POSTER BİLDİRİLER

[Abstract:0086]

CDH1 Mutation and Gastric Signet Ring Cell Cancer Detected in a 16-Year-Old Patient Without a Family History: A Case Report

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Abstract

Objective: Hereditary diffuse gastric cancers are one of the genetically inherited cancer syndromes that include pathogenic or likely pathogenic mutations in various genes, including the CDH1 (Cadherin 1) gene. This gene plays a critical role in genetic diffuse gastric cancer and lobular breast cancer.

Pathogenic variants of this gene exhibit an autosomal dominant inheritance pattern, and diagnosis is usually made before the age of 20. Isolated diffuse gastric cancer may occur, or it may be seen in first- or second-degree relatives. Family history is not neccessary for diagnosis.

Case: A 16-year-old female patient presented to the emergency department in February 2024 with complaints of abdominal pain. Laboratory tests showed glucose: 430 mg/dL, creatinine: 1.3 mg/dL, positive urinary ketones, and venous blood gas pH: 7.0, leading to a diagnosis of diabetic ketoacidosis, and the patient was admitted for treatment. Due to persistent abdominal pain during follow-up, antibodies for Celiac disease, which can be associated with Type 1 DM, were tested. Because of Anti-tissue transglutaminase IgG antibodies were positive, endoscopy was performed. Endoscopic imaging revealed polypoid lesions throughout the stomach, and multiple biopsies were taken. Histological examination of the biopsies showed findings consistent with signet ring cell carcinoma (diffuse) of the stomach. Imaging studies performed for disease staging revealed localized disease, and the patient was referred for surgery. Postoperative pathological evaluation confirmed signet ring cell carcinoma. A germline next-generation DNA sequencing analysis was performed, revealing a heterozygous, autosomal dominant CDH1 gene mutation (c.187>T p(Arg63)). According to the patient's surgical pathology, the tumor was staged as T1aN0M0, classified as Stage I. Since there was no need for adjuvant therapy, the patient was placed under follow-up. Annual breast ultrasound screening was recommended for lobular breast cancer surveillance, and family screening was also advised.

Conclusion: Here, we present a case of a 16-year-old with no family history who was found to have a CDH1 mutation and diffuse carcinoma of the stomach. If positive, patients should also be evaluated and followed up for lobular breast carcinoma. The follow-up and treatment of such cases should be conducted by a multidisciplinary team, including molecular geneticists, medical oncologists, and surgical oncologists.

Keywords: CDH1, Diffuse gastric cancer, Family history, Lobular breast carcinoma

Author To Editor: Bildiriyi göndermekte ki amacım; aile öyküsü olmadan da hastalarda mutasyon bakmanın önemini göstermektektir. Bu sayede hastalarda önleyici onkolojik tarama ve taramalar yapılabilmektedir.

[Abstract:0099]

Multiple Primary Cancers with BRCA Mutation: Two Case Reports

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Abstract

Objective: Hereditary breast and ovarian mancer attributable to pathogenic variants in BRCA1/2 is characterized by an autosomal-dominant pattern of inheritance, markedly increased susceptibility to breast and ovarian cancer, with an especially early onset of breast cancer, and an increased incidence of tumors of other organs,such as the fallopian tubes, prostate, male breast, and pancreas. Multiple primary tumours are usually metachronous or synchronous, depending on the time of presentation between the two malignancy diagnoses. Although synchronous diseases often occur as a result of exposure to similar carcinogens, metachronous ones are more often related to the treatment of the primary tumour.

Case: A 64-year-old woman the biopsy taken from the omentum was found as ovarian serous carcinoma metastasis. She was given 6cycles of paclitaxel-carboplatin treatment with a diagnosis of stage 4 ovarian carcinoma. In the response evaluation of the patient,a complete response to liver metastasis was obtained on abdominal MRI.TAH+BSO was performed and pathological complete response was obtained.After 1 year of treatment-free follow-up, a 2.5x1.5 cm lesion was detected in the head of the pancreas in the control examination.The patient underwent whipple operation.Pathology was evaluated as pancreatic adenocarcinoma.After adjuvant treatment a 15 mm nodular lesion with pathological FDG uptake in the right breast.Breast tru-cut biopsy was evaluated as invasive ductal carcinoma. The patient underwent modified radical mastectomy.Adjuvant letrozole treatment was started. According to NGS results the patient carries the BRCA1 gene mutation.mCase 2:A 72-year-old patient was examined with cough and shortness of breath.Pet-CT revealed a
pleura-based 74*42*73 mm mass (SUVmax:11.51) in the lower lobe of the right lung and heterogeneous involvement in the prostate.Right lung lower lobectomy was performed. Pathology was evaluated as squamous cell carcinoma.He received 4cycles of carboplatin-paclitaxel treatment. TRIB pathology result was compatible with prostate adenocarcinoma with Gleason score 3+3=6.Androgen deprivation therapy was started. In the 10th month of follow-up,a 3 cm lesion compatible with metastasis in the pancreas. The patient underwent whipple operation. Pathology was evaluated as pancreatic adenocarcinoma (T2N0M0.)According to NGS results the patient carries the BRCA 1 gene mutation

Conclusion: Inherited mutations in BRCA1 and BRCA2 genes increase the risk of development of cancer in organs especially in breast and ovary. Prevention and screening in BRCA mutation carriers are of high importance

Keywords: BRCA carriers, multiple primary tumors, synchronous tumor

[Abstract:0100]

A Rare Case: Germline PRKN Mutant Primary Peritoneal High Grade Serous Carcinoma

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Objective: Primary peritoneal serous carcinoma (PPSC) is an extremely rare malignancy. It is an epithelial tumor arising from the peritoneum and is histopathologically similar to serous ovarian carcinoma. The prognosis is poor and the median survival time is 11-17 months. Because the frequency of BRCA mutations in peritoneal and ovarian cancer cases is similar, PPSC is thought to be part of the hereditary breast-ovarian cancer syndrome. Parkin (PRKN) gene mutations are not common. But many studies have demonstrated Parkin gene alterations in a wide variety of cancers. It is associated with poor survival in patients with advanced breast cancer. However, its clinical significance in primary peritoneal cancers is unknown. In this case report, it is aimed to contribute to the literature by presenting a case of primary peritoneal high grade serous carcinoma with germline parkin gene mutation, to better recognize this extremely rare clinical problem and to describe its clinical features.

Case: A 38-year-old pregnant woman had a cesarean section at 31 weeks of pregnancy due to respiratory problems. Peritonitis carcinomatosis was detected during surgery. Peritoneal biopsy sampling revealed a histopathological diagnosis of high-grade serous carcinoma. The patient was administered 3 cycles of carboplatin-paclitaxel protocol. Then, debulking surgery was performed and 8 cycles of carboplatin-paclitaxel were completed. A partial response was achieved. In the NGS analysis; BRCA 1/2 was wild type, PRKN gene was mutant. After 3 months of niraparib treatment, progression was detected and the patient was started on the cisplatin-gemcitabine-bevacizumab protocol. The patient, who was found to have a complete response on PET-CT taken 6 cycles later, was continued with maintenance bevacizumab. Liposomal doxorubicin was started in the patient whose disease progressed after 6 months of maintenance bevacizumab. The patient, who was given the second course of liposomal doxorubicin 2 weeks ago, continues to live with an overall survival of approximately 50 months.

