimens for the first line treatment. Progression-free survival for fist line treatment ranged from 4 to 9 months. The overall survival of patients ranged from 9 months to 25 months.

Consistent with our cases SCNEC carries a poorer prognosis when compared to cervical squamous cell carcinomas or adenocarcinomas [3]. The optimal treatment standards remain undefined. The prognosis tends to be quite dismal, and patients are typically diagnosed in advanced stages.

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BIBLIOMETRIC ANALYSIS OF NURSING STUDIES ON SUPPORTIVE CARE NEEDS OF CANCER PATIENTS

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ABSTRACT

This bibliometric research was carried out to identify and visualize the trends in nursing researches on the supportive care needs of individuals with cancer in the area of nursing between 2013 and 2022 and to identify the recent advances in the field of nursing. Bibliometric analysis was performed using statistical and bibliometric visualizations. The "Web of Science Core Collection" data base was utilized to obtain the research data. The database was searched using the keywords "Supportive Care", "Supportive Care Needs", "Nursing", "Cancer Patient". It was seen that there were a total of 2089 researches in this field in the analyzed database. The number of researches that met the criteria for inclusion in the bibliometric analysis was 432. It was determined that the number of researches included in the research increased over the years, 200 authors from 55 different countries contributed to the researches, the researches were published in 168 different journals, the number of citations to 432 publications was 1215 in total, and the most frequently used keywords in the published researches were supportive care (n= 110), supportive care needs (n= 36) and unmet needs (n=36). Bibliometric researches provide guiding information for researchers who want to learn about the subject and conduct research. In this research, it was seen that there is a need for nursing researches to determine the supportive care needs of patients diagnosed with cancer and to analyze the results of the applied nursing interventions.

Keywords: *Supportive care, bibliometric analysis, nursing, cancer*

Introduction

Individuals diagnosed with cancer face many difficulties in psychological, physical, social and spiritual areas starting from they receive the diagnosis of the disease. Pain, inability to performing activities of daily living, lack of information, economic difficulties, changes in family relationships, deterioration in spiritual processes and changes in sexual life constitute a significant part of the problems associated with cancer diagnosis and affect the patient negatively throughout the process [1,2,3]. Nursing care of individuals diagnosed with cancer requires a careful approach to these processes and prioritizes individualized and supportive care [4,15]. In the literature on nursing care, patient-centered care is accepted as a criterion for quality care of individuals affected by chronic conditions such as cancer [4,15]. Diagnosing and meeting the supportive care needs of individuals from a holistic approach by putting the patient at the center provides effective care [3,4].

Supportive care is the identification and effective meeting of the patient's care needs with a patient-centered approach. Supportive care can be described as patient-centered, comprehensive care that should help the person diagnosed with cancer and his/her relatives to manage the diagnosis and treatment of cancer, and should be provided in all stages from preliminary diagnosis to the definitive treatment and diagnosis process, recovery or end-stage and death[5,6]. Throughout the cancer experience; situations such as information about the treatment and the care plan, getting acquainted with health professionals who will provide care, access to evidence-based information, receiving emotionally-oriented support, and some measures such as transportation, activities at home, support and prosthesis provision are accepted within the scope of supportive care needs [5,6,7]. Meeting supportive care needs will contribute to reducing boredom, low quality of life and satisfaction with the care and may prevent an increase in the use and the cost of healthcare resources.

In the field of nursing, researches on the supporting care needs of people with cancer tend to increase worldwide [8]. The increase in the number of researches makes it difficult for researchers to access current researches and follow the results. For this reason, it is important to identify the tendencies of the researches conducted in the nursing field on the supportive care needs of people with cancer, to map the latest developments and to identify research gaps.

Bibliometric analysis is the mapping of research conducted by people or institutions in a specific field, in a specific period and in a specific region, and the mapping of the relationships among such research and the numerical analysis of trends [9]. Bibliometric analysis method was first used by Wyndham Hulme under the name Statistical bibliographers, and this concept is considered as the examination of books or other media communication tools using mathematical and statistical methods [10]. The use of bibliometric methods for purposes such as quantitative analysis of scientific publications, seeing the change and development in science, analyzing the connections of any research with other researches, and revealing general trends in any subject or field is becoming increasingly widespread and increasing in various disciplines.

Although the use of bibliometric analysis in the field of nursing is new, the number of such researches conducted to identify trends and research gaps in the relevant subject has been increasing in recent years [11]. Bibliometric analysis researches can be performed through different programs. In our research, VOSwiever program was used for bibliometric analysis. VOSviewer was introduced by Nees Jan van Eck and Ludo Waltman (Leiden University) in 2010. VOSviewer is a software utility for building maps and exploring maps that are based on web data. It is designed to analyze primarily academic recordings, but can be used with any kind of web database [12].

There is no bibliometric analysis of researches on the supportive care requirements of individuals with cancer in the field of nursing in the literature. With this research, it is aimed to analyze the bibliometric characteristics of articles published in the field of nursing on the supportive care requirements of individuals with cancer and to contribute to the reflection of existing evidence, to learn about the structure of the supporting needs of people with cancer, to understand the research gaps and to develop innovative ideas for researches on the supporting care requirements of people with cancer.

This bibliometric research was carried out to identify the tendencies of the articles on the supportive care needs of individuals with cancer in the field of nursing between 2013 and 2022 and to illustrate the latest advances.

Method

In the current research, bibliometric research was conducted by using statistical and bibliometric visualizations to conduct a bibliometric analysis of the researches published in the area of nursing on the supportive care needs of people diagnosed with cancer. In this direction, the research examined the change in the publication numbers of the researches by number of years, analysis of authors, countries and institutions, journal and citation analyses, and word count analysis.

"Web of Science Core Collection" data base was utilized to obtain the data for the research. The "Web of Science Core Collection" database was preferred because it is compatible with the VOSviewer program, is the most widely accepted database for analyzing scientific publications, and provides access to citation statistics and bibliographic data of scientific publications. Data were collected between August and September 2023 in compliance with the included and excluded criterion.

Criteria for inclusion: Articles published in English between 2013 and 2022 in the field of nursing related to the supportive care requirements of individuals diagnosed with cancer.

Congress proceedings, book chapters, case researches, letters to the editor and case researches published in the relevant date range were determined as exclusion criteria.

"Supportive Care", "Supportive Care Needs", "Nursing", "Cancer Patient" " keywords were used and 2089 researches conducted between 1991 and 2023 were reached. Among these researches, the total number of researches published between 2013-2022 is 453. The number of researches that are not articles and reviews is

12 (papers, book chapters and editorial materials n=12). The number of researches whose language is not English is 9 (Korean=4, German=2, French=1, Polish=1, Russian=1). The number of researches meeting the criteria for inclusion in the bibliometric analysis is 432. In the analysis of the data; all bibliographic data obtained in the research were downloaded from the database. Bibliometric analysis was performed using the VOSviewer program, which allows uploading metadata from multiple files.

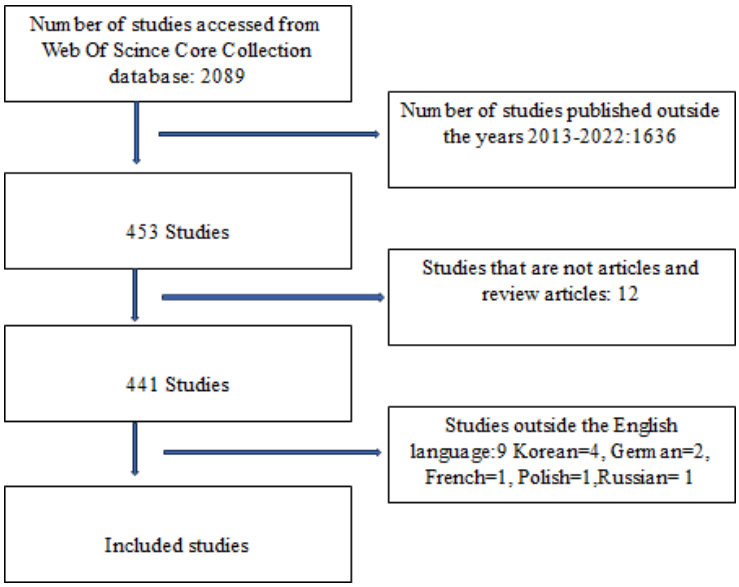


Figure 1. *Flow diagram of research data selection*

Since this research was not conducted on any individual and document analysis was used as a data collection method, ethics committee approval was not required.

Results and Discussion

Part 1.

Distribution of Researches by Year

Of the researches published in the field of nursing on the supporting care needs of individuals diagnosed as having cancer, 380 were articles and 52 were review articles. When the researches included in the research were analyzed according to years, it was seen that the number of researches in the relevant years varied between 66 and 29, with the most researches conducted in 2022 (n=66) and the least researches conducted in 2014 (n=29) (Figure 2). In addition, it was determined that 11 of the researches included in the research were conducted in randomized controlled design and 369 of them were descriptive.

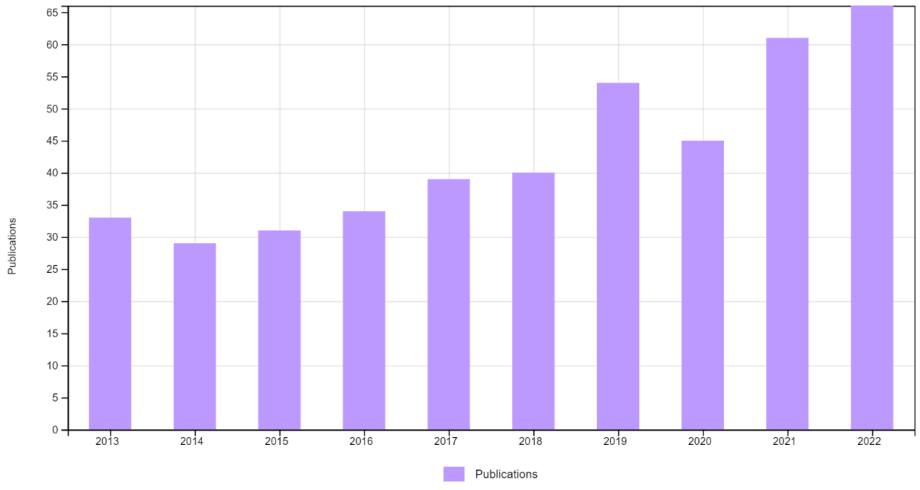


Figure 2. *Distribution of researches by years*

Figure 3. *Distribution of studies by type*

Table 1. *Distribution of researches by type*

Document Types	Record Count	% of 432
Article	380	87.963%
Review Article	52	12.037%

Author, Country and Institution Analyses

In the field of nursing, 200 authors from 55 different countries contributed to the researches published on the supportive care needs of people diagnosed with cancer. The top three authors who contributed the most to the literature on the subject are Karla Gough (n=9), Catherine Paterson (n=9) and Penelope Schofield (n=8). The top 10 countries contributing the most to published articles on the topic are the USA (n=105), Australia (n=78), the UK (n=42), Canada (n=34), Germany (n=28), China (n=27), the Netherlands (n=25), Sweden (n=21), Denmark (n=19) and Iran (n=18). 201 institutions contributed to the researches, with the top three institutions being the University of Sydney (n=26), the University of Melbourne (n=16) and the Peter Maccallum Cancer Center (n=15).

Table 2. *Top 10 authors who contributed the most to the subject, number and percentages of publications*

Field: Authors	Record Count	% of 432
Paterson C	9	2.083%
Gough K	8	1.852%
Schofield P	8	1.852%
Aranda S	5	1.157%
Butow P	5	1.157%
Kotronoulas G	5	1.157%
Krishnasamy M	5	1.157%
Maguire R	5	1.157%
Yates P	5	1.157%
Eicher M	4	0.926%

Journal and Citation Analysis

The researches published on the supportive care needs of the cancer-diagnosed individuals in the field of nursing were included in 168 different journals. The highest number of publications was in Supportive Care in Cancer (n=35). Supportive Care in Cancer was followed by Cancer Nursing (n=26), European Journal of Oncology

Nursing (n=26), Seminiars in Oncology Nursing (n=25), Journal of Clinical Nursing (n=24), Clinical Journal of Oncology Nursing (n=13), European Journal of Cancer Care (n=13), Oncology Nursing Forum (n=13), Pallaative supportive Care (n=11), Psycho Oncology (n=9).

