POSTER PRESENTATION ABSTRACTS

PP1- Investigation of miR-21, miR-150, miR-155 Expression Levels in Chronic Myeloid Leukemia Patients

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Purpose: In this study, the relationship between CML and the expression levels of miR-21, miR-150, and miR-155, which could be used in the follow-up of CML patients, was investigated.
Materials and Methods: RNA and miRNA were extracted from peripheral blood samples of patient and control samples. Targe-ted miRNA expression levels from cDNA samples were analyzed by real-time PCR method.
Results: miRNA expression level was determined as 1.0 in the control group. In the newly diagnosed group, the mean miR-21 fold change was 0.6, miR-150 fold change was 0.3, and miR-155 fold change was 0.5. fold changes for miR-21, miR-150 and miR-155 were found to be 1.4, 0.5 and 2.4 fold, respectively, in the imatinib treatment group. In the nilotinib treatment group, miR-21 level was 3.5, miR-150 level 0.5, and miR-155 level 4.3. In the dasatinib treatment group, fold change was 0.8 for miR-21, 2.1 for miR-150, and 0.5 for miR-155. The mean miR-21 level was found to be 3.2, miR-150 level 1.0 and miR-155 level 2.8. MiR-150 levels were found to be lower in the newly diagnosed group, imatinib group and nilotinib group than in the control samples. This differen-ce between the new diagnosis group ($p=0.07484$) and the nilotinib group ($p=0.01541$) is statistically significant. No significant difference was found between patients and controls in terms of miR-21 and miR-155 levels.
Conclusion: These results support that miRNA-150 can be used as a parameter in the monitoring of treatment of CML patients and can contribute to the early detection of drug resistance.

PP2- Strategic Early Detection of Urolithiasis Through Blood Metabolite Analysis

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Relevance. Urolithiasis is among the most prevalent urological disorders globally, with regional incidence rates ranging from 7% to 20% (Murushidi et al., 2023; Shatylko et al., 2019). In Kazakhstan and other Central Asian countries, the disease is notably widespread, largely due to climatic conditions, dietary patterns, and genetic predispositions (Kaprin et al., 2022). Recurrence rates are high, with up to 67% of patients experiencing stone formation within five years of the initial episode (Alfimov et al., 2023), highlighting the urgent need for early detection and preventive strategies. The epidemiology of urolithiasis in Kazakhstan reveals distinctive features, including potentially higher prevalence compared to global averages, often attributed to limited public awareness and insufficient preventive measures (Kaprin et al., 2022). Key contributing factors include metabolic disorders such as hyperuricemia and hypercalciuria, which are central to the disease's pathogenesis (Chernenko et al., 2018; Eliseev, 2018). Moreover, urolithiasis is frequently associated with comorbidities like osteoporosis and metabolic syndrome, necessitating an integrated, multidisciplinary approach to management and prevention (Krishtopa et al., 2022; Sharvadze et al., 2017).
Key words: urolithiasis, early detection, prevention, kidney stone, metabolites.
Aim. To develop early diagnostic strategies for urolithiasis aimed at optimizing treatment, prevention, and metaphylaxis by analyzing the spectrum and relative concentrations of key urinary metabolites.
Methods. For sensitive and comprehensive metabolomic profiling, high-performance liquid chromatography (HPLC) was employed due to its efficiency and relatively simple sample preparation. Mass spectrometry was utilized for the identification, characterization, and quantification of proteins and metabolites. Metabolite identification was performed using specialized spectral databases based on fragmentation patterns. The Human Metabolome Database (HMDB), which contains 217,920 annotated metabolite entries detected in human blood, was used to classify metabolites by their concentrations and reference ranges (Wishart et al., 2022).