Conclusion: The clinical significance of parkin gene mutation in primary peritoneal high-grade serous carcinoma, a very rare malignancy, is unknown. More data are needed to better define the clinical significance of PRKN gene mutation in these patients.

Keywords: Peritoneal cancer, PRKN gene mutation, serous carcinoma

[Abstract:0101]

A Rare Case of Genetic Skin Tumor: Brooke-Spiegler Syndrome

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Introduction: Brooke-Spiegler syndrome (BSS) is a rare autosomal dominant disorder associated with mutations in the CYLD gene. It is characterized by the development of cutaneous tumors, including basal cell carcinoma (BCC), cylindroma, and multiple trichoepitheliomas. The syndrome typically presents in childhood or early adulthood as slow-growing, painless skin lesions. If untreated, it can lead to significant tissue destruction in advanced stages. Herein, we report a rare case of BSS diagnosed at an advanced stage, notable for familial predisposition and extensive tissue involvement.

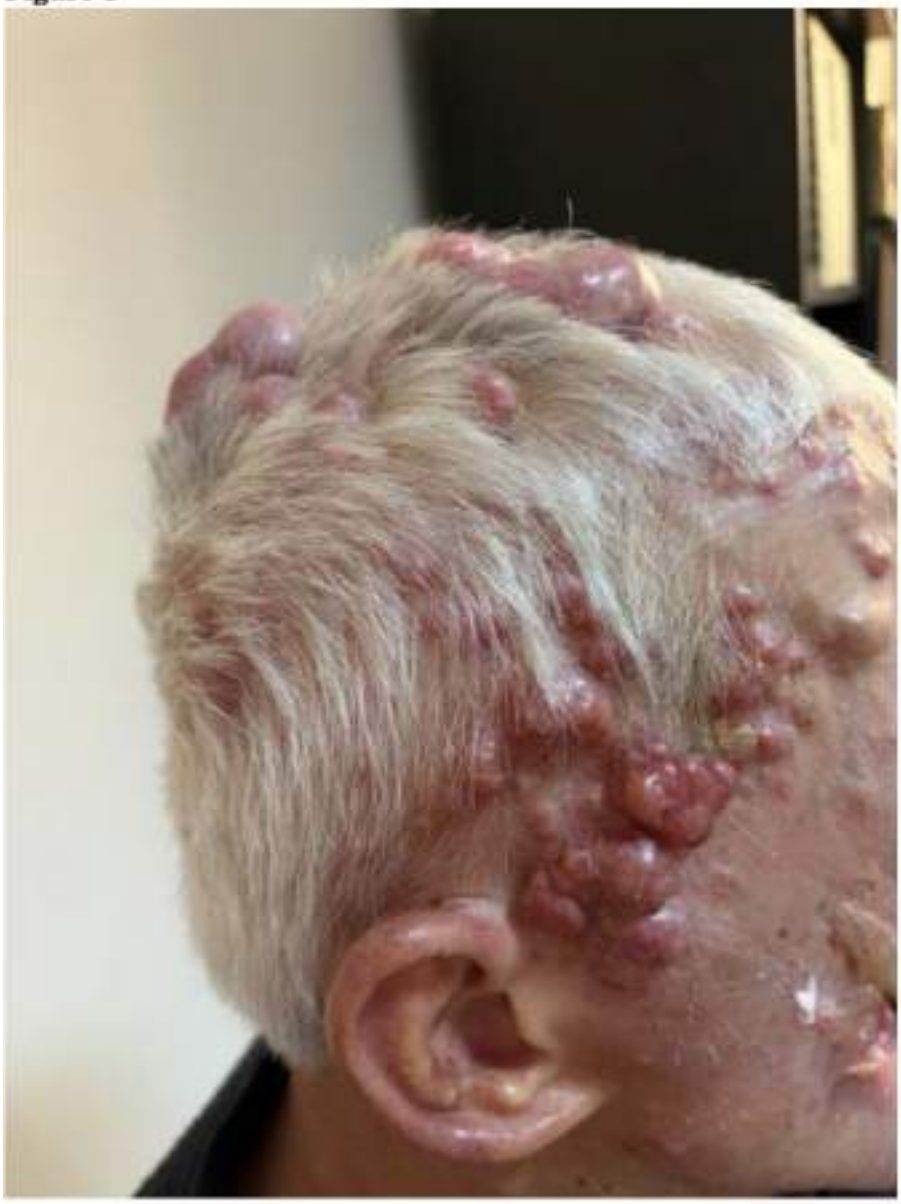
Case: A 56-year-old male presented to the dermatology clinic with a progressively enlarging lesion on the side of his nose over the past 10 years. His family history revealed similar scalp lesions in a cousin and an aunt. A biopsy of the nasal lesion confirmed the diagnoses of BCC and cylindroma. The patient was referred to our clinic with a diagnosis of Brooke-Spiegler syndrome and BCC. On physical examination, significant destruction of the right side of the face, including the mandible and maxilla, was observed, with exposed teeth in the affected area. Multiple nodular lesions were noted on the scalp and bilaterally on the face. Radiological evaluation revealed a thick-walled necrotic lesion measuring 14x15 mm in the left maxillary sinus, and a 3 mm nodule in the posterobasal segment of the right lower lung lobe on chest CT. The nodular scalp lesions were considered consistent with cylindroma. Skin biopsies confirmed BCC in the nasal region and cylindroma in the forehead, with histopathological findings indicating tumor persistence at the surgical margins. The patient was started on vismodegib, a targeted Hedgehog pathway inhibitor, at a daily dose of 150 mg. He was also referred to the medical genetics department for comprehensive analysis of CYLD gene mutations.

Conclusion: This case highlights the diagnostic challenges and treatment strategies for Brooke-Spiegler syndrome. A thorough family history is crucial for early diagnosis. In advanced cases, combining targeted therapies with surgical interventions can lead to successful outcomes.

Identification of CYLD gene mutations can guide genetic counseling and family screening. This report underscores the clinical features and management of a rare disease at an advanced stage.