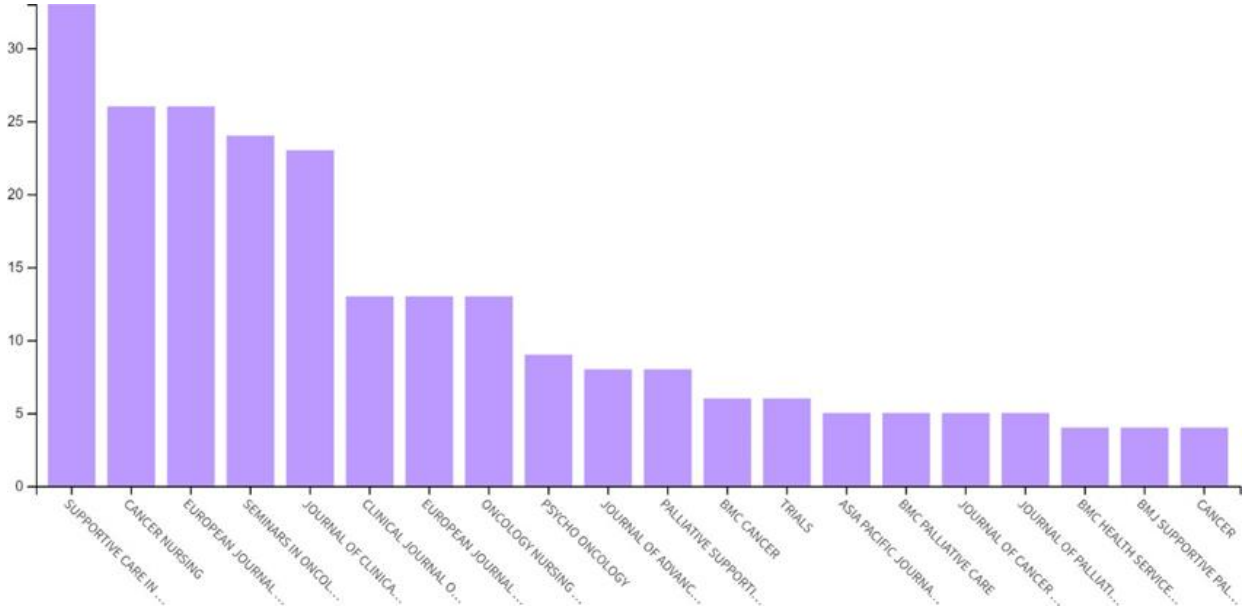
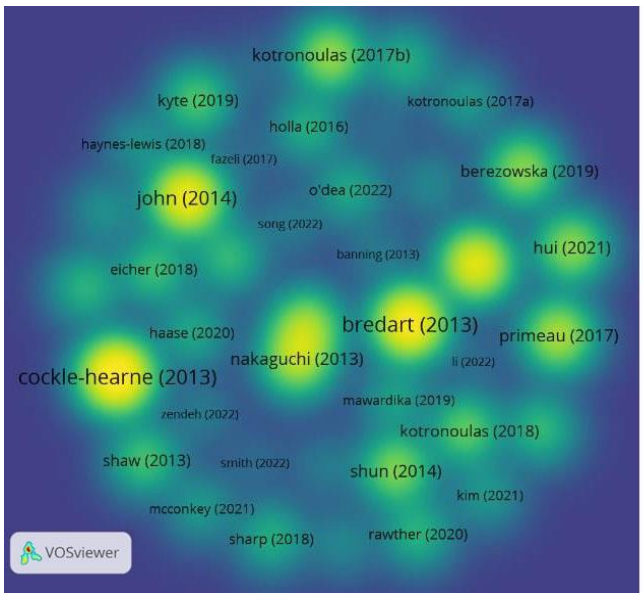
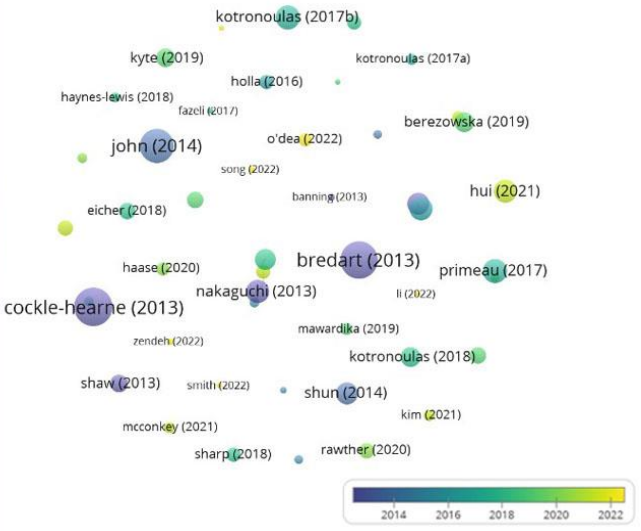


Figure 4. *Distribution of researches according to the journal in which they were published*

Citation analysis allows analyzing the relationships between publications by identifying the most influential publications in a research field [13]. Within the scope of citation analysis, it was seen that the h-index of the researches published on the supportive care needs of individuals diagnosed with cancer in the field of nursing was 33. The number of citations to 432 publications published on the subject is 1215 in total.

The most cited research (n= 298) is the publication titled "The effect of supportive nursing care on the needs of men with of prostate cancer: a research cross seven European countries" published by Cockle-Hearne J. et al. in 2013. This research is followed by the research titled "Assessment of needs, and health-related quality of life, and satisfaction with care in Breast cancer patients to better target supportive care" published by Brédart, A., Kop. et al. in 2013 with 271 citations. The research entitled " Inequalities in self-perceived unmet needs for supportive care among patients with lung cancer in the Cancer Care Outcomes Research and Surveillance Advisory Consortium" (n=173) was ranked third.





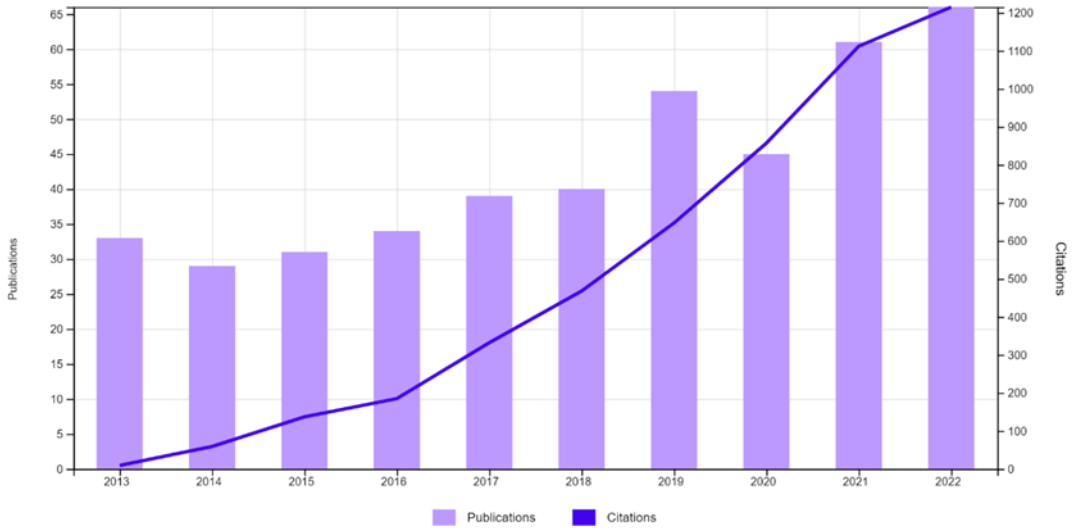
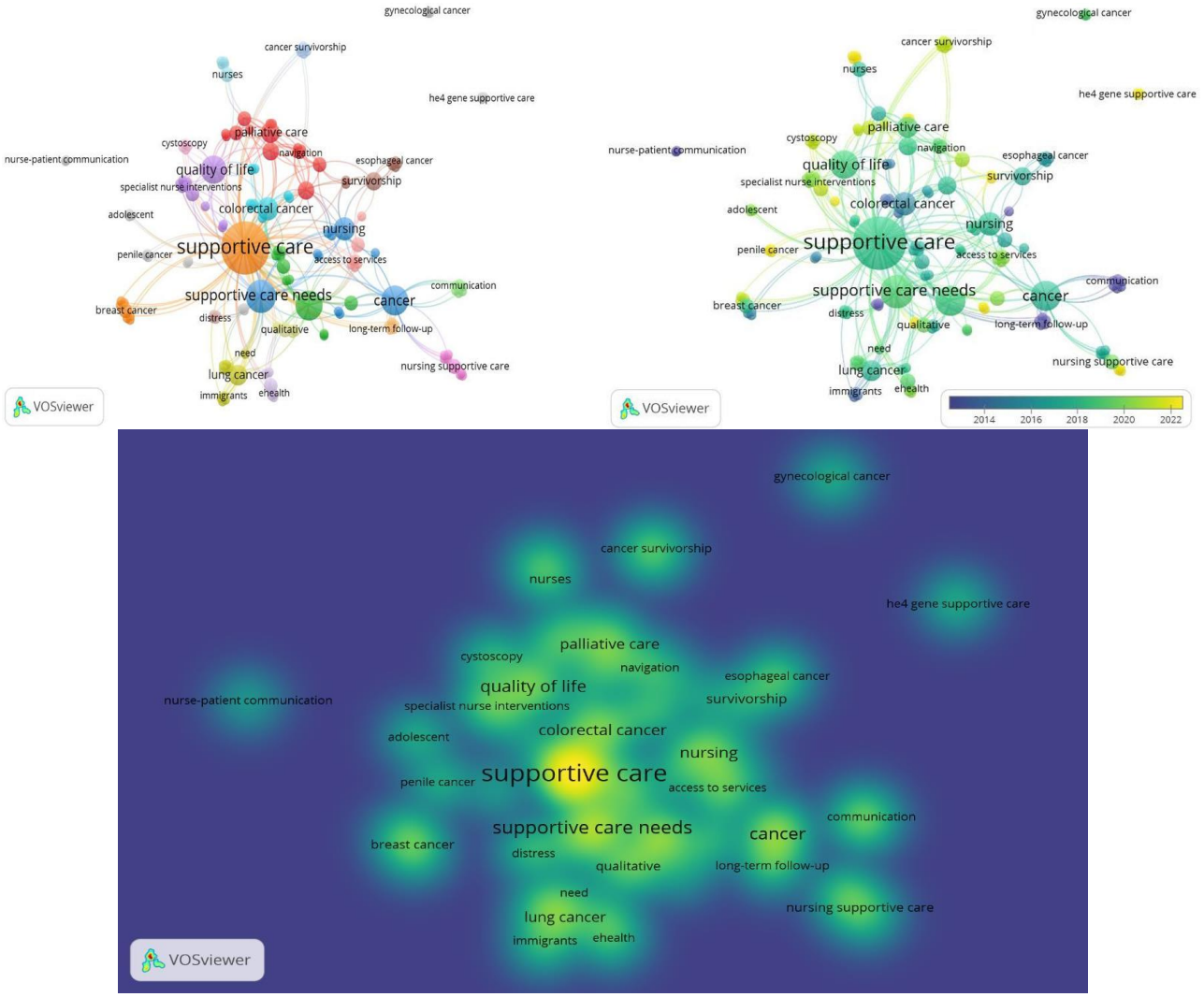


Figure 5. *Citation Analysis of Researches*

Word Analysis

In the word network analysis, the most commonly used keywords in published researches were analyzed. The top ten words analyzed were supportive care (n= 110), supportive care needs (n= 36), unmet needs (n=36), cancer (n=35), quality of life (n=28), nursing (n=21), colorectal cancer (n=20), lung cancer (n=18), palliative care (n=18), oncology (n=17).



Part 2.

In this research, a bibliometric analysis of 432 researches on the supportive care needs of people diagnosed with cancer in the field of nursing was conducted through the VOSviewer program. In the research, it was observed that the number of researches related to the supportive care needs of cancer patients published in the field of nursing has increased over the years. It can be said that this situation contributes to the deepening of the literature on the supporting care requirements of people diagnosed with cancer. It is thought that the rise in the number of people diagnosed with cancer over time, the evolution of nursing care to an individual-centered understanding and the increase in the quality of care have contributed to this interest and the increase in scientific productivity.

In the research, it was seen that Karla Gough, who ranked first in the list of authors who contributed to the researches published in the field of nursing on the supportive care needs of people diagnosed with cancer, had 9 researches, followed by 9 and 8 publications. This situation suggests that there are authors who produce consistent researches in the field of nursing regarding the supportive care requirements of people diagnosed with cancer. The most support for researches on the subject came from the USA. This is thought to be a result of the high accessibility of individuals diagnosed with cancer to nursing care and the contribution of research nurses to the literature to increase the care quality of cancer patients.