Results. This study presents findings from high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC-MS/MS), visualized through a Venn diagram to compare the number of detected metabolites in patients with urolithiasis and their healthy relatives. Blood samples from individuals diagnosed with urolithiasis (urolithiasis group) and their unaffected relatives (control group) were collected using the dried blood spot (DBS) method. The initial phase focused on optimizing metabolite extraction conditions from DBS to maximize yield. Specifically, extraction efficiency was assessed at pH 2, 7, and 9 for both groups. Comparative analysis of the metabolomic profiles under different pH conditions revealed distinct metabolite sets between the groups, with Venn diagrams highlighting overlapping and unique features.

The analysis showed that the highest number of metabolites was detected at pH 9. The presence of a substantial set of shared compounds at this pH enables the broadest coverage of the metabolome, facilitating the identification of potential diagnostic biomarkers specific to urolithiasis.

Conclusion. This study highlights key metabolic features of urolithiasis identified through high-performance liquid chromatography and tandem mass spectrometry. The greatest number of metabolites was extracted at pH 9, suggesting a distinct biochemical environment potentially linked to stone formation. Comparative profiling revealed notable differences between patients and healthy relatives, indicating the presence of disease-specific metabolites. Future research will focus on characterizing these biomarkers for early diagnosis and targeted therapy, with special attention to overlapping and unique metabolites as well as those consistently present in affected individuals. The inclusion of healthy relatives offers insight into protective and predisposing metabolic factors, paving the way for improved preventive strategies.

PP3-The influence of ADIPOQ gene polymorphisms and alleles on metabolic syndrome and it is components.

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Introduction

Metabolic syndrome (MetS) is a significant public health issue worldwide. It encompasses a cluster of disorders that collectively increase the risk of developing serious diseases — the likelihood of type 2 diabetes increases fivefold, and the risk of mortality from cardiovascular conditions rises by 2.5 times [1,2]. ADIPOQ gene, is a key protein secreted exclusively by adipocytes and plays an important role in the regulation of metabolic processes [3,4].

Methods

A cross-sectional descriptive study was conducted involving 190 patients. All participants underwent biochemical analysis, assessment of anthropometric parameters, blood pressure measurement, and PCR-RFLP was performed.

Results

The prevalence of genotypes and alleles of the ADIPOQ gene polymorphism was studied. The results of the study showed the following genotype and allele frequencies of the ADIPOQ gene: CC genotype – 48.9%, CG genotype – 37.9%, GG genotype – 11.1%. The frequency of the C allele was 63.9%, and the G allele – 36.1%. A statistically significant direct association was found between ADIPOQ gene genotypes and triglyceride levels ($\chi^2 = 9.29$, $p = 0.014$), as well as between the G allele and the component abdominal obesity ($\chi^2 = 4.34$, $p = 0.034$). No statistically significant associations were found with other components of MetS.

Conclusion

In our study, the G allele was more frequently observed in patients with abdominal obesity. The presence of these polymorphisms may serve as a useful tool for assessing the risk of developing MetS and holds clinical significance for the prevention and treatment of metabolic disorders.

Keywords

ADIPOQ gene polymorphism, metabolic syndrome, abdominal obesity.

PP4- The role of MC4R gene polymorphisms and alleles in metabolic syndrome and it is components

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Introduction

The high prevalence of overweight and obesity is one of the most serious public health problems in the 21st century. The pathogenesis of metastases includes many genetic and acquired factors that fall under the definition of insulin resistance and low-grade chronic inflammation. Over the past decade, advances in single-nucleotide polymorphism genotyping technologies have facilitated genome-wide association studies to identify various risk loci/single-nucleotide polymorphisms associated with an increased risk of obesity and type 2 diabetes mellitus [1,2]. The MC4R gene is known to play a central role in regulating energy and appetite, which leads to better control of obesity [3].

Methods

A cross-sectional descriptive study was conducted involving 190 patients. All participants underwent biochemical analysis, assessment of anthropometric parameters, blood pressure measurement, and PCR-RFLP was performed.