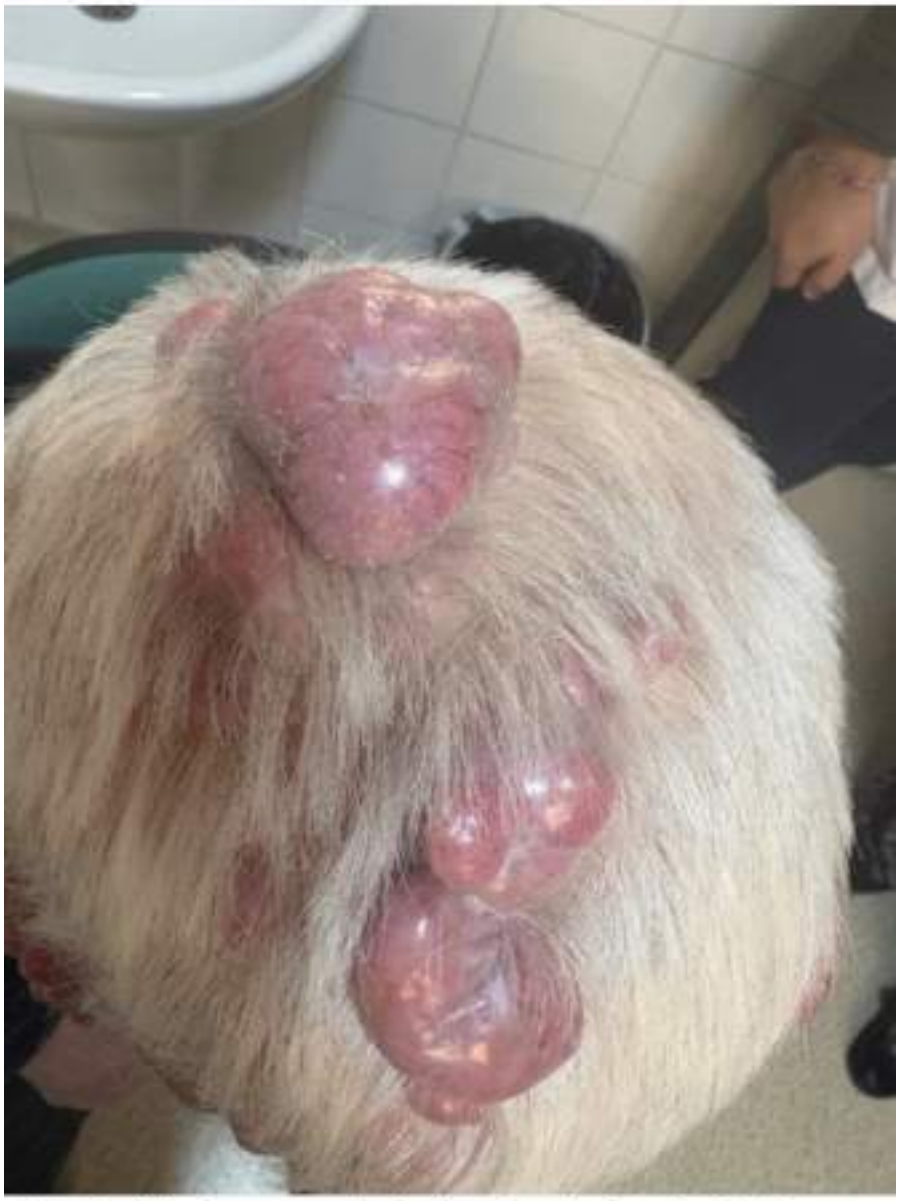
Keywords: Brooke-Spiegler syndrome, CYLD gene mutation, basal cell carcinoma, cylindroma, genetic skin tumors

Figure 1



Nodular Lesions Observed on the Scalp and Face Associated with Brooke-Spiegler Syndrome

Figure 2



Giant Nodular Lesions on the Scalp in Brooke-Spiegler Syndrome

Author To Editor: Sayın Bildiri Değerlendirme Kurulu Üyeleri, Sizlere nadir görülen genetik bir deri tümör sendromu olan Brooke-Spiegler sendromuna ait bir olguyu sunmaktan mutluluk duyuyoruz. Çalışmamızda, ileri evrede tanı almış ve belirgin klinik bulgularla karakterize bu olguyu literatüre katkı sağlayacak şekilde detaylı olarak ele aldık. Genetik, klinik ve radyolojik açıdan kapsamlı bir şekilde değerlendirilmiş olan bu hasta, Brooke-Spiegler sendromunun tanı ve tedavi süreçlerindeki zorluklara ışık tutmaktadır. Bu bildiriyi, ilgili alandaki farkındalığı artırmak ve bilimsel toplulukta tartışma yaratmak amacıyla dikkatinize sunuyoruz. Değerlendirme sürecinde göstereceğiniz kıymetli katkılarınız ve önerileriniz için şimdiden teşekkür ederiz. Ayrıca, bildirinin değerlendirilmesinde başarılı bulunması halinde verilecek olan kurs ödülüne büyük bir ilgi ve heyecan duyduğumu belirtmek isterim. Bu ödülün, bilimsel bilgi birikimimi geliştirme ve mesleki donanımımı artırma yönünde önemli bir fırsat sunacağına inanıyorum. Bu vesileyle, bildirime gösterdiğiniz değerli zaman ve ilginiz için tekrar teşekkür ederim.
Saygılarımla, Dr. Gülhan Özçelik Köker Akdeniz Üniversitesi Tıbbi Onkoloji Yandal Asistanı

Dear Members of the Scientific Committee, It is a great pleasure to present a case of Brooke-Spiegler syndrome, a rare genetic skin tumor syndrome, to your esteemed committee. In our study, we have detailed this case, which was diagnosed at an advanced stage and is characterized by prominent clinical findings, in a way that contributes to the literature. This patient has been comprehensively evaluated from genetic, clinical, and radiological perspectives, shedding light on the diagnostic and therapeutic challenges associated with Brooke-Spiegler syndrome. We submit this abstract to increase awareness in the field and to foster discussion within the scientific community. We are sincerely grateful for your valuable contributions and suggestions during the evaluation process. Furthermore, I would like to kindly express my great interest and excitement regarding the course award that will be given following the evaluation of the abstracts. I believe this award represents a unique opportunity to enhance my scientific knowledge and professional skills. Once again, I thank you for the time and attention you have devoted to reviewing my abstract.
Kind regards, Dr. Gülhan Özçelik Köker Medical Oncology Fellow, Akdeniz University

[Abstract:0106]
Familial Adenomatosis Polyposis Coli

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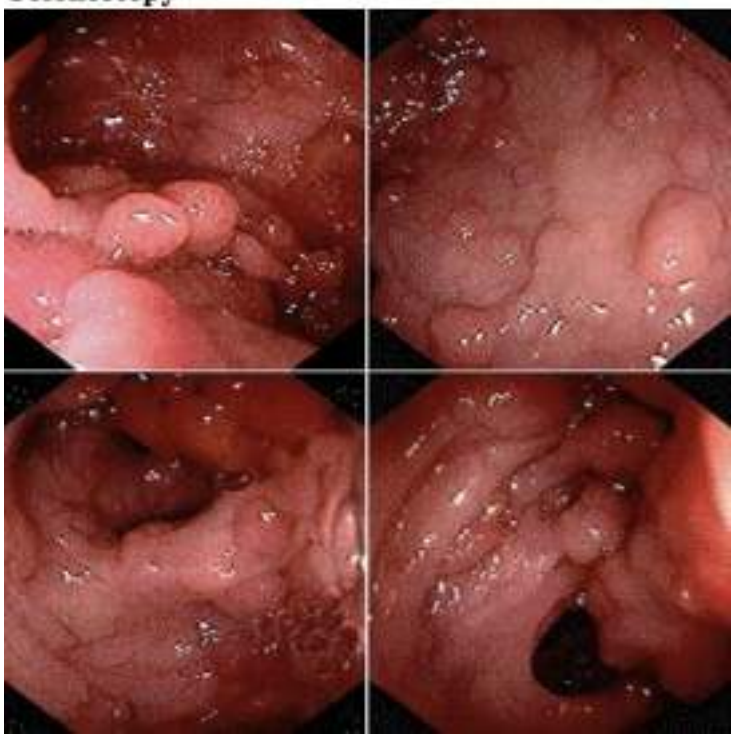
Objective: Familial adenomatous polyposis is a genetic disorder that predisposes you to develop precancerous colon polyps called adenomas. Colon polyps are abnormal growths in the lining of your colon or rectum. They aren't cancer, but certain types, like adenomas, can change into colorectal cancer. Without treatment, the risk of developing colorectal cancer with familial adenomatous polyposis is close to 100%. It also develops relatively earlier and faster with FAP than in those without. Children in families known to be affected by the syndrome begin yearly colonoscopy screenings at the age of 10.
Case: A 32-year-old male patient who applied due to diarrhea was examined because his father had a history of colon cancer. During the colonoscopy, multiple polyps were detected covering the entire colon, the largest measuring 3cm. An ulcerovegetating mass was observed covering 50% of the distal wall of the rectum. In the polyp biopsy taken, the polyps in the colon were detected as tubular adenoma. Rectum biopsy revealed adenocarcinoma. A mutation in the APC gene was detected in the somatic genetic test. Abdominal MRI performed for staging purposes revealed a T4aN2nM0 high + mid rectum tumor. No distant metastases other than the primary tumor were detected in the PET/CT scan. Total colectomy was planned after 12 courses of neoadjuvant FOLFIRINOX. Chemotherapy was started after the patient's blood test and echocardiography were found to be normal. His treatment is still ongoing.
Conclusion: Without timely treatment, the median life expectancy is 42 years. But with appropriate care, you can live a normal life. Once your colon has been removed, your biggest risk is from other gastrointestinal cancers or problematic desmoid tumors. These occur much less frequently than colorectal cancer.
Keywords: FAP, colorectal cancer, polyposis