In the research, the researches published on the supportive care needs of individuals diagnosed with cancer in the field of nursing were included in 168 different journals. Supportive Care in Cancer is the journal in which the most articles on the subject were published. The impact factor of the journal is 3.1, the Journal Citation Indicator of the journal is 0.94 for 2022 and 1.01 for 2021. The journal is also ranked Q2 in Health Care Science and Q1 in Rehabilitation. Supportive Care in Cancer is followed by Cancer Nursing (n=26), European Journal of Oncology Nursing (n=26), Seminiars in Oncology

Nursing (n=25), Journal of Clinical Nursing (n=24), Clinical Journal of Oncology Nursing (n=13), European Journal of Cancer Care (n=13), Oncology Nursing Forum (n=13), Palliative Supportive Care (n=11), Psycho Oncology (n=9). In the field of nursing, it is seen that researches on the supportive care needs of individuals diagnosed with cancer have been published in many journals in the literature.

Within the scope of the citation analysis conducted in the research, it was seen that the h-index of the researches published on the supportive care needs of cancer diagnosed patients in the field of nursing was 33. The number of references to 432 publications published on the subject is 1215 in total. The most cited research among the researches (n= 298) is the research titled "The impact of supportive nursing care on the needs of men of prostate cancer: a research across seven European countries" published by Cockle-Hearne J. et al. in 2013. This research was followed by the research titled "Assessment of needs, health-related quality of life, and satisfaction with care in breast cancer patients to better target supportive care" published by Brédart, A., Kop. et al. in 2013 with 271 citations. The research titled "Disparities in perceived unmetful need for supportive services among patients with lung cancer in the Cancer Care Outcomes Research and Surveillance Consortium" (n=173) published by Dolly A. John et al. in 2014 ranked third. Citation analysis enables the analysis of the relationships between publications by identifying the most influential publications in a research field (8). In this context, it is thought that deepening the literature will contribute to obtaining more meaningful data on citation analysis.

In the word network analysis conducted in the research, the most frequently used keywords in the researches published in the field of nursing regarding the supportive care needs of people diagnosed with cancer were analyzed. The top ten words analyzed were supportive care (n= 110), supportive care needs (n= 36), unmet needs (n=36), cancer (n=35), quality of life (n=28), nursing (n=21), colorectal cancer (n=20), lung cancer (n=18), palliative care (n=18), oncology (n=17). It is seen that the words selected for bibliometric analysis in the research are among the top 10 most used words. In addition, the fact that cancer types stand out as marginal words in the visualized mapping suggests that researches on the supportive care needs of people diagnosed with cancer, for example, researches on the need for supportive care of people diagnosed with gynecological cancer, will be encountered more frequently in the literature.

There are a limited number of bibliometric analysis researches in the literature in the field of nursery. In a research in which a bibliometric analysis of researches on heart failure in the area of nursing was conducted (Kavradım & Özer, 2022), it was shown that the number of researches on heart failure increased over the years, and

the reason for this situation was the incidence of the disease and developments in the area of nursing. In another research conducted in Türkiye and indexed in the Web of Science database, in which a bibliometric analysis of researches on breast cancer in the field of nursing was conducted, it was stated that the number of researches has been increasing in recent years and that the country with the largest number of such researches is the USA [14].

The limitations of the research include the fact that the literature review of the research was conducted through a single database, only researches published in English language were included and the type of research included in the research was limited.

Conclusion

This bibliometric analysis revealed the current situation regarding the supportive care needs of individuals diagnosed with cancer in the field of nursing, the authors who published the most publications on the research topic, the institutions and countries where the most publications were made, the journals where the research on the subject was published the most, and the word analysis on the subject. The fact that there is no research in the literature in which bibliometric analyses and trends regarding the supportive care needs of people diagnosed with cancer in the field of nursing are supported with visuals reveals the unique value of this research. It is envisaged that the research will provide guiding information to researchers who want to learn about the subject and who want to conduct research.

Conflict of interest

The authors have no conflict of interest.

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BIBLIOMETRIC ANALYSIS OF PUBLICATIONS ON HEAD AND NECK CANCER

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ABSTRACT

Objective

Cancers occurring in the oral cavity, salivary glands, paranasal sinuses, nasal cavity, pharynx, nasopharynx, oropharynx, hypopharynx, larynx, and upper neck lymph nodes are collectively referred to as head and neck cancers [1]. Due to their heterogeneous biology, treatments are complex, and most patients typically undergo combined therapies such as surgery, radiotherapy, and/or chemoradiotherapy [2].

Bibliometric analysis is employed to statistically examine academic literature in a specific research field. This study aims to conduct a bibliometric analysis of the literature related to head and neck cancers.

Methods

In the Web of Science (WoS) database, publications using the keyword "head and neck cancer" in journals indexed under SCI-Expanded from 1980 to 2022 and published in English were included in the analysis, totaling 22,857 publications.

Results

Upon examining the bibliometric map, the most frequently used keywords in studies related to "head and neck cancer" were found to be "rehabilitation," "survival," "surgery," "adaptation," and "body image." These keywords reflect the primary areas of research focusing on improving the quality of life and treatment outcomes of head and neck cancer patients. Additionally, they emphasize the impact on patients' physical and psychological well-being.

Figure 1, it can be observed that the most commonly preferred keywords in studies related to "head and neck cancer" are, in order, "rehabilitation," "survival," "surgery," "adaptation," and "body image."

When analyzing keyword co-occurrences, the following groups emerged: the first group included "chemoradiotherapy," "goals," and "survivorship"; the second group contained "function," "adaptation," "body image," "coping," and "psychosocial"; the third group featured "enteral nutrition" and "surgery"; the fourth group included "chronic aspiration" and "dysphagia"; and finally, the fifth group consisted of "human papillomavirus," "alcohol," "epidemiology," and "tobacco."

Another significant outcome of the study was the identification of highly cited articles in the field of "head and neck cancer." These articles have made substantial contributions to advancements in this field and have had a significant impact on the scientific community.

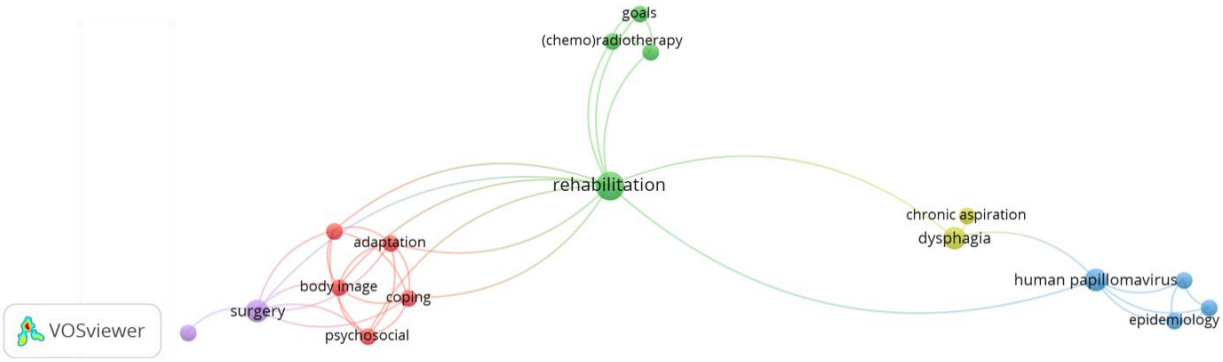

Figure 1.

Conclusion

An analysis of the distribution of research on "head and neck cancer" over the years reveals an increasing trend in research activity and importance in this area. Particularly in recent years, there has been a noticeable increase in the number of studies, indicating the growing significance of this topic and heightened interest among researchers. Highly cited articles have played a pivotal role in advancing this field. The identified keywords in the bibliometric analysis reflect the primary focus areas of research, emphasizing the importance of strategies to enhance patients' quality of life.

Future research may concentrate on more personalized approaches to head and neck cancer treatment. Characterizing cancers at the genetic and molecular levels can lead to a better understanding of individualized treatment responses and tailored therapies. This may optimize factors such as drug selection, dosage, and treatment duration for individual patients [3].

Immunotherapy and targeted therapies are significant areas of development in head and neck cancer treatment. Future research may focus on how immunotherapy and targeted therapies can be effectively integrated into head and neck cancer treatment [4]. Combination strategies to enhance the effectiveness of these treatment methods may also be explored.

Studies aimed at improving the quality of life for head and neck cancer patients are crucial. Research examining the effects of factors such as rehabilitation, psychosocial support, nutrition, and oral hygiene on cancer patients' quality of life can enhance both their life expectancy and quality of life [5]. Research exploring risk factors and epidemiological patterns associated with head and neck cancer can help understand its causes and develop preventive strategies. Further research is needed to understand the roles of risk factors such as alcohol, tobacco, and HPV in cancer development [6]. Studies that involve communication strategies to raise awareness about head and neck cancer among the general public and promote early diagnosis are also essential. Early diagnosis is crucial in the treatment of head and neck cancer and can save lives.

Keywords: *Head and neck cancer, Bibliometrics, Publication Trends*

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THE EFFECT OF COMPOUND B-84 CONTAINING AZOMETHINE GROUP ON *NQO1* GENE

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ABSTRACT

Osteosarcoma is a primary neoplasm known for osteoid or bone formation and is the second most common primary neoplasm worldwide [1]. Oxidative stress is a series of mechanisms that lead to cell death by inducing tumor development [2]. Osteosarcoma causes dysfunction of bone homeostasis as a result of osteoblast and osteoclast cells being affected by oxidative stress [3]. Compounds containing the azomethine group contain antioxidant, antifungal, antibacterial, antipyretic, anti-inflammatory properties. and has begun to be used as a new chemotherapeutic target due to its anticancer activities [4] In this study, azomethine group compound B-84 was first synthesized and applied to the bone tumor (SAOS-2) at eight different concentrations (100µg/ml-0.5µg/ml). The cytotoxic activity of the compound was determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) method at a wavelength of 570 nm. Then, the IC50 dose was determined as 70 µg/ml with the Graphpad Prism8 program. The determined dose was applied again to the SAOS-2 cell line, RNA was isolated and cDNA was synthesized in accordance with the kit protocol. He then performed Q-PCR analysis. At the end of the analysis, it was determined that the expression of the *NQO1* gene was reduced compared to the control group.

Keywords: *Azomethine, cancer, gene expression, NQO1*

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THE EFFECT OF COMPOUND B-104 CONTAINING AZOMETHINE GROUP ON PRDX1 GENE

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ABSTRACT

Osteosarcoma is a tumor characterized histologically by the presence and production of malignant mesenchymal cells in the bone stroma [1]. There is an imbalance in the redox system of all tumor cells. When this balance is disrupted, the rate of production of highly active substances exceeds the body's antioxidant regulatory ability range, ultimately leading to oxidative stress. Oxidative stress can help tumors grow and develop, but one of the cancer treatments is to increase the level of oxidative stress to increase the apoptosis of tumor cells. In recent years, scientists have been continuing their research on new compounds with anticancer activity. It is thought that the use of new compounds containing the azomethine group, one of these compounds, may be a promising method in cancer treatment [2]. In this study, first the compound B-104 was synthesized, and then this compound was applied to the bone tumor (SAOS-2) cell line at eight different concentrations (100µg/ml-0.5µg/ml). Cytotoxic activity was determined at a wavelength of 570 nm using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) method. IC50 value was determined as 15µg/ml with Graphpad Prism 8 program. The determined concentration of compound B-104 was applied to the SAOS cell line, and then RNA isolation and cDNA synthesis were performed. Expression levels of oxidative stress-related genes were determined using the RT-PCR method. When the results were examined, it was determined that the B-104 compound decreased PRDX1 expression in the SAOS cell line compared to the control group.

Keywords: *Azomethine, cancer, gene expression*

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PERCUTAN TRANSTORACIC LUNG BIOPSY; ONE CENTER EXPERIENCE

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ABSTRACT

We aimed to retrospectively evaluate the lung lesions occurring in PTAB in our hospital and investigate the radiological features of the lesions, pathological diagnoses, and complications, as well as single-center clinical experiences.

89 patients (13 females, 76 males) who underwent CT guided PTLB in our clinic between January 2021 and December 2022 were included in the study. In our study, the radiological features of the lesions, PTAB's complications,lesions Suv max values and pathology results were examined. Tru-cut biopsy was performed in 89 lesions, using an 19 G needle by single needle method.

Of the 89 patients included in our study, 86 were diagnosed and the diagnostic adequacy rate was 96,6%. Pneumothorax was detected in 15 patients (%16,9). Pneumothorax developed in 4 of 65 patients with pleural-based lesions (6.2%). Pneumothorax developed in 11 of 24 patients with non pleural based lesions(45.8%).

When the Suv max values of the patients were compared according to their pathological diagnoses, the difference was found to be statistically significant (p = 0.021).

CT guided PTLB has highly diagnostic adequacy rate, easy to administer and complications with acceptable levels.