Results

According to the results of the genetic study, the frequency of occurrence of MC4R genotypes and alleles of the gene was: CC genotype - 20.5%, TC genotype – 40%, TT genotype - 33.7%, C allele – 45,1%, T allele – 54,9%. A statistically significant direct relationship was found between MC4R genotypes and

triglyceride levels ($\chi 2$ =8,9, p=0.028). Statistically significant associations were found with all components of the MetS.

Conclusion

The results of our study may help to understand the main genetic variations in this gene for better management of the decline in the development of the components of MetS.

Keywords

MC4R gene polymorphism, metabolic syndrome, abdominal obesity.

PP5- Evaluation of balanced chromosomal aberration frequency in healthy Turkish Cypriot couples

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Background:A chromosomal aberration is a condition involving structural or numerical changes in one or more chromosomes.These abnormalities are a significant genetic factor contributing to reproductive issues. Balanced chromosomal aberrationsspecifically refer to structural changes in chromosomes that maintain the proper amount of genetic material, without any loss orgain. Carriers of balanced translocations often face fertility challenges due to improper chromosome segregation during gameteformation. This can result in implantation failure, miscarriages, or birth disorders. However, these individuals are typicallyhealthy and exhibit no developmental abnormalities, which means they are often unaware of their condition. In contrast,unbalanced chromosomal rearrangements can cause developmental issues or spontaneous pregnancy loss. Balancedtranslocation carriers account for approximately 0.2-0.4% of the general population. The purpose of this study was todetermine the prevalence of balanced translocations in the Turkish Cypriot population.

Material and Methods: The study analyzed 50 healthy Turkish Cypriot couples planning to conceive. Chromosomal analysis wasperformed using G-banding karyotyping to identify potential balanced translocations.

Results: Results revealed that 4% of the participants exhibited chromosomal alterations. The most common aberrationsobserved included inversion 9, balanced translocations between chromosomes 4 and 7, derivative chromosome 22, andtranslocations involving chromosomes 4 and 10.

Conclusion: Cytogenetic analysis of conception products plays a critical role in uncovering the causes of miscarriages. Inconclusion, the frequency of chromosomal alterations found in the Turkish Cypriot population, consisting of 80,000 individuals,represents an important finding. This insight is crucial for family planning considerations and shaping government policies.

Keywords: Balanced translocation, cytogenetics, chromosomal aberrations

PP6- Evaluation of the pathogenicity of variants of uncertain significance in the *BRCA2* gene through ın silico analyses and clinical correlation

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Introductıon:

The *BRCA2* gene plays a key role in DNA repair and tumor suppression, with variants often linked to breast and ovarian cancers. Variants of uncertain significance (VUS) pose challenges in risk assessment. This study aimed to evaluate the pathogenicity of *BRCA2* VUS detected by next-generation sequencing (NGS) in patients at the Çanakkale Onsekiz Mart University Medical Genetics Clinic and explore their clinical relevance.

Methods:

VUS interpretations were performed using Franklin, ClinVar, and QCI databases. Functional effects were assessed using in silico tools including SIFT, MutationTester2021, FATHMM, PANTHER, and AlphaMissense. Disease associations were evaluated using PHD-SNP and SNPs&GO, while MUpro and I-Mutant assessed protein stability. HOPE and Swiss-Model were used for 3D structural analysis. Findings were correlated with patients' personal and family cancer histories.

Results:

Among 193 *BRCA2* variants, 53% were benign/likely benign, 21% pathogenic/likely pathogenic, and 24% VUS. The study focused on 48 VUS—all missense variants, mostly in exon 11. In silico analyses reclassified 7 as pathogenic/likely pathogenic and 29 as benign/likely benign. Conflicting results were observed for 12 variants. Additionally, 7 novel variants were identified.