Colonoscopy



[Abstract:0115]

Belzutifan Treatment in von Hippel-Lindau Disease: A Case Report

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Abstract

Objective: Von Hippel-Lindau (VHL) disease is a rare autosomal dominant genetic syndrome, characterized by germline pathogenic variants in the VHL gene. Its prevalence is estimated to be approximately 1-2/39,000 cases of. VHL disease is characterized by the presence of multiple benign and malignant tumors, including clear cell renal cell carcinomas (RCCs), central nervous A study published in 2021 investigated VHL-associated kidney cancer in an open-label clinical trial involving 61 patients diagnosed with VHL-associated kidney cancer based on a VHL germline alteration and with at least one measurable tumor in the kidney. The study reported an overall response rate of 49% in patients with VHL-associated renal cancer, 63% in 24 patients with measurable central nervous system haemangioblastomas, and 83% in 12 patients with measurable pancreatic neuroendocrine tumors. The objective of presenting this case is to raise awareness of this rare disease.

Case: A 28-year-old female patient was evaluated in March 2013 with complaints of hirsutism. Two masses compatible with malignancy were detected in the right kidney. Following the right partial nephrectomy on 07.03.2013, the pathology result was reported as renal cell carcinoma (RCC). The patient was subsequently observed without undergoing any further treatment. In 2020, a genetic examination revealed a positive Von Hippel-Lindau (VHL) mutation, identified following the detection of RCC in the patient's family, specifically her mother and sisterDuring the follow-up period at the Göztepe Prof. Dr. Süleyman Yalçın City Hospital, approximately 11 years later, on 24/02/2024, pancreatic cysts and Bosniak Type 3 cysts (with high malignant potential) in the kidney were detected on abdominal magnetic resonance imaging (MRI); 2 mm diameter lesions compatible with cerebellar hemangioblastoma were detected on brain MRI. Following the approval of overseas drug use, Belzutifan 120 mg was initiated in March 2024. Subsequent follow-ups revealed that the patient's masses remained stable and exhibited no active complaints, except for Grade 1 anemia.

Conclusion: Belzutifan is vital in treating Von Hippel-Lindau (VHL) disease and is an indispensable agent in the treatment protocol.To evaluate responses to treatment in this rare disease, multicentre clinical trials involving a large patient population are required.

Keywords: Von Hippel Lindau Disease, Renal Cell carcinoma, hemangioblastomas, Belzutifan, effectiveness

[Abstract:0117]

Clinicopathologic Features of Male Breast Cancer Patients: A Single Center Experience

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Objective: Breast cancer is rare in men, accounting for about 1% of all breast cancer patients and 0.2% of cancers in men.The risk of male breast cancer appears to be higher with inherited BRCA2 rather than BRCA1 mutations. We aimed to retrospectively evaluate the clinicopathologic features of our male breast cancer patients.
Materials-Methods: All breast cancer patients admitted to Pamukkale University Medical Oncology Clinic between September2005 and July2022 were screened and 21 male breast cancer patients were included. Age at diagnosis,family history,localization of the primary tumor, presenting symptom, stage, histological type,ER,PR,HER2,Ki67,BRCA mutation,
chemotherapy, surgery, progression-free and overall survival data were evaluated and the literature was reviewed.
Results: The median age of the patients was 59+11.7(40-82)years.Stage1 was 5(23.8%),Stage2 was 6(28.6%),Stage3 was 4(19%),and Stage4 was 6(28.6%).The presenting symptom was a palpable mass in the breast or axilla in 16(76.2%) patients. Primary tumor localization was right breast in 11(52.4%),nipple/central in 12(57.1%)and upper outer quadrant in 2patients(23.8%).4patients(19%)had multicentric tumors.The most common histologic type was invasive ductal carcinoma in 14 patients(66.7%). According to hormone profile,16(76.2%) patients were ERpositive,13(61.9%) patients were PRpositive,4(19%)patients were Her2positive and 14(66.7%)patients had Ki67 of 20% or higher.Accordingly, LuminalA was 4(19%),Luminal B/her2negative 10(47.6%),Luminal B/her2 positive 2(9.5%),Her2 positive/nonluminal 2(9.5%)and triple negative 3(14.3%). Grade3-4 according to tumor grade was detected in 11patients (52.4%).16(76.2%)patients underwent MRM or simple mastectomy.There were 4(19%) patients with BRCA1 mutation and 10 (47.6%)patients with BRCA2 mutation. Adjuvant chemotherapy 9(42.9%)and adjuvant radiotherapy 8(38.1%).All hormone receptor positive patients received Tamoxifen treatment. Triple negative patients received anthracycline-taxane based chemotherapy.There were 7 (33.3%)patients with a family history of cancer. Progression developed in 2 patients(9.5%) and 6 patients(28.6%)died.mPFS was 96.5+7.3(95%CI 82.2-110.9) months and mOS was 87.2+11.5(95%CI 64.6-109.8)months.
Conclusion: As with breast cancer in women, a family history of breast cancer in first-degree relatives is associated with an increased risk of breast cancer in men. The BRCA1 and BRCA2 gene leads to the majority of cases of known hereditary breast cancer in women. Genes other than BRCA may also play a role in predisposing men to breast cancer. PTEN mutation, PALB2, Cowden syndrome, Li-Fraumeni syndrome and Lynch syndrome have been associated with an increased risk of breast cancer in men. Diagnosis of male breast cancer at an early stage, hereditary gene analysis and appropriate treatment are very important for a good prognosis.
Keywords: Male breast cancer, clinicopathologic features, BRCA

[Abstract:0135]

Rare Genetic Insights: A Young Colorectal Cancer Patient with MUTYH Heterozygosity

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Objective: To present a rare case of early-onset colorectal cancer in a young patient with heterozygous MUTYH mutation, highlighting the clinical challenges, genetic implications, and potential considerations for personalized management and family screening strategies.