Keywords: *Lung, computed tomography, image-guided biopsy, pneumothorax*

Introduction

Percutaneous transthoracic lung biopsy (PTLB)is a type of lung biopsy that can be performed under CT, USG, and USG guidance and is suitable for peripheral lesions that cannot be reached bronchoscopically. [1,2]. Nowadays, CT-guided PTLB is frequently preferred, and it is pleura-based in the required amounts and can be an auxiliary method and guide[3]. In our center, due to the higher radiation dose than other methods, it can be performed in the form of repeated shots using a marker under CT guidance. In our research, we aimed to retrospectively evaluate the lung lesions occurring in PTAB in our hospital and investigate the radiological features of the lesions, pathological diagnoses, and complications, as well as single-center clinical experiences.

Method

89 patients who underwent CT-guided transthoracic biopsy and had a PET CT scan between January 2021 and December 2022 were retrospectively evaluated and included in our study. The parameters reviewed are patients age and gender, location of the lesions (side and lobe) mean diameter and density of the lesions, number of lesions (solitary or multiple), margins of the lesion (lobulated, spiculated, smooth), whether the lesion is pleural based or not, distance between lesion and pleura, SUVmax values of lesions at PET scans, complications after the biopsy procedure and pathology results.

The mean diameter of the lesion is determined as the average of the two longest diameters perpendicular to each other taken from the axial CT images obtained to estimate the needle entry site before PTLB. Mean density is determined as the average of three measurements taken from the solid parts of the lesion.

All patients were informed about the purpose, method, and possible complications of the biopsy procedure, and an informed consent form was obtained from all patients for the biopsy.

After the patient was positioned appropriately to pass the shortest distance and the marker material was placed, 3 mm thick sections were obtained with a 64-slice Aqqulion x model Toshiba CT. The biopsy specimens were evaluated by the same pathologist. Control CT images were taken after the biopsy procedure was completed for possible complications. After PTLB, all patients were admitted to the chest diseases department and were kept under observation for possible complications, and a PA chest radiography was obtained and evaluated within the first hour.

Results and Discussion

Findings

Of the 89 patients in our study, 76 (85.4%) were male and 13 (14.6%) were female. The average age of women is 69.08±12.36(40-94); the average age of men was determined as 68.88±9.35 (46-89). When pathology results were evaluated with PTLB, the diagnosis could not be made in 3 (3.4%) patients. It was reported as suspicious for malignancy in 6 (6.7%) patients. 54 of the patients (60.7%) had non-small cell carcinoma, 4 (4.5%) had small cell carcinoma, 4 (4.5%) had tumor necrosis, and 7 (7.9%) had inflammation tissue and other pathological diagnoses were made in 6 (6.7%) patients.

Of the biopsied lesions, 30 were located in the right upper lobe, 5 in the right middle lobe, 14 in the right lower lobe, 25 in the left upper lobe, 12 in the left lower lobe, and 3 in the lingula.

In our study, the diagnosis was achieved in 86 of 89 patients, and when the biopsy results were evaluated together, the diagnostic rate was determined as 96.6%.

A total of 15 (16.9%) patients developed pneumothorax after PTLB, and only 6 (6.7%) of these patients required a chest tube, and a chest tube was inserted. No patient developed hemothorax, and ground glass areas in the needle trace, suggestive of minimal alveolar hemorrhage, were ignored.

When the development of pneumothorax was compared according to the location of the lesions, the difference between the groups was not significant (p = 0.13) Table 1

Table 1. *Distribution of pneumothorax development according to lung lobes*

	Pneumothorax present	**Pneumothorax absent**
Right upper	5(%5,6)	25(28.1%)
Right medium	0(%0)	5(5.6%)
Right lower	3(%3,4)	11(12.4%)
Left upper	2(%2,2)	23(25.8%)
Lingula	2(%2,2)	1(1.1%)
Left lower	3(%3,4)	9(10.1%)

Pneumothorax developed in 4 of 65 patients with pleural-based lesions (6.2%). Pneumothorax developed in 11 of 24 patients with non pleural based lesions(45.8%).

The average lesion diameter was determined as 48.60±22.98mm in patients who developed pneumothorax, and 64.36±31.06mm in patients who did not develop pneumothorax. As the lesion size increased, pneumothorax developed less frequently.

While the distance to the pleura in patients who developed pneumothorax was 19.33 ± 16.72 mm, the average distance of the lesions to the pleura in patients who did not develop pneumothorax was 3.08 ± 7.71 mm. The difference between these groups was statistically significant (p = 0.001).

When the Suv max values of the patients were compared according to their pathological diagnoses, the difference was found to be statistically significant (p = 0.021). However, when the pathological diagnoses of the lesions were compared in terms of contours and densities, no significant difference was found (p b 0.05) Table 2.

While 57 (64%) of the patients who underwent PTAB had a solitary lesion, 32 (36%) patients had multiple lesions. All lesions for which PTAB was performed were solid.

Table 2. *Distribution of lesion density, contour feature and SUV max values according to pathological diagnoses*

	CT Density (HU)	Countour			Suv max
		Smooth(n)	Lobule(n)	Spiculated(n)	
Small cell carcinoma (n=4)	32,5±10,4	0	3	1	9,55±1,47
Non small cell carcinoma (n=54)	32,4±11,7	8	18	28	12,34±7,07
Tumor necrosis (n=4)	26,0±13,4	1	3	0	13,62±5,51
Inflamation (n=7)	34,1±14,1	0	2	5	6,96±1,45
Malign (suspicious) (n=6)	19,3±16,8	3	1	2	10,20±4,28
Metastasis(n=5)	27,4±15,8	2	1	2	6,90±3,65
Non diagnostic(n=3)	32,7±4,7	0	2	1	14,43 5,92
P value	p >0,05		p> 0,05		(p=0,021)

Discussion

CT-guided transthoracic biopsy is a frequently used method with a high diagnostic rate. The most common complications are pneumothorax, hemothorax, and lung bleeding, and are at an acceptable level. The PTLB method can be performed as fine needle lung biopsy (FNAB) or tru-cut needle biopsy. [one]. While the biopsy is performed with a 21-22 G needle in FNAB, an 18-20 G tissue sample is taken for tru cut biopsy [4].

The most common complication in the PTAB procedure is pneumothorax, and its frequency has been reported to vary between 22-45% in different studies [5]. In our study, the pneumothorax rate was determined as 16.9%, which is below the rate reported in the literature. In studies, discussions have been made about the risk of developing pneumothorax if the lesion size is small, the depth of the lesion is high, the lesion is located in the lower lobes, the patient cannot hold his breath due to his advanced age, the fissure is passed with a needle, and the presence of emphysema increases the risk of developing pneumothorax [5,6]. Since the number of patients with emphysema was relatively small in our study, a reliable evaluation could not be made in terms of pneumothorax development. The pneumothorax rate in patients with lesions in the lower lobes is 6.8%, and the pneumothorax rate in patients with lesions in the upper lobes is 7.8%, which is below the rates reported in the literature.

Cox et al. [6] reported in their study that there was a relationship between small lesion size and the development of pneumothorax, and it was suggested that the surrounding ventilated lung area was injured more by the back and forth movements of the needle during aspiration sampling from small lesions than in large lesions. In our study, the average lesion diameter was determined as 48.60±22.98mm in patients who developed pneumothorax, and 64.36±31.06mm in patients who did not develop pneumothorax. As the lesion size increased, pneumothorax developed less frequently, supporting the literature.

Cox et al. [6] emphasized in their study that there is no significant difference between the depth of the lesion and the development of pneumothorax, but the development of pneumothorax is significantly lower in patients whose lesion is pleural-based and the needle does not travel any distance within the lung. In Tuncel et al.'s studies [3], the average lesion depth was determined to be 21.8 mm in patients who developed pneumothorax and 18.3 mm in patients who did not develop pneumothorax, and they could not find any significant difference. In our study, the distance to the pleura in patients who developed pneumothorax was 19.33 ± 16.72 mm, while the average distance of the lesions to the pleura in patients who did not develop pneumothorax was 3.08 ± 7.71 mm, and the difference between these groups was statistically significant.

Tuncel et al. [3] In their study, the pneumothorax rate in patients with pleural-based lesions was 10%, and the pneumothorax rate in patients with non-pleural-based lesions was 36.7%, and there is a significant difference. Similarly, in our study, pneumothorax developed in 65 patients with pleural-based lesions, 4 of them (6.2%) and 11 of 24 patients with non-pleural-related lesions (45.8%), and there was a significant difference between the two groups and there was no statistical difference. The difference was significant ($p < 0.001$).

The frequency of pneumothorax cases requiring treatment varies between 3-15% [2]. Tuncel et al. [3] stated that the rate of pneumothorax requiring treatment was 1.3% in their study, which was lower than reported

in the literature. In our study, the rate of pneumothorax requiring treatment was found to be 5.6% and is compatible with the literature.

Complications such as hemothorax, parenchymal hemorrhage, systemic air embolism, pericardial tamponade, and hemothorax mentioned in the literature were not detected in our study.

Pneumothorax develops immediately after or within the first hour of the PTAB procedure [5]. For this reason, it is recommended that the patient be observed and evaluated for asymptomatic pneumothorax with a standing PA chest x-ray in the first hour [5].

Çalışkan et al. [7] found in their study that the water max of small cell cells was 12.2±5.5. In our study, this value was found to be 9.55±1.47. When we evaluated the SUV max without distinguishing between non-small cell cells in our study, the SUV max was found to be 12.34±7.07, while Çalışkan et al. [7] found this value to be 10.9±5.6 in adenocarcinomas and 15.2±7.6 in squamous cell carcinomas. Liu et al. [8] In their study, they found the SUV max value in primary lung cancer to be 6.9 ± 2.7 and in metastasis to be 6.2 ± 3.2. In our study, we found the SUV max value to be 6.90 ± 3.65 in metastases, which is incompatible with this study. This difference may have varied depending on the activity of the primary tumor.

The limitations of our study include the retrospective nature of the study and the decrease in the number of patients due to the malfunction of our tomography unit for a while.

In conclusion; The diagnostic accuracy and complication rate of PTAB performed in our hospital is consistent with large-scale studies, and as long as it is performed by experienced radiologists, it is seen that it is successful and the complication rates are significantly low.

Conclusion

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A CASE-BASED APPROACH TO MEDULLARY THYROID CANCER

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ABSTRACT

Medullary thyroid carcinoma (MTC) constitutes approximately 5-10% of all thyroid cancers. Although the tumor forms in the thyroid, it doesn't originate from thyroid cells, but from the C cells or parafollicular cells which produce and release a hormone called calcitonin (CT) [1]. Medullary tyroid cancer diagnosed with İİAB [2].

Surgery is the best treatment of this disease but radiotherapy must be useful in the treatment of metastatic lesions.The benefit of chemoteraphy with vandetanib has been recently demonstrated.

This report aims to brings a perspective to the treatment approaches of medullary cancer a rare type of thyroid cancer through a case that recurred 3 times.

Keywords: *Medullary tyroid carcinoma, vandetanib, lutetium*

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ANTIPROLIFERATIVE ACTIVITY INVESTIGATION OF *MALVA NEGLECTA* WALLR.

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ABSTRACT

Natural products have played an important role in the treatment of various diseases including cancer. Medicinal plants and plant-derived compounds have attracted increasing attention in cancer treatment due to their selectivity against cancer cells, lower side effect profiles, and different cell death mechanisms. The genus *Malva* L. is widespread in subtropical, tropical, and temperate regions of Africa, Asia, and Europe and contains species frequently used in folk medicine [1]. *Malva neglecta* Wallr., called "küçük ebegümeci", is traditionally used in the treatment of cold, cough, bronchitis, and inflammation in Anatolia. *M. neglecta* has analgesic, antioxidant, antimicrobial, anti-inflammatory, antiemetic, anti-ulcerogenic, wound healing, neuroprotective, and antidiabetic effects and contains phenolic compounds and acids, amino acids, sugars, and fatty acids [2]. This study aims to evaluate the antiproliferative activity of *M. neglecta* on lung carcinoma cell lines, A549. The methanol extracts prepared from root and aerial parts of *M. neglecta* were tested at concentrations of 1-100 µg/mL by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. According to the results, while the root extract did not show a significant decline in cell viability, the methanol extract of aerial parts of *M. neglecta* showed moderate inhibition at the highest dose (Cell viability= %62,2). This extract may be promising for further anticancer activity studies.