Conclusıon:

In silico tools were effective in reassessing *BRCA2* VUS, reducing the VUS rate from 24% to 6%. These results support the integration of computational predictions into clinical genetics workflows. Further functional studies are needed to clarify the biological impact of unresolved variants and improve genetic counseling in hereditary cancer.

Keywords: *BRCA2*, VUS, in silico, clinic correlation

PP7- Evaluation of the hereditary cancer relationship of the fanconi anemia gene family

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Introduction: The Fanconi Anemia(FA) pathway is crucial for DNA repair and genomic stability. While biallelic mutations

in the FA pathway are linked to Fanconi anemia, the role of heterozygous mutations in certain FA genes in cancer development is still unclear. This study aims to assess the association of heterozygous pathogenic or likely pathogenic variants in FA gene family members, excluding cancer related *BRCA1,BRCA2,BRIP1,PALB2,RAD51C* and *RAD51* with hereditary cancer risk and their effects on DNA repair mechanisms.

Materials and Methods: In this retrospective study, patients who applied to our clinic and were found to have heterozygous pathogenic or likely pathogenic variants in the *FANCA,FANCB,FANCC,FANCD2,FANCE,FANCF,FANCG,FANCI,FANCM,SLX4,ERCC4,XRCC2,UBE2T,MAD2L2,RFWD3,FANCL* genes as a result of NGS analysis were examined.

Conclusions: Nineteen patients with variants in FA genes were analyzed. Four had a personal history of cancer, including breast cancer (2 cases), thyroid cancer, and a CNS tumor. Fourteen patients had family or personal histories of cancer, with breast cancer being most common, alongside lung, colon, stomach, pancreas, endometrium, prostate, bladder, larynx cancers, leukemia, Wilms tumor, and CNS tumors. Five patients had no personal or family history of cancer. It has been determined that the cancer risk is increased by 2.37 times in individuals carrying the mutation.

Discussion: This study adds to the literature by exploring the impact of heterozygous FA mutations on cancer susceptibility. The findings suggest that individuals with heterozygous variants in FA genes may be at an increased risk for various cancers, which may inform future strategies for cancer diagnosis, prevention, targeted therapies, and genetic counseling.

Keywords: cancer, DNA repair, Fanconi anemia

PP8- Renpenning Syndrome: Frameshift PQBP1 Variant in a Patient with Fragile X-Like Phenotype

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Background/Objectives: PQBP1 gene encodes the polyglutamine-binding protein 1 (PQBP1), which is involved in mRNA splicing and transcription. Pathogenic variants in this gene cause X-linked mental retardation disorders collectively referred to as Renpenning syndrome; characterized by microcephaly, short stature, small testes, and dysmorphic facial features. This report aims to present a case featuring intellectual disability along with dysmorphic characteristics, linked to a pathogenic mutation in the PQBP1 gene.

Methods: Following DNA isolation from peripheral blood; array-CGH analysis, CGG trinucleotide repeat analysis of the FMR1 gene and, whole exome sequencing (WES) analysis using the xGenExomeResearch Panel v2 kit via the NGS method were conducted.

Results: A 7-year-old male patient was referred to our clinic due to developmental and language delay with a preliminary diagnosis of Fragile X syndrome. The patient has speech delay, developmental delays, and learning difficulties, and unable to cooperate with the intelligence test. In a physical examination, microcephaly, long triangular face, sparse eyebrows, prominent eyelashes, thin upper lip, long philtrum, upslanted palpebral fissures, and proximally placed thumb were observed. Chromosome analysis and Fragile x, microarray, analyses were found to be normal. In WES analysis (NM_001032382.2) PQBP1 c.450_453delCAGA;p.D150fs*44 pathogenic frameshift deletion was detected.

Conclusion: Renpenning syndrome, due to its initial resemblance to Fragile X syndrome, requires considering Fragile X syndrome as a differential diagnosis. Clinical parameters such as head circumference, testicular volume, and height play a role in distinguishing between the two syndromes during first examination, thereby guiding further diagnostic tests and improving diagnostic accuracy.