Case: A 34-year-old male patient with a significant family history of colorectal cancer presented with rectal bleeding in 2017. His father, two paternal uncles, and a cousin had been previously diagnosed with colorectal cancer, suggesting a potential hereditary predisposition. The patient had no known comorbidities or history of regular medication use. Colonoscopy performed due to lower gastrointestinal bleeding revealed two polyps in the descending colon and an ulcerovegetative mass in the ascending colon, which was partially obstructing the lumen. Biopsy of the mass confirmed adenocarcinoma. Pathological staging revealed a T2N0, grade 2 lesion, consistent with stage 1 colon cancer. Immunohistochemical analysis showed the loss of MLH1 and PMS2 expression. Further molecular testing identified wild-type KRAS, NRAS, and BRAF. Due to a suspicion of hereditary colorectal cancer, a next-generation sequencing (NGS) solid tumor panel was performed, focusing on genetic mutations associated with colorectal cancer. The analysis detected a heterozygous c.36+11C>T p.(=) variant in the MUTYH gene, implicating a potential role of MUTYH-associated polyposis (MAP) in the carcinogenesis. The patient did not receive adjuvant chemotherapy or radiotherapy. Close clinical and radiological follow-ups were conducted as part of the management plan. At his most recent evaluation in January 2025, there was no evidence of recurrence or metastasis.

Conclusion: This case highlights the importance of thorough genetic evaluation in young-onset colorectal cancer patients with a significant family history. The identification of a heterozygous MUTYH mutation underscores the potential contribution of carrier status to early-onset colorectal cancer and emphasizes the necessity of genetic counseling and family screening in such scenarios. The absence of recurrence or metastasis in the patient reinforces the importance of individualized treatment and vigilant surveillance strategies in hereditary cancer syndromes.

Keywords: Hereditary cancer syndromes, young-onset colorectal cancer, heterozygous mutyh mutation

[Abstract:0141]

Spectrum of Germline Cancer Susceptibility Gene Mutations in Turkish Cancer Patients: A Single Center Study

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Objective: The application of multigene panel testing in the genetic investigation of hereditary cancer in the years of personalized medicine is crucial for clinical surveillance, therapeutic approach, and risk-reducing management. The aim of the study was to reveal the genetic predisposition in a Turkish cohort of individuals referred for hereditary cancer.

Materials-Methods: A total of 1,105 individuals were referred for multigene genetic testing using NGS technology, during the period 2020-2024 in the laboratory. Among the examined individuals, 48.14% were diagnosed with breast cancer, 5.4% with ovarian cancer, 3.50% with colorectal cancer, 2.80% with prostate cancer and 4.60% with pancreatic cancer. 11.2% were healthy with a significant family history of cancer, while ~6.5% had a different type of cancer.

Results: 19.8% of the examined individuals carried a pathogenic variant. Specifically, 49.8% of the patients had a pathogenic variant in a clinically significant gene (BRCA1, BRCA2, BRIP1, PALB2, RAD51C, PMS2, CDKN2A, MLH1, MSH2, TP53, APC and RAD51D), of whom 16.9% were referred with no family history. When age cut-off is applied, 35.5% of individuals over 50 years old were harboring mutations in the aforementioned. Among the different types of pathogenic variants detected, a significant percentage (4.7%) represented copy number variation (CNV). Additionally, in 49.8% of the individuals tested, a variant of uncertain significance (VUS) was detected.

Conclusion: Comprehensive multigene genetic testing is necessary for appropriate clinical management of pathogenic variants' carriers, regardless age of diagnosis and family history of malignancies. Additionally, the information obtained is important for determining the risk of malignancy development in family members of the examined individuals.

Keywords: Germline cancer, multigene panel testing, Turkish cohort

Figure 1. Cancer type distribution in 1,105 individuals tested with hereditary cancer panel of 52 genes.

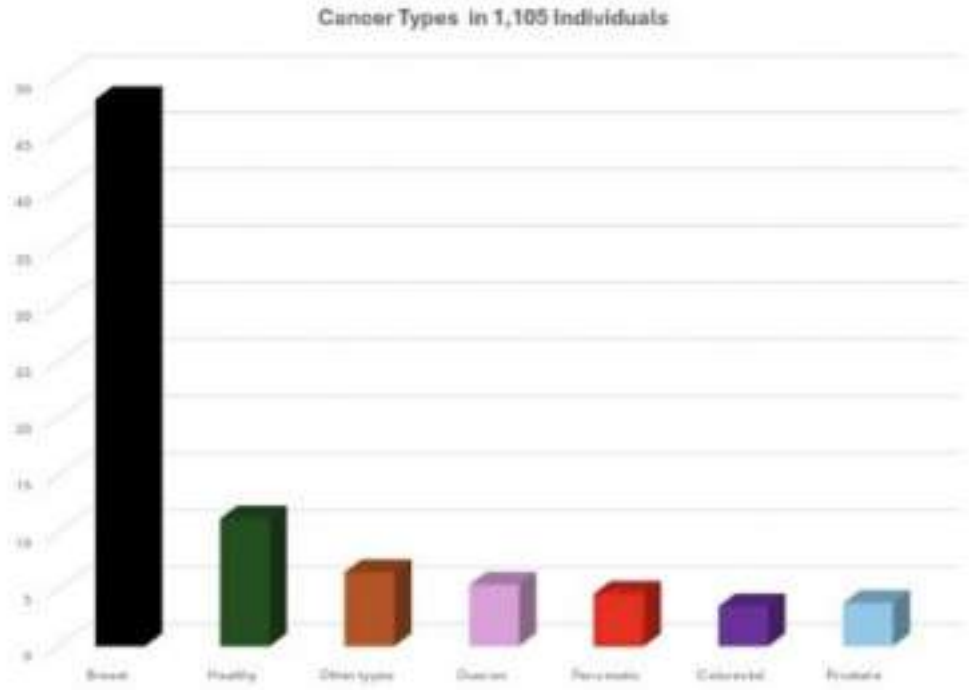
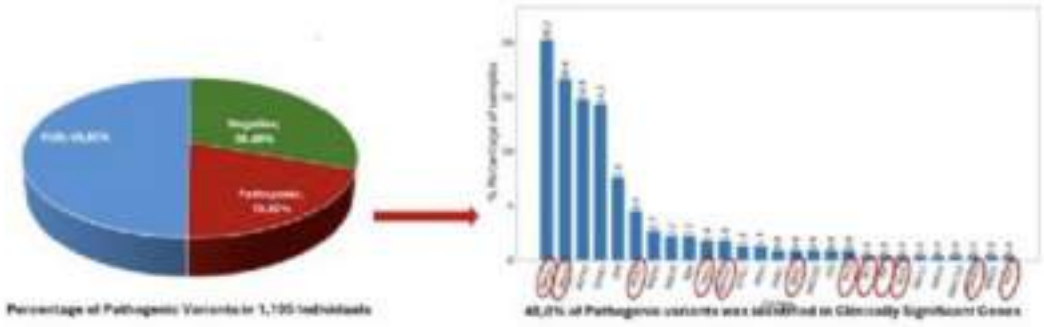


Figure 2. Mutational Distribution among positive (pathogenic) findings in 1,105 individuals