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TEN YEARS OF ENDOMETRIAL CANCER CASES INVESTIGATION OF THE DISTRIBUTION ACCORDING TO HISTOLOGICAL TYPES

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Introduction and Purpose

Cancer is the second leading cause of death in our country and in the world after cardiovascular diseases. Gynecologic cancers are one of the major causes of female mortality worldwide. Endometrium cancer is the most common gynecologic cancer in Türkiye and developed countries. Approximately 320,000 new cases are diagnosed worldwide each year and 76,000 patients die from the disease each year. Due to the rising prevalence of obesity, a strong endometrial carcinoma (EC) risk factor, its annual incidence is predicted to increase

According to Türkiye statistics, gynaecological cancers constitute 11.2% of all female cancers. Studies have shown that the most common gynaecological cancer is endometrial cancer, followed by ovarian and cervical carcinoma. According to 2018 data, the incidence of endometrial cancer in Türkiye is 6.

Endometrial cancers are divided into two types (type I and type II) according to their biological, molecular and clinicopathological characteristics. Tumours of type I or endometrioid histology account for 80% of cases(6,7). The most common cancer of the uterus in terms of histological type and site is endometrial adenocarcinoma.(3,4,5) Non-endometrioid type endometrial cancers (Type II) include carcinosarcoma, serous and clear cell carcinomas. The incidence rates of histological types are endometrioid 77%, mucinous 1%, serous 7%, clear cell 2%, mixed cell 8%, carcinosarcoma 3% (Table-1). Despite the lack of screening methods, stage I disease is diagnosed in almost 75 per cent of cases, resulting in a good prognosis.

The aim of this study is to examine the distribution of patients diagnosed with endometrial cancer and operated in Sivas Cumhuriyet University Practice and Research Hospital Gynecology and Obstetrics Clinic according to histological subtypes. The study is important in terms of contributing to the literature by revealing the similarities or differences of the results with the statistics of our country and the world and guiding the planned education and research on the subject.

Method

The population of this cross-sectional study consists of patients diagnosed with endometrial cancer and operated between 2011 and 2021. No sample selection was made in the study and all patients who were reported from the pathology department with a diagnosis of endometrial cancer and operated on were included in the study. The operation notes of the patients were obtained from the Gynaecology department. Permission was obtained from Sivas Cumhuriyet University Non-Interventional Clinical Research Ethics Committee for the retrospective study. Patients were classified according to histological subtypes of endometrial cancer. These types are endometrioid type, serous carcinoma, mucinous carcinoma, clear cell carcinoma, mixed type and carcinosarcoma.

Findings

The data of 214 patients who were diagnosed with endometrial cancer and operated in Sivas Cumhuriyet University Application and Research Hospital Gynaecology and Obstetrics Clinic between 2011 and 2021 were obtained. Accordingly, 81.7% (n=175) of our cases were endometrioid type, 8.4% serous type (n=18), 4.7% (n=10) mixed type, 2.8% (n=6) clear cell, 4% (n=1.9) carcinosarcoma, 0.5% (1) mucinous type. (Table-2).

Table 1. *Incidence rates of histological subtypes of endometrial cancer in the World*

Histological type	%
Endometrioid	77
Serous	7
Mucinous	1
Clear cell	2
Mixt tip	8
carcinosarkoma	3

Table-2. *Distribution of our patients with endometrial cancer according to histological subtypes*

Histological type	**n**	**%**
Endometrioid Tip	175	81.7
Serous	18	8.4
Mucinous	1	0,5
Clear cell	6	2.8
Mixt Tip	10	4.7
carcinosarkoma	4	1.9

Discussion

The geographical distribution of gynaecological cancers varies according to continents. Gynaecological cancers are more common in countries with poor economic development indices such as African countries and South American countries(9) The most commonly diagnosed cancer and the leading cause of death from cancer vary greatly between and within countries, depending on the degree of economic development and related social and lifestyle factors. It is important that statistics are available both at country and city level to guide screening and treatment programmes. (10,11,12). In the United States, endometrial cancer is the most common cancer in female reproductive organs. According to the American Cancer Society's 2023 estimates of endometrial cancer in the United States;

- Around 66,200 new cases of cancer will be diagnosed.
- Around 13,030 women will die from uterine cancer.

These estimates include both endometrial cancers and uterine sarcomas. Up to 10 per cent of uterine cancer cases are sarcomas.(13) The majority of EC cases are type 1 (i.e. low-grade endometrioid type), which is associated with high levels of circulating estrogens, age, obesity, nulliparity and unmet estrogen therapy. Type 1 ECs are typically associated with a relatively favourable prognosis with a five-year survival of approximately 85%.(14) In contrast, the less common type 2 ECs have been recognised to be clinically more aggressive and heterogeneous. Edmondson et al. showed that histological types such as serous and clear cell carcinoma arise as a result of a genetic mutation and that mutations in the tumour suppressor gene p53 play an important role in the development of serous endometrial cancer. According to the study by Johson et al., black women have a higher proportion of more aggressive histological types and a higher overall risk of death than white women(15) Some of these histological types can be considered as distinct diseases and may require specific therapeutic approaches, and more research is needed on the aetiology and prognosis for detailed type 2 EC subtypes. Mortality is not equally distributed among ethnic groups. Ethnic differences in EC are driven by the less common type 2 and, therefore, future studies of EC disparities should take this histological heterogeneity into account. In conclusion,

EC is a heterogeneous disease with significant differences in survival according to major histological type.

In this study, we have shown that there is no difference between the histological type results in our clinic and the world statistics. This should encourage us to take precautions against obesity, long-term endogenous or exogenous hyperestrogenism (polycystic ovary syndrome, tamoxifen treatment, anovulation, estrogen

replacement therapy), hypertension and diabetes mellitus, which are the most important risk factors identified in endometrioid endometrial cancer.

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INVESTIGATION OF THEORETICAL ACTIVITIES OF METHANONE DERİVATİVE MOLECULES AGAINST COLON CANCER PROTEINS

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ABSTRACT

Large intestine or colon cancer is one of the most common types of cancer in the world.

The large intestine consists of the colon and rectum. Colon cancer is when the layer covering the inner part of the large intestine grows abnormally and forms a protrusion. Some genetic conditions cause the progression of colon cancer. These genetic conditions are microsatellite instability (MSI), aneusomy (CIN), and chromosomal translocations.

In this study, the chemical and biological activities of methanone derived molecules will be compared. First, methanone derived molecules, Calculations were made on 6-31++G(d,p) basis set at HF, M062X, and B3lyp levels. Afterwards, these molecules were characterized by IR, ^{1}H NMR, ^{13}C NMR and UV-Vis spectrum analysis. Additionally, molecular docking calculations of the studied molecules were performed for colon cancer (PDB ID: 3DTC and 4UYA).

Keywords: *Computational, DFT, spectrum, methanone, docking*

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INVESTIGATION OF THEORETICAL ACTIVITIES OF PHENYLDIAZENYL DERİVATİVE MOLECULES AGAINST LUNG CANCER PROTEINS

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ABSTRACT

Lung cancer (LC) is the most common type of cancer that causes death in the world [1]. According to histological types, lung cancer is divided into small cell lung cancer and non-small cell lung cancer. At the beginning of cancer, the cells in the lung increase excessively over time and form a mass in the lung, and as a result of the resulting mass, it continues to multiply and spreads to other organs [2]. Cancer cells can interact directly with neighboring cells through membrane receptors and ligands or interact with distant cells by releasing cytokines, chemokines, and metabolites into the circulatory system. EGFR is a member of the tyrosine kinase 1 receptor family and regulates the growth of cells. EGFR activation and regulation leads to cell proliferation, apoptosis, and angiogenesis. [3].

In this study, the chemical and biological activities of phenyldiazenyl derived molecules will be compared. First, phenyldiazenyl derived molecules, Calculations were made on 6-31++G(d,p) basis set at HF, M062X, and B3lyp levels. Afterwards, these molecules were characterized by IR, ^{1}H NMR, ^{13}C NMR and UV-Vis spectrum analysis. Additionally, molecular docking calculations of the studied molecules were performed for lung cancer (PDB ID: 4ZXD and 5ZMA).

Keywords: *Computational, DFT, spectrum, phenyldiazenyl, docking*

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EVALUATION OF MYCOSIS FUNGOIDES CASES; A UNIVERSITY HOSPITAL EXPERIENCE

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ABSTRACT

Mycosis fungoides is the most common cutaneous T-cell lymphoma, characterized by clonal proliferation of atypical T-cells and a predilection for the skin. It usually affects middle-aged and older adults. The disease typically presents with symptoms such as patches, plaques, tumors, or erythroderma. According to the data obtained in this study, it was revealed that it was more common in women and those between the ages of 51-64. When the diagnoses are compared by years, it is seen that there is a decrease in the number of patients.

Introduction

Mycosis fungoides (MF) is the most common Cutaneous T-cell lymphoma. It covers 50% of cutaneous lymphomas [1]. The patch phase in MF is characterized by scaly and erythematous patches. The presence of these lesions in areas that are not exposed to sunlight, such as the trunk, is an important clinical symptom [2]. MF may progress to patch, plaque and tumor stages, respectively. To make a diagnosis of MF, correlation of clinical and histopathological examination is required. The diagnosis is made by seeing epidermotropism, atypical lymphocytes and Pautrier microabscesses in histopathological examination [3]. The incidence of MF is 6-7/10^6 and there are significant regional variations, with the incidence being higher in blacks. The disease is more common in adults and elderly patients. It is twice as common in men as in women. The etiology of MF is unknown. In some cases, it has been observed to be associated with chronic skin disorders and long-term exposure to various allergens, and genetic predisposition has been found to play a role in some cases. So far no strong association with viral infections has been demonstrated. MF has been observed in patients receiving solid organ transplants, suggesting that immune suppression may contribute to the development of the disease [4]. It has been stated that more than 90% of patients with early stage MF do not progress to the tumor stage and do not show extracutaneous symptoms of the disease throughout their lives [5].

Materials and Methods

The population of this cross-sectional study consists of patients diagnosed with MF in the Pathology Department of Sivas Cumhuriyet University Practice and Research Hospital between 01.01.2012 and 30.08.2023. The dependent variable of the study is the diagnosis of MF. Independent variables are year of diagnosis, patients' age, and gender. The age variable is classified as 30 and under, 31-50, 51-64, 65-79, 80 and over.

Data analysis

Data were analyzed with the statistical program SPSS-22 (SPSS INC., Chicago, IL, USA). Data stated by measurement are presented descriptively with mean and standard deviation (minimum - highest values), data specified by count are presented descriptively with number and percentage distribution. Chi-square test was used to analyze the data and $p<0.005$ was considered significant.

Results and Discussion

A total of 151 patients were diagnosed with MF within the specified date range. 53.0% (n=80) of these patients were female and 47.0% (n= 71) were male. The average age of the patients is 59.6±17.3 (minimum 22-maximum 99). When the distribution of diagnoses by years is evaluated, it is seen that the maximum number of patients was 36 patients in 2012 and the lowest number was 3 patients in 2019. When evaluated according to age groups, MF diagnosis is most common in the 51-64 age group (48/151, 31.8%). The age group where the disease is least common is 30 and under (6/151, 4.0%). When the relationship between age groups and gender was analyzed statistically, the result was considered significant (P<0.01).

Most of the lymphomas seen on the skin are of T-cell origin. Mycosis fungoides (MF) is the most common cutaneous lymphoma. It usually occurs between the ages of 45-60, but it can also be seen in adolescence and children. It is twice as common in men than in women [6,7]. In our study, similar to the literature, the average age of MF patients was found to be 59.6 years. The age group in which the disease is least common was found to be 30 years of age and below. Unlike the literature, the frequency of MF was seen more in women in our study. When the distribution of diagnoses by years is examined, it is seen that the frequency of diagnosis has decreased in recent years.

Conclusion

According to the data obtained in this study, it was revealed that it was more common in women and those between the ages of 51-64. When the diagnoses are compared by years, it is seen that there is a decrease in the number of patients. More comprehensive studies are needed to better understand the reasons for this.

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CHARACTERISTICS AND SURVIVAL OUTCOMES OF GASTRIC CANCER PATIENTS RECEIVING NEOADJUVANT THERAPY

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ABSTRACT

Today, the standard treatment in non-metastatic gastric cancer is surgery after neoadjuvant chemotherapy. One of the first studies investigating the efficacy of neoadjuvant chemotherapy in the literature is the MAGIC study. This study compared surgery after neoadjuvant chemotherapy with ECF (epirubicin, cisplatin, and fluorouracil) protocol versus surgery alone. Receiving neoadjuvant chemotherapy has been shown to improve overall survival (OS) and disease-free survival (DFS). The most recent study compared the neoadjuvant FLOT regimen with the ECF/ECX chemotherapy regimen in the FLOT4-AIO. OS was 50 months in the FLOT regimen and 35 months in the ECF/ECX regimen. After this study, neoadjuvant chemotherapy has become the standard treatment for tumors of T2 and higher. In our study, we aimed to evaluate the general characteristics and treatment results of our patients who received neoadjuvant chemotherapy. We included 29 patients who received neoadjuvant chemotherapy in our study. Before and after neoadjuvant chemotherapy, clinopathological features were recorded. The final status of the patients, whether recurrence/metastasis developed, OS and DFS were calculated and recorded. In 13 patients the primary tumor was in the corpus, in 8 patients in the esophagogastric junction-cardia, and in 8 patients distally. 20 patients received FLOT chemotherapy and 9 patients received FOLFOX chemotherapy as neoadjuvant treatment. 3 patients had pathological complete response, 13 patients had near pathological complete response/partial response and 13 patients had no response/poor response. Median OS was 29.8 months and median DFS was 16.7 months. In our study, complete response was obtained in 3 patients and almost complete response was obtained in 13 patients. Both rates were 54.4% in total. This is a high rate when compared to the literature, and we think that this is due to the low number of patients.