PP9- Copy number variants in pediatric epilepsy patients

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Abstract

Introduction:

Epilepsy is one of the most common chronic neurological disorders of childhood, affecting over 10 million children globally. Identifying the underlying cause is essential for appropriate treatment planning and prognosis estimation. This study aimed to determine the frequency of copy number variants (CNVs), known to be associated with neurodevelopmental disorders such as intellectual disability, autism, epilepsy, and psychiatric conditions, in patients diagnosed with epilepsy within the first 18 years of life, and to characterize the clinical features of those carrying pathogenic CNVs.

Materials and Methods:

Medical records of patients referred to the Medical Genetics Clinic of our hospital with a diagnosis of epilepsy between 2013 and 2025 were retrospectively reviewed, provided informed consent was obtained. Patients who underwent microarray analysis using the Illumina CytoSNP-12v2.1 BeadChip (315K) platform on DNA extracted from peripheral blood and were found to have CNVs were included.

Results:

Among 168 pediatric epilepsy patients, at least one CNV was

detected in 13 (7.7%). Of these, 7 (53.8%) were male and 6 (46.2%) female. The mean age was 6.77 years; the median was 6.39 years. CNVs included 7 duplications (53.8%) and 6 deletions (46.2%). The most commonly affected region was 16p11.2 (30.8%), linked to neurodevelopmental disorders. Deletions ranged from 660 kb to 1.1 Mb. CNVs involving sex chromosomes were observed in two patients, consistent with karyotype analysis. Three variants were of uncertain significance; nine were pathogenic. No reclassification occurred upon database review.

Conclusion:

CNVs are significant contributors to pediatric epilepsy. Microarray analysis offers valuable diagnostic insight, especially in early-onset, unexplained cases.

Keywords: Copy number variants, microarray analysis, pediatric epilepsy

PP10- Link between chronic tinnitus with *mir-30e*, *mir-206,* and *mir-124* polymorphisms modulating the brain-derived neurotrophic factor gene

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Introduction

Brain-derived neurotrophic factor (BDNF) is involved in early development of the central auditory pathway and inner ear sensory epithelium. Mounting evidence indicates that BDNF administration promotes miRNA production in neurons, despite the typical suppressive effect of miRNAs on *BDNF* expression. Therefore, miRNAs regulating *BDNF* expression may have an impact on the auditory pathway and could be potential gene polymorphisms affecting human hearing ability. This study aimed to examine the role of miRNA polymorphisms regulating *BDNF* in the pathophysiology of tinnitus.

Materials and Methods

The study recruited 70 tinnitus patients aged 18-55 from the ENT clinic, along with 70 control subjects of the same age range without tinnitus or systemic illnesses. Tinnitus assessment included tympanometric, audiological, and psychoacoustic evaluations. Seven *miRNA* SNPs (*miR-30e rs112439044, rs10489167, miR-206 rs16882131, miR-30a rs1491500379, miR-26b rs565919718, rs188612260,* and *miR-124 rs5315564*) regulating the *BDNF* gene were analyzed using the Fluidigm platform.

Results

Significant differences in genotype distribution were observed for *miR-30e rs112439044*, *miR-124 rs5315564*, and *miR-206 rs16882131* polymorphisms between the tinnitus and control groups ($p<0.05$). According to genetic inheritance-model analysis, the dominant and additive inheritance models revealed 0.20 and 0.83-fold risks for *miR-30e rs112439044*, respectively. The dominant inheritance model showed a 1.65-fold risk for *miR-124 rs5315564*, while the dominant model had an 11.1-fold protective effect for *miR-206 rs16882131* and the additive model had an 8.57-fold risk.

Discussion and Conclusions

The study results indicate that *miR-206*, *miR-30e*, and *miR-124* polymorphisms may influence the auditory pathway through the regulation of *BDNF* gene expression.