[Abstract:0170]

Transient Abnormal Myelopoiesis Associated with a Somatic Novel GATA1 Mutation in a Down Syndrome Case

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Abstract

Down syndrome (trisomy 21) is a genetic disorder caused by the presence of all or a portion of a third chromosome 21. Patients typically present with short stature, characteristic facial features, protruding tongue, conductive hearing loss, congenital heart defects, duodenal stenosis/atresia, imperforate anus, Hirschsprung disease, joint laxity, short, broad hands, mild to moderate intellectual disability, Alzheimer disease, hypothyroidism, leukemia (both ALL and AML) and growth retardation. Here, we report a newborn with dysmorphic features, respiratory distress, congenital pneumonia, chorioretinal atrophy, hypothyroidism, pericardial effusion, a small atrial septal defect (ASD), jaundice, widespread erythema and skin rashes, hepatomegaly, bilateral hydrocele, micropenis, leukocytosis, thrombocytopenia, and a peripheral smear showing a predominance of blastic white cells, along with transient abnormal myelopoiesis and acute myeloid leukemia (AML). Dysmorphic facial features included upslanting palpebral fissures, epicanthal folds, small ears, a flat nasal bridge, and a broad nasal bridge. Whole exome sequencing detected a nonsense variant in exon 2 of the GATA1 gene (NM_002049: c.168_185dup). We classified the variant as likely pathogenic according to the ACMG criteria. This study contributes to the role of next-generation sequencing in the detection of somatic mutations. However, it should be noted that somatic variants may not be blood-derived, and therefore, it is recommended to study non-hematopoietic samples such as buccal mucosa. This mutation was not reported previously in the literature. The mutation has been identified as novel.

Keywords: AML M5, Down syndrome, GATA1, Transient abnormal myelopoiesis

[Abstract:0181]

A Case Report of Low-Grade Serous Ovarian Carcinoma with Somatic BRCA Mutations and Discordant Germline Testing

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Objective: Low-grade serous ovarian carcinoma (LGSOC) is an uncommon subtype of epithelial ovarian cancer characterized by indolent behavior and resistance to conventional chemotherapy. BRCA mutations are rarely associated with LGSOC (1). This report aims to present a unique case of LGSOC with somatic BRCA1 and BRCA2 mutations, contrasting with the negative germline BRCA findings and highlighting its clinical and therapeutic implications.

Case: A 53-year-old woman presented with abdominal pain. She had no known family history of ovarian or breast cancer. Initial imaging in 2020 revealed a 92x93 mm solid pelvic mass, but the patient did not seek further medical attention. A pelvic MRI in February 2024 identified a 14x10.5 cm lobulated, heterogeneously enhancing mass. Total abdominal hysterectomy and bilateral salpingo-oophorectomy revealed bilateral low-grade serous carcinoma of the ovaries. Staging with FDG-PET in March 2024 revealed no evidence of distant metastasis. Adjuvant chemotherapy with six cycles of carboplatin and paclitaxel was initiated. Next-generation sequencing in the tumor tissue revealed three pathogenic frameshift mutations: BRCA1 c.1961delA (p.K654fs47, allelic fraction 4.4%), BRCA2 c.1813delA (p.I605fs9, allelic fraction 2.56%), and BRCA2 c.9097delA (p.T3033fs*29, allelic fraction 2.73%). Variant interpretation followed ACMG/AMP guidelines, with all mutations classified as Tier IA. Germline BRCA1/2 testing via liquid biopsy and MLPA analysis using the SALSA MLPA Probemix P002-D1 BRCA1 kit confirmed the absence of deletions, duplications, or pathogenic variants, supporting the somatic nature of the mutations. Immunohistochemistry demonstrated estrogen receptor positivity, leading to the initiation of letrozole therapy.

Conclusion: This case highlights the discordance between somatic and germline BRCA findings in LGSOC. Somatic BRCA mutations may expand therapeutic options, but data on the efficacy of PARP inhibitors in LGSOC remain limited and investigational (2). Further studies are required to evaluate the therapeutic potential of PARP inhibitors and other targeted therapies in LGSOC with somatic BRCA alterations.

Keywords: Low-grade serous ovarian carcinoma, Somatic BRCA mutations, BRCA testing discordance

References

1. Slomovitz B, Gourley C, Carey MS, et al. Low-grade serous ovarian cancer: State of the science. Gynecol Oncol.
2. Sanchez-Lorenzo L, Sancho L, Iscar T, Grisham R, Chiva L. Management challenges in low-grade serous ovarian cancer with a BRCA mutation. Int J Gynecol Cancer. 2024;34(4):631-636.

[Abstract:0187]

Identification of Pathogenic and Novel Variants in BRCA1 and BRCA2 Genes Using Next-Generation Sequencing in Hereditary Cancer Patients

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Objective: BRCA1 and BRCA2 mutations are significant contributors to the risk of various cancers, particularly breast and ovarian cancers. Accurate identification of these mutations is essential for risk assessment, management, and treatment strategies. This study investigates BRCA1 and BRCA2 mutations in a cohort of 30 cancer patients using next-generation sequencing (NGS) to identify pathogenic variants and their association with different cancer types.
Materials-Methods: Genomic DNA from peripheral blood samples of 30 hereditary cancer patients was analyzed for BRCA1 and BRCA2 mutations via next-generation sequencing. Variants were classified according to the American College of Medical Genetics and Genomics (ACMG) guidelines.
Results: The study cohort included 22 breast cancer, 5 ovarian cancer, 2 endometrial cancer, and 1 prostate cancer case. A pathogenic variant in either BRCA1 or BRCA2 was detected in 5 individuals, one of which was novel. Additionally, two distinct variants of uncertain significance (VUS) were identified in two cases. Three frameshift variants in BRCA2 (c.1773_1776del, c.3545_3546del, c.4772_4773del) were detected in two ovarian and one breast cancer case. Two distinct truncating variants were detected in the BRCA1 gene (c.2395A>T and c.844_850dup) in a breast cancer and an ovarian cancer patient, respectively.
Conclusion: This study highlights the role of BRCA1 and BRCA2 mutations in hereditary cancer syndromes, particularly in breast and ovarian cancers. Among the cohort of 30 patients, 5 individuals harbored pathogenic variants, including a novel mutation, demonstrating the utility of next-generation sequencing in identifying rare and potentially clinically relevant genetic variations. The detection of three frameshift variants in BRCA2 and two distinct truncating variants in BRCA1 further underscores the genetic heterogeneity of these mutations and their implications for different cancer types. The identification of two VUSs emphasizes the need for continued research and functional studies to determine their clinical relevance. These findings reinforce the importance of comprehensive genetic testing and interpretation to guide personalized cancer risk management and treatment strategies.
Keywords: BRCA1, BRCA2, genetic testing, hereditary cancer, next-generation sequencing

[Abstract:0221]

Development of a targeted mass spectrometry-based workflow for endometrial cancer biomarker verification