Keywords: *Gastric cancer, neoadjuvant chemotherapy, pathologicaly complet response*

Introduction

Gastric cancer is one of the most common malignancies worldwide. Most patients are diagnosed in advanced stages due to mild early disease symptoms and low regular screening rates. The treatment of gastric cancer is curative resection in the form of D2 gastrectomy. However, more than 30% of gastric cancers present as locally advanced disease, making them unresectable. Neoadjuvant chemotherapy was introduced to eliminate micro-metastasis and improve resectability before surgery, which increases R0 resection rates [1,2].

The MAGIC study enrolled patients with resectable stage 2 or higher gastric cancer, lower esophageal cancer and esophagogastric junction (EGJ) cancer. Patients were divided into preoperative 3 cycles of epirubicin, cisplatin, fluorouracil (ECF) surgery and postoperative 3 cycles of ECF or surgery only arms. The 5-year overall survival (OS) in the group receiving neoadjuvant therapy was 36.3%, while the 5-year OS in the group that underwent surgery first was 23% (HR 0.75; p=0.009). Disease-free survival (DFS) was significantly better in the group receiving neoadjuvant chemotherapy compared to the other group (HR 0.66; P<0.001) [3]. In a meta-analysis comparing neoadjuvant chemotherapy regimens with surgery alone, neoadjuvant chemotherapy was associated with a statistically significant benefit in terms of OS and DFS. Neoadjuvant chemotherapy increased the R0 resection rate and did not increase the risk of operative complications and postoperative complications [4].

The phase II/III FLOT4-AIO study compared a flourouracil, dosataksel, oxaliplatin (FLOT) regimen with epirubicin-based triple therapy. In a report of 300 patients with gastric or EGJ adenocarcinoma enrolled in the phase II portion of the study, the FLOT regimen was associated with a higher pathologic complete response rate (16 % vs 8%) and toxicity appeared to be approximately similar. The phase III component of the study included 716 patients with resectable gastric (44%) or gastroesophageal junction (56%) tumors. FLOT was found to have significantly higher median overall survival (50 vs. 35 months, HR 0.77) [5]. Following this study, perioperative FLOT chemotherapy has become the standard treatment for gastric and GEJ adenocarcinoma at cT2 and higher stages.

In this study, we aimed to analyse the characteristics and treatment results of our patients who received neoadjuvant chemotherapy for gastric ca in our clinic.

Method

Twenty nine patients who received neoadjuvant treatment were included in our study. Initial clinicopathological characteristics of the patients and pathological response status after surgery, surgical stage, whether there was nux/metastasis or not, final status of the patient, OS and DFS were evaluated.

Results and Discussion

Of the patients included in the study, 65.5% were 65 years of age or younger and 34.5% were older than 65 years. 14 patients were female and 15 patients were male. In 13 patients the primary tumour was in the corpus, in 8 patients in the EGJ-cardia, and in 8 patients distally. 7 of 29 patients had signet-ring cell histology component. 27 patients had clinical stage 3 and 2 patients had clinical stage 2. 20 patients received FLOT chemotherapy and 9 patients received FOLFOX chemotherapy as neoadjuvant treatment. 21 patients underwent total gastrectomy and 8 patients underwent partial gastrectomy. 23 patients underwent D2 dissection. 3 patients had pathological complete response, 13 patients had near pathological complete response/partial response and 13 patients had no response/poor response (Table 1). 19 patients developed nux/metastasis. Nux/metastasis sites were peritoneum in 9 patients, lymph node in 5 patients, liver in 4 patients and lung in 1 patient. 17 patients had an exitus during follow-up. Median OS was 29.8 months and median DFS was 16.7 months (Figure 1-2).

Table 1. *Patient characteristics in gastric cancer receiving neoadjuvant chemotherapy*

Variable (n)	**(n:29)**
Age	
≤ 65 years	19 (65.5%)
> 65years	10 (34.5%)
Gender	
Female	14 (48.3%)
Male	15 (51.7%)
Tumor location	
GEJ-Cardia	8 (27.6%)
Corpus	13 (44.8%)
Distal	8 (27.6%)
Histological type	
Adenocarcinoma	22 (75.9%)
Singlet cell carcinoma	7 (24.1%)
Clinical stage	
Stage 2	2 (6.9%)
Stage 3	27 (93.1%)
Grade group	
Grade 1-2	15 (51.7%)
Grade 3	14 (48.3%)

Perineural invasion	
Yes	12 (41.4%)
No	17 (58.6%)
Lymphovascular invasion	
Yes	14 (48.3%)
No	15 (51.7%)
Neoadjuvant chemotherapy agent	
FLOT	20 (68.9%)
FOLFOX	9 (31.1%)
Surgery type	
Total gastrectomy	21 (72.4%)
Partial gastrectomy	8 (27.6%)
Dissection type	
D1	6 (20.7%)
D2	23(79.3%)
pT	
pCR	3 (10.4%)
pT1	1 (3.4%)
pT2	7 (24.1%)
pT3	13 (44.8%)
pT4	5 (17.3%)
pN	
pN0	12 (41.4%)
pN1	7 (24.1%)
pN2	4 (13.8%)
pN3	6 (20.7%)
Pathological response	
CR	3 (10.4%)
Near to CR and PR	13 (44.8 %)
Poor response and no response	13 (44.8 %)

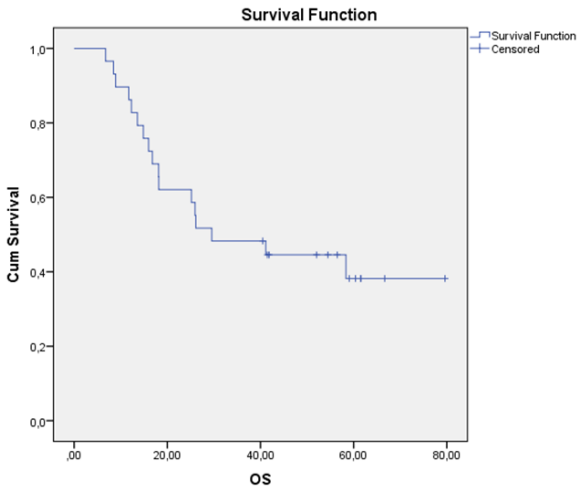

Figure 1. *Median overall survival in gastric cancer patients receiving neoadjuvant chemotherapy*

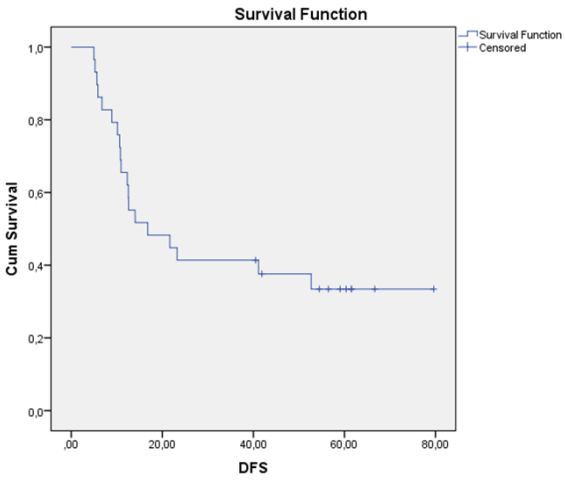

Figure 2. *Median disease-free survival in gastric cancer patients receiving neoadjuvant chemotherapy*

Conclusion

In our study, 3 patients had complete response, while 13 patients had near complete response. Both rates totaled 54.4%. This is a high rate compared to the literature, and we think that the reason for this is the small number of patients. Recently, Turkish data investigating the efficacy of neoadjuvant FLOT treatment in gastric and EGJ tumors have been published, in this study, the rate of complete and near complete pathological response was found to be 23%. In the FLOT4-AIO study, 16% pathologic complete response was achieved in the FLOT arm, while 8% pathologic complete response was achieved in the ECF/ECX arm.

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BIOCHEMICAL INVESTIGATION OF THE PROTECTIVE EFFECTS OF DEXPANTHENOL ON 5-FLUOROURACIL-INDUCED NEPHROTOXICITY AND HEPATOTOXICITY IN RATS

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ABSTRACT

5-Fluorouracil (5-FU) is a broad-spectrum chemotherapeutic used in the treatment of colorectal adenocarcinoma, gastric adenocarcinoma, pancreatic adenocarcinoma and breast carcinoma (1). It leads to the death of rapidly proliferating tumor cells through DNA damage (2). 5-FU, like many other chemotherapeutics, has toxic effects on the liver and kidneys (3-5). Dexpanthenol (DXP), known for its anti-inflammatory and antioxidant properties, is a derivative of pantothenic acid, also known as provitamin B5 (6). In our study, we aimed to evaluate the protective effects of DXP on 5-FU-associated nephrotoxicity and hepatotoxicity.

The study was carried out at the Experimental Animal Research and Application Center with the approval of Sivas Cumhuriyet University Animal Experiments Local Ethics Committee. The animals included in the study were housed in an experimental room with a temperature of 22-24 °C and 40-60% humidity in a 12-hour alternating light-dark environment in accordance with standard care and feeding procedures. feed and tap water were given ad libitum. After a one-week adaptation period, a total of 24 16-week-old male Wistar Albino rats weighing 240-260 g were randomly divided into 4 groups (n=6/group). In the control group rats, sterile saline was given intraperitoneally at a dose of 1 mL/kg for 8 days. 5-FU group rats received 5-FU intraperitoneally at a dose of 35 mg/kg for 5 days, 5-FU+DXP 500 group rats received 5-FU at a dose of 35 mg/kg for 5 days and DXP 500 mg/kg for 8 days intraperitoneally starting on the same day, 5-FU+DXP 1000 group rats received 5-FU at a dose of 35 mg/kg for 5 days and DXP 1000 mg/kg for 8 days intraperitoneally starting on the same day.

At the end of the study, serum samples were analyzed for renal (BUN, creatinine, total protein, albumin, uric acid) and liver (AST, ALT, ALP, total bilirubin, direct bilirubin, LDH) function tests. Data were analyzed by one-way analysis of variance and post hoc Tukey test in GraphPad prism 8.0.1 software program. Results were presented as mean ± standard error. $p<0.05$ was considered statistically significant.

Statistically significant impairment was recorded in both liver and kidney function tests in 5-FU treated rats compared to the control group. In the graphs shown in Figure 1, 5-FU caused a significant increase in AST ($p<0.001$), ALT ($p<0.001$), ALP ($p<0.001$), total bilirubin ($p<0.05$), direct bilirubin ($p<0.05$) and LDH ($p<0.001$) levels in rats. When DXP was given with 5-FU at doses of 1000 mg/kg, all parameters decreased significantly. DXP 1000 mg/kg caused a highly significant decrease especially in AST, ALT, ALP and LDH levels ($p<0.001$). The 500 mg/kg DXP dose did not show a positive effect on total bilirubin and direct bilirubin. However, significant decrease was observed in other parameters.

In the graphs shown in Figure 2, 5-FU caused significant changes in BUN ($p<0.05$), creatinine ($p<0.01$), uric acid ($p<0.001$), total protein ($p<0.001$) and albumin ($p<0.001$) levels in rats. When DXP was administered with 500 mg/kg 5-FU, a highly significant ($p<0.001$) decrease in uric acid level and a significant ($p<0.05$) decrease in BUN and creatinine levels were observed. No significant positive effect on total protein and albumin was recorded. When DXP was given with 5-FU at a dose of 1000 mg/kg, a highly statistically significant improvement was found on uric

acid and total protein levels. Significant improvement was also observed in BUN ($p<0.01$), creatinine ($p<0.05$) and albumin ($p<0.05$) levels.