Keywords: Chronic tinnitus; *BDNF* gene; *BDNF* gene regulating *miRNAs;* Single nucleotide polymorphism

PP11- A rare syndromic immunodeficiency caused by *ZBTB24* gene

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Introduction: Immunodeficiency-Centromeric Instability-Facial Anomalies Syndrome (ICF syndrome) is a rare genetic disorder characterized by humoral immunodeficiency, dysmorphic facial features, and marked genomic instability, notably in the centromeric regions of chromosomes 1, 9, and 16. The syndrome is inherited in an autosomal recessive manner and four genes have been identified associated with the relevant phenotype: DNMT3B, ZBTB24, CDCA7, HELLS. Here, we present a case with ICF syndrome caused by a homozygous nonsense ZBTB24 variant.

Case Report: 7-year-old male patient was referred from the department of allergy and immunology for a definitive molecular diagnosis. He first presented at the age of 8 months with recurrent fever and bronchiolitis. Further evaluation was significant for hypogammaglobulinemia and dysmorphic facial features, including flat and wide nose bridge, hypertelorism, upslanting palpebral fissures, and a bilateral sandal gap deformity. Based on these findings, the patient was clinically diagnosed with ICF syndrome and scheduled for regular follow-up with IVIG injections. He also has speech delay and specific learning disorder. To clarify underlying pathology, karyotyping was initially performed, which demonstrated chromosomal instability. Subsequently, he underwent Clinical Exome Sequencing (QIA-

seq-Actionable Exome Kit), in which homozygous p.R320* variant was identified in the ZBTB24 gene.
Conclusion: This case highlights the importance of considering ICF syndrome in patients presenting with immunodeficiency and facial dysmorphism. Karyotyping that reveals genomic instability remains a valuable method where molecular tests are not available in patients with suspected ICF syndrome.
keywords: syndromic, immunodeficiency, ZBTB24, ICF

PP12- A Novel homozygous *CUL7* variant in a patient with 3M syndrome: Clinical presentation and molecular diagnosis

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Abstract:
Background: 3M syndrome is a rare autosomal recessive disorder characterized by severe pre- and postnatal growth retardation, characteristic facial dysmorphism, skeletal anomalies, and normal intelligence. Pathogenic variants in *CUL7*, *OBSL1*, and *CCDC8* genes are known causes.
Case Presentation: We report a 2-year and 3-month-old female patient referred from pediatric endocrinology due to marked short stature and coarse facial features. She was born at 33 weeks of gestation to consanguineous parents (G2P2A0), weighing 1350 grams, and required 2.5 months of neonatal intensive care for respiratory distress syndrome. Psychomotor development was normal. Newborn screening, hearing, and vision tests were unremarkable. Family history revealed short stature in the father's aunt and uncle. On physical examination, height was 71 cm (<0.02 percentile), weight 8.9 kg (0.25 percentile), and head circumference 48 cm (43.25 percentile). Dysmorphic features included dolichocephaly, coarse facial appearance, thick eyebrows, synophrys, depressed nasal bridge, broad nasal tip, anteverted nostrils, long philtrum, high narrow palate, and a simian crease on the left hand. Abdominal ultrasound, skeletal survey, echocardiography (closed VSD), and metabolic screening were normal.
Results: Clinical exome sequencing identified a novel homozygous frameshift variant in *CUL7* (NM_014780.5:c.317del, p.Val106Glyfs*9), classified as likely pathogenic (PM2, PVS1) according to ACMG criteria.
Conclusion: A comprehensive phenotypic evaluation is crucial in patients with growth retardation to identify underlying genetic causes. 3M syndrome should be considered in individuals with characteristic craniofacial and skeletal features. The novel *CUL7* variant identified in our patient adds to the mutational spectrum of this rare syndrome and highlights the importance of molecular genetic analysis in diagnosis.
Keywords: 3M syndrome, *CUL7* gene, short stature