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Abstract

Endometrial cancer (EC) is the most common gynecologic disease in developed countries, with increasing incidence and mortality among women. Proteomics offers a promising approach for the discovery of novel biomarkers that can aid in early detection of disease. Mass spectrometry (MS)-based proteomics provides robust analytical capabilities and in-depth understanding of protein changes. Among MS techniques, multiple reaction monitoring mass spectrometry (MRM-MS) has emerged as a powerful tool for biomarker verification. It effectively meets the need for a high-throughput, selective and reliable method to verify candidate biomarkers identified in discovery studies. The aim of this study was to develop MRM-MS method to validate nine candidate protein biomarkers (Q01995, P14618, P40121, P09211, P28838, Q00688, P62937, P04179) that were previously identified as candidate biomarkers for EC. Nine unique peptides (LVNSLYPDGSKPVK, IYVDDGLISLQVK, QAALQVAEGFISR, MLLADQGQSWK, AAGIDEQENWHEGK, LEIEPEWAYGK, FEDENFILK, DSSTWLTAFVLK, and HHAAYVNNLNVTEEK) were determined to represent the nine candidate proteins. The development of an MRM method includes selecting transitions, optimizing instrument and chromatographic conditions. Isotope-labeled standard peptides ([13C6,15N2]-lysine or arginine) were used to develop the MRM-MS method for quantifying nine biomarkers in the representative tissue samples. Representative tissue samples were collected in Memorial Hospital (Ankara, Türkiye). Representative samples were subjected to protein extraction in Tris-HCl buffer (pH 7.6) using a homogenizer and protein digestion steps: denaturation in sodium deoxycholate, alkylation with dithiothreitol, reduction with iodoacetamide, and enzymatic digestion using Trypsin/Lys-C. The MRM-MS method has been successfully developed to ensure reliable results. The methods effectively monitor nine target proteins. The analytical merits including linearity, limit of detection, and matrix effect in tissue samples were extensively studied. The method performance was also tested using Quality control (QC) samples to assess variations arising from sample processing and instrumental analysis. The results demonstrated consistent performance with low variability and high reproducibility. Discovering and verifying biomarkers is essential for enhancing cancer diagnosis and prognosis. This is particularly important for hereditary cancers, as early detection can significantly improve disease outcomes. Our findings show the potential of MRM-MS to validate diagnostic biomarkers for EC. The method has been applied to a clinical cohort and data analysis is in progress.

Keywords: Biomarker, endometrial cancer, mass spectrometry, proteomics

[Abstract:0222]

A Case Report of MEN 1 Syndrome with Confirmed Mutation and Complete Clinical Features in Multiple Affected Family Members

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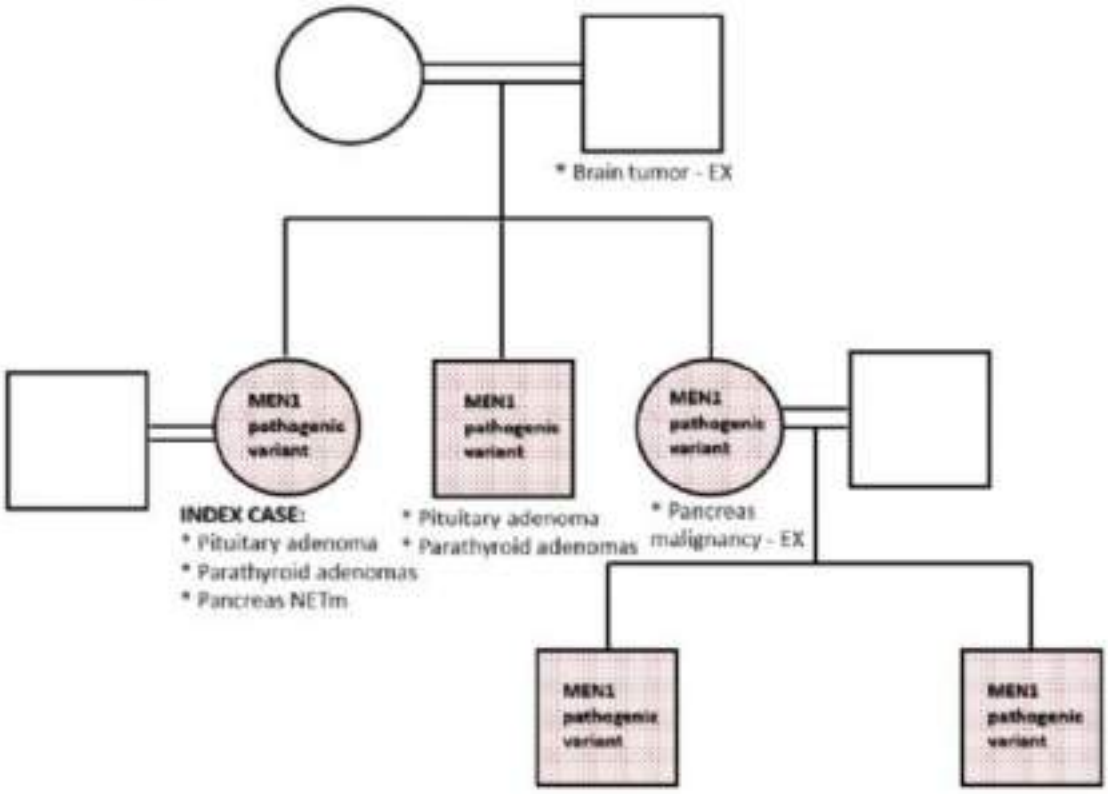
Objective: Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant inherited disorder, typically presenting with parathyroid, pituitary, and gastro-pancreatic neuroendocrine tumors (NETs), caused by germline heterozygous mutations in the MEN1 gene on chromosome 11q13.
Case: A 40-year-old female patient underwent surgery for prolactinoma in 2006. During routine follow-up, hypercalcemia and hyperparathyroidism were detected, and further investigations revealed a parathyroid adenoma. As a result, a right inferior parathyroidectomy was performed in 2007. While under observation without treatment for 13 years, the patient was referred to a tertiary care hospital in 2020 after the detection of hypercalcemia and hyperparathyroidism. Investigations revealed four parathyroid adenomas, which were subsequently excised. Upon suspected MEN 1, the patient underwent MR imaging of the pancreas. A mass lesion measuring 23x19 mm was identified in the body-tail region of the pancreas. Following this, a Ga-68 peptide (DOTA-TATE) PET scan was performed, which revealed a hypodense lesion with approximately 2 cm in diameter and a SUV max of 24.74, showing intense uptake of increased activity in the body-tail junction of the pancreas. The chromogranin level was found to be 65.5 ng/ml. The patient underwent distal pancreatectomy. The pathology report confirmed a grade 2, well-differentiated neuroendocrine tumor. The tumor was positive for chromogranin and synaptophysin, and the Ki-67 proliferation index was 5%. During the evaluation of the pancreas, genetic testing for MEN 1 was conducted, revealing a heterozygous c.1594C>T (p.Arg532*) nonsense mutation in exon 10 of the MEN1 gene. This was considered a pathogenic variant, leading to a diagnosis of MEN 1 syndrome. Family members who received genetic counseling also carry the same pathogenic variant.mAfter the pancreatic neuroendocrine tumor surgery, the patient received somatostatin therapy for one year based on a multidisciplinary decision involving medical oncology and endocrinology specialists. The patient's family history is detailed in the pedigree (Figure 1).
Conclusion: MEN 1 is a very rare disease. The diagnosis in our patient was made 13 years after the identification of a pituitary adenoma and parathyroid adenoma. Early diagnosis allows for the prediction and early intervention of the developing neoplasms.
Keywords: Neoplasia, neuroendocrine, parathyroid, pancreatic, pituitary

Pedigree chart illustrating the inheritance pattern of MEN1 and the clinical profiles of affected family members.