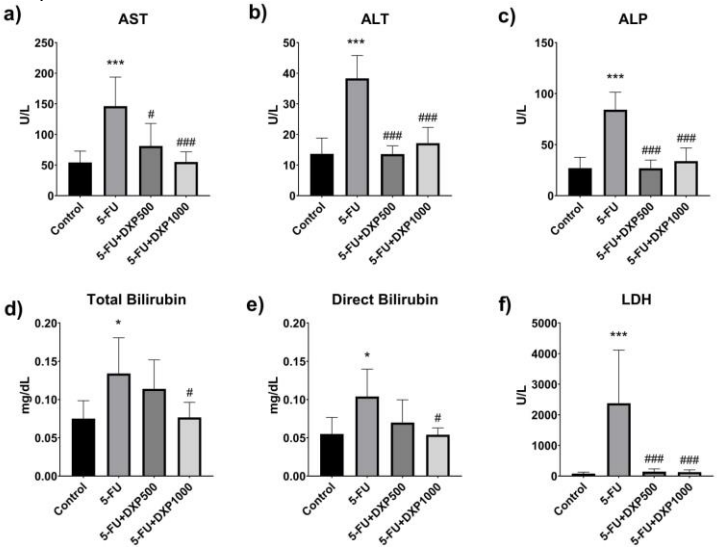

Figure 1. *Positive effects of DXP 500 mg/kg and 1000 mg/kg doses on 5-FU-induced liver dysfunction*

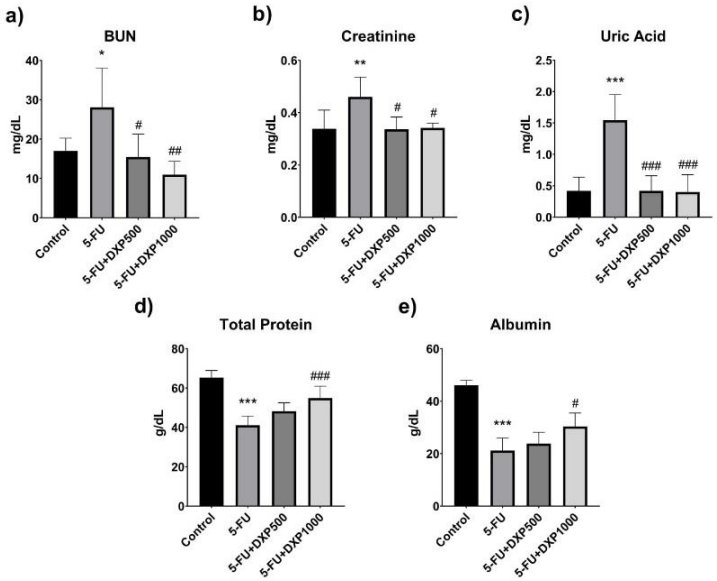

Figure 2. *Positive effects of DXP 500 mg/kg and 1000 mg/kg doses on 5-FU-induced renal dysfunction*

In our study, we have biochemically demonstrated that administration of DXP, especially at a dose of 1000 mg/kg, has favorable effects on 5-FU-associated hepatotoxicity and nephrotoxicity in rats.

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INVESTIGATION OF THE HEMATOLOGIC EFFECT OF DEXPANTHENOL ON 5-FLUOROURACIL -ASSOCIATED MYELOSUPPRESSION IN RATS

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Introduction

The antitumor agent 5-Fluorouracil (5-FU), which is used in the treatment of many cancers including skin, colorectal and breast cancer, was first introduced in 1957. 5-FU shows its cytotoxic effect by disrupting normal DNA and RNA synthesis. Common side effects seen with systemic administration are nausea, vomiting, diarrhea, leukopenia and hair loss. However, serious side effects such as anaphylaxis, myocardial ischemia, pancytopenia and acute cerebellar syndrome may also be observed.

Dexpanthenol, also known as provitamin B5, is the active alcohol of pantothenic acid (PA), one of the B-complex vitamins. When administered parenterally or orally, it is rapidly absorbed in rats and other mammalian tissues and converted to pantothenic acid in the body. PA enters the liver through the portal circulation and is incorporated into the structure of coenzyme A and distributed to all body tissues. Coenzyme A is involved in many vital enzymatic reactions. Studies have shown that PA plays an important role in cell defense and repair systems against damage caused by oxidative stress and inflammatory response. PA is a substance with high biological importance because it is included in the structure of coenzyme A. In our study, we aimed to investigate the hematologic effect of DXP on 5-FU-induced bone marrow suppression in rats.

Materials and Methods

A total of 24 16-week-old male Wistar Albino rats weighing 240-260 gr were randomly divided equally into 4 groups (n=6/group). In the control group rats, sterile saline was given intraperitoneally at a dose of 1 mL/kg for 8 days. 5-FU group rats received 5-FU 35 mg/kg intraperitoneally for 5 days.

5-FU+DXP 500 group rats received 5-FU 35 mg/kg intraperitoneally for 5 days and DXP 500 mg/kg intraperitoneally for 8 consecutive days starting on the same day. 5-FU+DXP 1000 group rats were given 5-FU 35 mg/kg intraperitoneally for 5 days and DXP 1000 mg/kg intraperitoneally for 8 consecutive days starting on the same day. At the end of the study, intracardiac blood samples were taken from the rats euthanized by decapitation method. The samples were analyzed by complete blood count.

Statistical Analysis

Data were analyzed with GraphPad Prism 8.0.1 using one-way analysis of variance followed by post hoc Tukey test. Results are presented as mean ± standard error. A value of $P<0.05$ was analyzed statistically.

Results-1

WBC, neutrophil and platelet/lymphocyte ratio (PLR) values were statistically significant and lower in the groups receiving 5-FU compared to the control group ($P<0.05$).

In addition, although lymphocyte, monocyte and neutrophil/ lymphocyte ratio (NLR) values were numerically lower, there was no statistically significant difference between the control and 5-FU groups ($P>0.05$).

Treatment intervention of dexpanthenol at both doses did not show any ameliorative effect on the parameters (P>0.05).

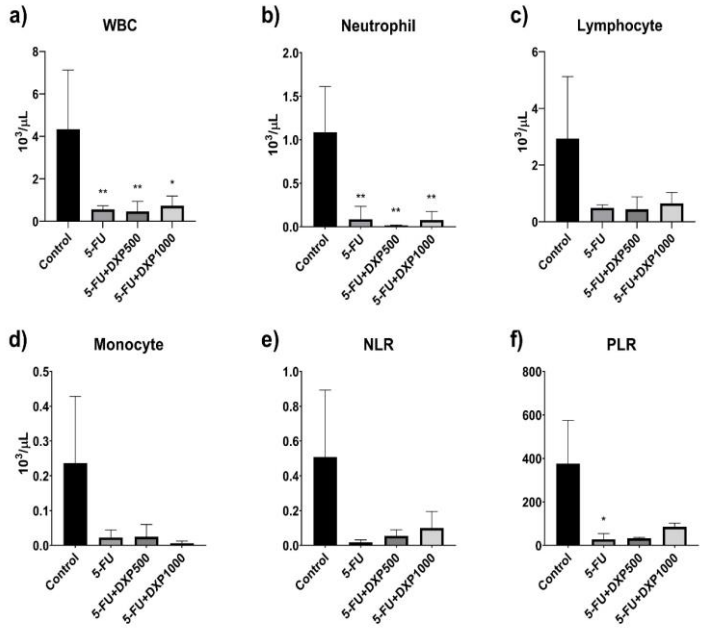

Figure 1. *Effect of DXP on 5-FU induced leukocyte, lymphocyte, granulocyte count changes and NLR and PLR changes. *P<0.05, **P<0.01 and ***P<0.001 indicate statistical significance compared to the control group. ##P<0.05, ##P<0.0.1 and ###P<0.001 indicate statistical significance compared to 5-FU group*

Results-2

Red blood cell count (RBC), hemoglobin (hgb) and hematocrit (hct) values were significantly lower in 5-FU and 5-FU+DXP500 groups compared to the control group (p<0.05).

When 1000 mg/kg dose of DXP was given together with 5-FU, RBC, hgb and hct values were significantly increased (p<0.01). 5-FU showed suppressive effect on platelet (PLT) count. Both treatment doses of DXP failed to reverse this effect (p>0.05).

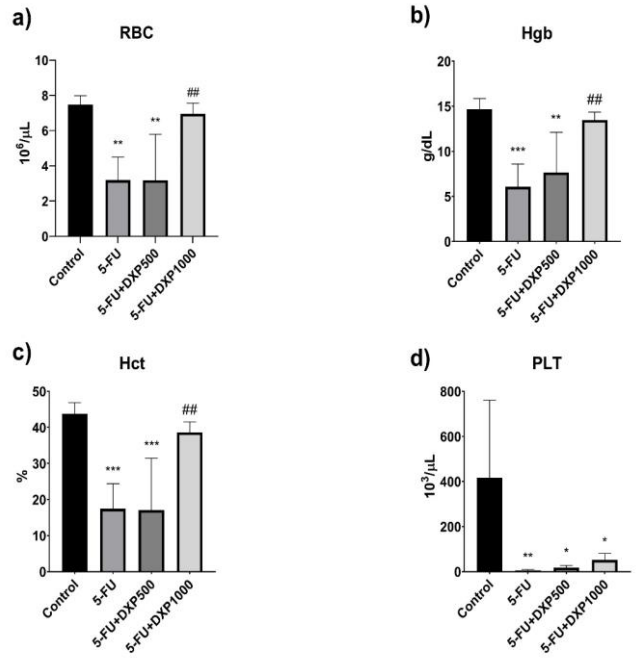

Figure 2: *Effect of DXP on 5-FU-induced erythrocyte count changes. *p<0.05, **p<0.01 and ***p<0.001 indicate statistical significance compared to the control group. ##p<0.05, ##p<0.0.1 and ###p<0.001 indicate statistical significance compared to 5-FU group.*

In an animal experiment with anacardic acids from Amphipterygium adstringens, it was shown that anacardic acids have significant myeloprotective and antineoplastic effects and can protect the organism against the toxic effects of drugs such as 5-FU and carboplatin by increasing the effectiveness of chemotherapeutics.

In a study investigating the effect of high dose uridine on 5-FU-induced myelosuppression, it was found that intermittent iv uridine infusion starting 3 hours after 5-FU administration and lasting for 72 hours corrected leukopenia but had no effect on thrombocytopenia.

Thus, this study demonstrated that high doses of uridine can reduce the severity of myelosuppression caused by 5-FU.

Conclusion

In our study, DXP at a dose of 1000mg/kg significantly improved RBC, hgb and hct levels.

Further studies are needed to find the optimal dose regimen of DXP and to understand its mechanism of action.

The number of studies with drug combinations instead of costly treatments such as erythrocyte suspension, platelet apheresis, Granulocyte Colony Stimulating Factor (G-CSF) should be increased against myelosuppression side effects of antineoplastic drugs.

More research is needed to increase the antineoplastic efficacy of drug combinations and reduce side effects such as myelosuppression.

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BIBLIOMETRIC ANALYSIS ABOUT GASTRIC CANCER

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ABSTRACT

In this study conducted a bibliometric analysis to identify the most influential publications in the field of gastric cancer. Bibliometrics is a quantitative research method that examines publication, citation and co-citation patterns to identify research trends, hot topics and influential authors in a given field. In this study, 2,270 articles published between 1990 and 2022 were selected from the Web of Science database and co-citation maps and keyword co-occurrence maps were created using VOSviewer software. Co-citation maps show the most influential articles and authors in the field, while keyword co-occurrence maps show the most frequently used keywords in the field and their relationships.

The analysis showed that the number of publications on gastric cancer has increased over the years, indicating a high level of interest and research activity in the field. The majority of articles were published in specific journals, highlighting the importance of journal publication for researchers in the field of gastric cancer. The analysis also showed that the United States, China and Japan were the most prolific countries in terms of publications, keywords such as "Gastric Cancer", "Helicobacter Pylori", "Diet", "Mortality", "Stomach Neoplasms" and "Epidemiology" were most frequently used, and research trends covered topics such as diagnosis, treatment, molecular mechanisms, epidemiology, risk factors, early detection, screening, health disparities and access to care.

The results of this study can guide future research and clinical practice in the field of gastric cancer. Researchers can use the findings of this study to identify the most influential articles and authors in the field and explore research trends and hot topics in the field. The findings can also help clinicians stay abreast of the latest advances in gastric cancer diagnosis and treatment.

This study also has some limitations. The search was limited to the Web of Science database, other databases were not included. The analysis was limited to articles only, other materials (congress proceedings, books, etc.) were not included. The analysis focused on the number of publications and citations on the other hand other measures of research impact such as H-index were not used.