[Abstract:0226]

Case Presentation: A Case of Pancreatic Gastrointestinal Stromal Tumor Associated with Medullary and Papillary Thyroid Carcinoma

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Introduction: Gastrointestinal stromal tumors (GISTs), the most common mesenchymal tumors of the gastrointestinal tract, are characterized by a 5% hereditary etiology. Known hereditary GIST syndromes are caused by germline mutations in the c-KIT, PDGFR-alpha, neurofibromin 1, and succinate dehydrogenase subunits. Results from several single-center case series have shown that approximately 1 in 9 patients with sporadic GISTs develop synchronous and metachronous secondary malignancies. We present a case of a patient who, approximately two years after being diagnosed with a pancreatic GIST, developed concurrent medullary and papillary thyroid carcinoma.
Case: A 70-year-old female patient presented with abdominal pain in 2022, which prompted further investigation. Imaging revealed a 46x39 mm cystic mass in the head of the pancreas. The patient underwent a Whipple procedure, during which a 6 cm tumor was identified. The mitotic index was high, with 10 mitoses per 5 mm^2. Given these high-risk features, c-kit mutation analysis was performed, which confirmed a positive result. As a result, adjuvant imatinib therapy was initiated. Two years after the start of imatinib therapy, the patient developed a multinodular goiter, which led to the decision for total thyroidectomy. During surgery, multifocal papillary thyroid carcinoma and unifocal medullary microcarcinoma were identified. Post-thyroidectomy, the patient received radioactive iodine therapy and has since been followed up in remission.
Conclusion: This case presents a rare coexistence of pancreatic GIST with papillary and medullary thyroid cancers. GISTs are primarily associated with c-kit and PDGFRA mutations, while BRAF and RET mutations dominate in thyroid cancers. The genetic profiles of GISTs typically differ from those of papillary and medullary thyroid cancers. However, some studies have reported the presence of RET mutations in both cancer types, although this association is rare. The BRAFmutation is commonly found in papillary thyroid cancer and rarely in GISTs. Treatment approaches targeting genetic alterations, such as imatinib for GISTs and BRAF inhibitors for papillary thyroid cancer, share certain similarities In conclusion, while the genetic relationship between GISTs and thyroid cancers remains unclear, it is emphasized that such rare cases should be managed with a multidisciplinary approach.
Keywords: Gastrointestinal stromal tumor, hereditary syndromes, tyroid carcinoma

[Abstract:0227]

Atypical Clinical Course in Nijmegen Breakage Syndrome: A Case Presented with Cancer

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Introduction: Nijmegen Breakage Syndrome (NBS) is a chromosomal instability disorder inherited in an autosomal recessive manner, characterized by microcephaly, immunodeficiency, intellectual disability, dysmorphic facial features, and a predisposition to various cancers. The gene responsible for NBS, NBN (NBS1), is located on chromosome 8q21, and its product, the Nibrin protein, is thought to play a critical role in the repair of DNA double-strand breaks and the activation of DNA damage response checkpoints. Here, we present a case of NBS diagnosed in a patient with isolated ovarian cancer without the typical findings associated with the syndrome.

Case: A 45-year-old female patient with serous ovarian cancer was referred to us for hereditary cancer evaluation. Physical examination revealed a prominent nose and a high-arched palate. Her family history showed that her sister had undergone a hysterectomy at the age of 38 due to uterine myoma, and her parents were not consanguineous. Pathogenic variants were not detected in BRCA1 and BRCA2 genes by MLPA and sequencing analysis. However, sequencing analysis of a hereditary cancer panel encompassing 226 genes identified a homozygous ENST00000265433.3:c.163_171+3del variant in the NBN gene. This variant was classified as "Pathogenic" according to the American College of Medical Genetics (ACMG) criteria (PVS1, PM2, PM3, PP5). Karyotype analysis was reported as 46,XX. The patient was referred to relevant specialties to evaluate additional findings related to NBS. Advanced investigations and consultations revealed no additional findings associated with NBS. Segregation analysis was planned for the family.

Conclusion: NBS is a cancer predisposition syndrome in which both lymphoid and solid malignancies can be observed. The alternative splicing mechanism in NBN transcription may contribute to a milder phenotype. This case highlights the atypical presentation of NBS and emphasizes that it can manifest in isolation with cancer. These findings shed light on the genetic and clinical diversity of NBS. Moreover, while the NBN gene is responsible for NBS, it can also predispose individuals to cancer.

Therefore, it is crucial to consider this gene in hereditary cancer evaluations and include it in hereditary cancer panels.

Keywords: Hereditary cancer, Nijmegen breakage syndrome, NBN gene

[Abstract:0230]

Case Report of DICER1-Associated Bilateral Cystic Nephroma

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Objective: This study presents a 4-year-old male patient diagnosed with bilateral cystic nephroma, in whom a pathogenic germline DICER1 variant was identified.
Case: The patient was referred to our clinic after the parents noticed an abdominal mass when the child was 1 year old. An abdominal ultrasound revealed a multilocular cystic structure in the left kidney, prompting further evaluation with a differential diagnosis of nephroblastoma and nephroma. After performing a left radical nephrectomy, the pathology result confirmed cystic nephroma. Clinical exome sequencing (CES) analysis revealed the DICER1 (NM_030621.4): c.1525C>T (p.Arg509Ter) (heterozygous) variant. The variant was classified as pathogenic according to ACMG criteria. Pedigree analysis revealed a history of nephrolithiasis in the mother and maternal grandmother, as well as a family history of kidney tumors in the maternal grandmother's brother's son. Parent segregation analysis showed that the variant was inherited from the healthy father.
Conclusion: DICER1 syndrome is a pleiotropic tumor predisposition disorder caused by pathogenic germline variants in the DICER1 gene, which encodes an endoribonuclease crucial for the processing of microRNAs. DICER1 tumor predisposition is characterized by an increased risk of pleuropulmonary blastoma (PPB), pulmonary cysts, thyroid neoplasms, ovarian tumors, and cystic nephroma. Less common tumors associated with this syndrome include ciliary body medulloepithelioma, nasal chondromesenchymal hamartoma, embryonal rhabdomyosarcoma, pituitary blastoma, pineoblastoma, central nervous system sarcoma, other central nervous system tumors, and presacral malignant teratoid tumors. Most tumors are observed in individuals under the age of 40. DICER1 syndrome is inherited in an autosomal dominant manner with low penetrance. In individuals with DICER1 syndrome who carry pathogenic variants in the germline DICER1 gene, approximately 80% of variants are inherited from one parent, while about 20% are de novo. Cystic nephroma (CN) is a rare benign kidney tumor characterized by cysts of various sizes within the kidney, accounting for less than 1% of all kidney tumors. It usually presents with an asymptomatic, enlarging abdominal or flank mass. This study highlights the importance of low penetrance DICER1 gene analysis in patients diagnosed with bilateral cystic nephroma and contributes a new patient to the literature.
Keywords: Bilateral cystic nephroma, DICER1 syndrome, Hereditary cancer syndrome