POSTER PRESENTATIONS

CURRENT APPROVED TARGETED THERAPY DRUGS USED IN SPESIFIC CANCER TYPES

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ABSTRACT

Today, it is critical to increase effective treatment options in order to reduce the death rate from cancer diseases. In addition to developing new drugs in increasing effective treatment options, studies on existing drugs and diversification of usage alternatives are among the researches. As a result of studies, targeted therapy drugs approved for use on specific cancer types are published by institutes of cancer [1-3]. Drug treatment in cancer diseases requires a relatively long time and high cost, so the need for health care's services increases in long-term treatment of patients. Successful and cost-effective approaches to cancer treatments have been the subject of researches in recent years [4-6]. In this presentation, the current status of drugs approved for use for specific cancer types by the American Food and Drug Agency and their license status in Türkiye is going to be given on the basis of 2023. Pharmaceutical dosage forms and routes of administration of these drugs is also be going to be given, and the need for healthcare personnel in treatment is going to be evaluated.

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FIBROEPITHELIAL POLYP MIMICKING SARCOMABOTRYOID CARCINOMA- A RARE CASE PRESENTATION

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ABSTRACT

Objective

Fibroepithelial polyps in the vaginal canal are uncommon lesions with well-established histological characteristics. However, these polyps may display unusual morphological features in exceptional cases, leading to diagnostic challenges and potential misinterpretations. Here, we present a case of a fibroepithelial polyp in the vaginal canal that closely resembled sarcomabotryoid carcinoma, emphasizing the significance of precise diagnosis and appropriate management.

Case Presentation

A 54-year-old postmenopausal female patient presented with a sudden onset of a firm, nodular mass measuring approximately 2.5 cm in size. The patient noticed this mass over a period of three days. Upon further examination, it was noted that the palpable vaginal mass exhibited a smooth surface and did not appear to be associated with pain or any signs of bleeding (Figure 1) The polypoid mass was found to be affixed to the left lateral vaginal wall via a stalk measuring approximately 0,5 cm in length. The mass was excised locally, and the pathology report indicated a fibroepithelial polyp. Upon a follow-up visit three months later, no recurrence was observed in the patient.

Conclusion

Fibroepithelial polyps are characterized as mucosal polypoid lesions featuring a central core of connective tissue, enveloped by a benign squamous epithelium. We documented an unusual occurrence of concomitant fibroepithelial polyps originating from the vaginal wall in a 54-year-old female patient. Following surgical intervention, she had a smooth postoperative recovery, devoid of any complications, suggesting that surgery is the most effective approach for managing such tumors.

Keywords: *Fibroepithelial polyp, sarcomabotryoides, pseudosarcoma botryoides, mesodermal stromal polyp*

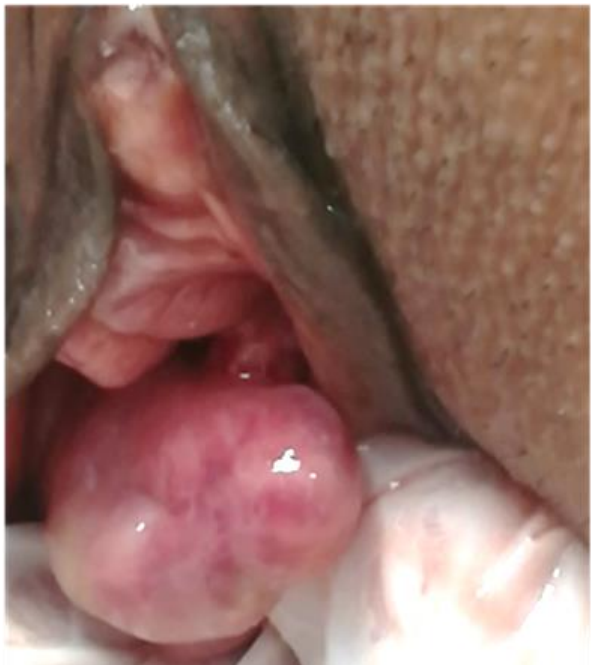

Figure 1. *Surface appearance of the vaginal mass*

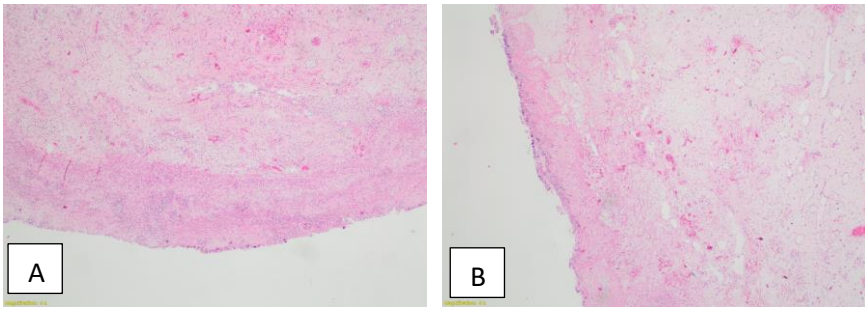

Figure 2. *A. Polyp section with completely dissapeared surface epithelium, enlargement of basal layer cells, and hypocellular stroma in H&E sections (x20). B. There are benefits for peaople who do not undergo nuclear options in H&E sections (x20).*

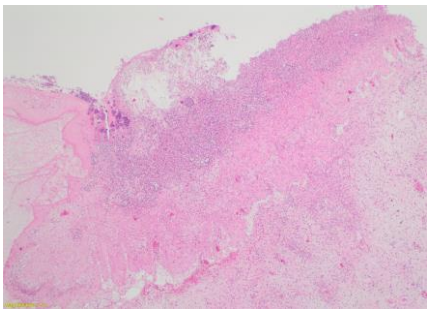

Figure 3. *In H&E sections, inflammatory exudate is seen on the surface and inflammatory granulation tissue is seen in the stroma(x20).*

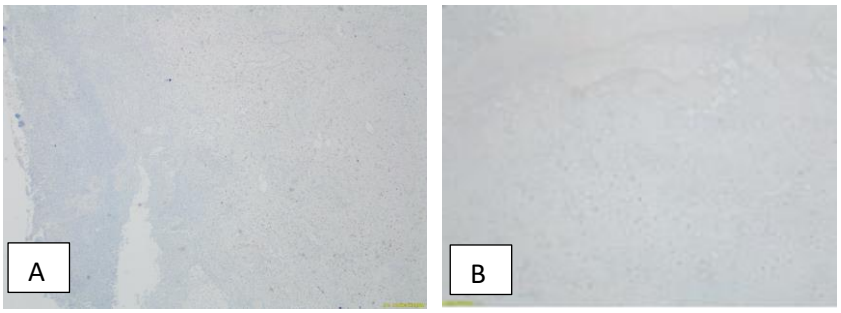

Figure 4. *Immunohistochemically, stromal cells stained positively for estrogen and progesterone (x20)*

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PROTECTIVE EFFECTS OF THIAMINE PYROPHOSPHATE AND CINNAMON (*Cinnamomum verum*) AGAINST OXIDATIVE LIVER DAMAGE INDUCED BY ISONIAZID AND RIFAMPICIN COMBINATION IN RATS

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ABSTRACT

Isoniazid and rifampicin are effective drugs against mycobacteria and are used in the treatment of pulmonary tuberculosis as part of the combined treatment approach recommended by the World Health Organization[1]. Isoniazid and Rifampicin Combination (IRC) has been shown to cause hepatotoxicity[2].In the literature, oxidative stress and inflammation have been reported to play a role in the pathogenesis of IRC-induced hepatotoxicity[2].Antioxidative and anti-inflammatory effects of thiamine pyrophosphate (TPP) and Cinnamon Extract (CE) have been shown in previous studies[3]. The aim of this study was to investigate the protective effect of TPP and CE against possible liver damage caused by IRC treatment in rats. In our study, 24 male albino Wistar rats were used. Experimental animals were divided into four groups as healthy control group (SG), Isoniazid (50 mg/kg) + Rifampicin (50 mg/kg) group (IRG), TPP (25 mg/kg) + Isoniazid (50 mg/kg) + Rifampicin (50 mg/kg) group (TIRG) and CE (100 mg/kg) + Isoniazid (50 mg/kg) + Rifampicin (50 mg/kg) group (CIRG). The doses given once a day for 7 days. At the end of this period, the animals were euthanized by giving 50 mg/kg thiopental sodium intraperitoeal and the liver tissues were removed.Levels of MDA, tGSH, SOD, CAT, TNF-α, IL-6, IL-1β and NF-κB biomarkers were measured in the excised tissues.According to our biochemical analysis results, the increase in oxidants and decrease in antioxidants indicate that IRC causes oxidative stress in liver tissue. TPP and CE treatments inhibited these changes in oxidants and antioxidants ($p<0.001$). TPP was more successful than CE in this inhibition ($p<0.001$). IRC treatment induced hepatotoxicity due to oxidative and inflammatory damage in rat livers and TPP and CE reduced this damage. In conclusion, the addition of TPP to IRC treatment may be a novel therapeutic strategy to prevent the hepatotoxic effect of IRC.

Keywords: *Thiamine pyrophosphate, cinnamon, Isoniazid, rifampicin, rat*

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INVESTIGATION OF THEORETICAL ACTIVITIES OF DIFLOROBENZENE DERIVATIVE MOLECULES AGAINST COLON CANCER

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ABSTRACT

Colon cancer is a type of cancer that develops in the colon or rectum, the last part of the intestines. They often start as polyps in the intestines and can slowly turn into cancer [1]. Colon cancer often has no symptoms in the early stages, so regular screenings are important. Symptoms include abdominal pain, bloody stools, weight loss, and changes in stool habits. The chance of cure is higher when diagnosed early, and treatment options may include surgery, chemotherapy and radiotherapy. Healthy lifestyle choices are important in reducing the risk of colon cancer [2,3].

In this study, the chemical and biological activities of diflorobenzene derived molecules will be compared. First, diflorobenzene derived molecules, calculations were made on 6-31^{++}G(d,p) basis set at HF, M062X, and B3lyp levels. Afterwards, these molecules were characterized by IR, ^{1}H NMR, ^{13}C NMR and UV-Vis spectrum analysis. Additionally, molecular docking calculations of the studied molecules were performed for prostate cancer (PDB ID: 6XXP and 3RUK).

Keywords: *Computational, DFT, spectrum, diflorobenzene, docking*

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EVALUATION OF THE ATTITUDES AND AWARENESS LEVELS OF THE COMMUNITY REGARDING CERVICAL CANCER AND HUMAN PAPILLOMAVIRUS INFECTION

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ABSTRACT

Cervical cancer is a highly prevalent cancer among women worldwide and is associated with significant morbidity and mortality [1]. Human Papillomavirus (HPV) infection is responsible for 99.7% of cervical cancer cases [2]. While HPV infection is primarily transmitted through sexual contact, it can also be transmitted through skin-to-skin contact in the genital area. More than half of sexually active men and women become infected with HPV at some point in their lives [3]. The majority of HPV infections are transient and harmless, with approximately 70% of infections resolving on their own within one year [4]. Persistent and recurrent HPV infections, particularly in areas such as the cervix, vagina, vulva, penis, anus, base of the tongue, and tonsils, can lead to the development of cancer [5].

A study conducted in Türkiye from 2019 to 2023 aimed to determine the relationship between cervical cancer and HPV, assess articles related to HPV vaccination, and gauge the knowledge and awareness levels of the community. A search was conducted in Turkish and English using keywords such as "Cervical Cancer, HPV, HPV knowledge level, HPV awareness, HPV vaccine, Türkiye" on Google Scholar, PubMed, and Dergipark databases. The search yielded 127 articles on Google Scholar, 131 on PubMed, and 44 on Dergipark. After applying inclusion criteria, 98 articles were evaluated.

The knowledge of HPV being sexually transmitted varies, with rates ranging from 20.53% to 99.4% among university students, 28.6% to 92.4% among women, and 76.9% to 96.9% among healthcare workers. Awareness of HPV vaccine was found in 47.3% to 92.7% of university students, 39.2% to 56.9% of women, and 64.1% to 100% of healthcare workers. When examining the rates of HPV vaccine uptake, university students ranged from 0.07% to 8.6%, women from 3.4% to 9.5%, and healthcare workers from 1.8% to 15.3%. About 72.2% of doctors believe that HPV vaccination should be included in routine vaccination schedules [6]. In another study, it was observed that only 24.5% to 49.8% of women had undergone Pap smear tests, and 73% of women had never undergone gynecological examinations [7,8,9].

In Türkiye, it was found that awareness of the relationship between cervical cancer and HPV is at a moderate level, and knowledge about HPV vaccine is inadequate. Healthcare workers play a crucial role in influencing individuals' decisions to get vaccinated, with 93.8% being a determining factor [10]. Providing in-service training to healthcare workers and implementing community-wide projects can increase awareness about the relationship between cervical cancer and HPV, as well as HPV vaccination, which is essential for women's health and can be prevented through vaccination.

Keywords: *Cervical Cancer, Human Papillomavirus, HPV knowledge level, HPV awareness, HPV vaccine, Türkiye*

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