PP13- Clinical and genetic evaluation of 16 patients diagnosed with Prader-Willi Syndrome

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Introduction: Prader-Willi syndrome (PWS; OMIM #176270) is a rare genetic disorder characterized by hypotonia, intellectual disability, short stature, hypogonadotropic hypogonadism, and a distinct nutritional trajectory-initial feeding difficulties followed by hyperphagia and obesity. It results from abnormal DNA methylation in the 15q11.2–q13 region, most commonly due to paternal deletions, followed by maternal uniparental disomy and imprinting defects.
Materials and Methods: We retrospectively evaluated the demographic and clinical characteristics of 16 patients diagnosed with PWS and followed at our clinic between 2014 and 2025. Data were analyzed using SPSS version 20.
Results: Eight of the patients were female (50%). The median age at diagnosis was 5 months and 10 days, and 12 patients (85.7%) were diagnosed during infancy. IUGR was present in 8 patients (50%), and 15 (93.7%) required NICU admission. All had neonatal hypotonia; 13 (81%) had feeding difficulties, and 10 (62.5%) experienced respiratory distress. At last follow-up, five patients were still in infancy, with a median weight SDS of -1.86 (range: -2.84 to -0.78) and head circumference SDS of -2.49 (range: -3.16 to -1.45). Among the 10 patients aged 2 years and older at the last follow-up, 7 were found to be obese (BMI > +2 SDS). Genetic analysis revealed deletions in 64% of patients and uniparental disomy in the remainder; no imprinting center defects were detected.
Conclusion: PWS should be considered in neonates presenting with IUGR, hypotonia, feeding difficulties and respiratory distress. Early diagnosis is critical to address nutritional management and prevent neuromotor delays.
Keywords: Prader-Willi Syndrome, genetics, nutrution, obesity.

PP14- A Novel Splice-site Variant in A 17-year-old Male Patient with Basilicata-Akhtar Syndrome

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Introduction: Basilicata-Akhtar Syndrome (MRXSBA) is characterized by global developmental delay, feeding difficulties, hypotonia, poor or absent speech, unsteady gait and spasticity. Additional findings include dysmorphic facial features and mild distal skeletal anomalies. MRXSBA is caused by variations in *MSL3*. We present a 17-year-old male patient who has been diagnosed by clinical exome sequencing (CES).

Material, Methods: A 17-year-old male patient was consulted to our clinic for mental retardation, neurodevelopmental delay, joint contractures, and sensorineural hearing loss. The patient had a history of achilles tendon contracture and cryptorchidism surgeries. It was known that the mother had intellectual disability. In our physical examination, brachycephaly, pectus carinatum, joint stiffness and increased muscle tones were observed. The facial dysmorphic features included Widows's peak, left epichantal fold, long and narrow chin, posterior rotated prominent ears, and dental anomalies. Cranial MRI findings were as follows; cerebral and cerebellar atrophy, thin pituitary gland, and gliotic changes in the periventricular and subcortical white matter.

Discussion: To elucidate underlying pathology, chromosomal microarray analysis and karyotyping were performed, both of which resulted normal. Subsequent clinical exome sequencing revealed a hemizygous splice variant in *MSL3* gene (NM_078629.4:c.1282-1G>A). This variant was interpreted as likely pathogenic according to ACMG 2015 variant classification and considered to be associated with patient's phenotype.

Conclusion: Thus far, over 40 patients with Basilicata-Akhtar Syndrome have been documented, and all reported variants were *de novo*. In our case, due to the presence of intellectual disability in the mother, a family study is being conducted to investigate a possible hereditary transmission. A novel splice-site variant was identified at the acceptor side of exon 11, within the region encoding the critical MRG domain.

KeyWords: Basilicata-Akhtar Syndrome, MSL3, splice variant

PP15- Identification of a novel pathogenic *EXT1* gene mutation in a patient with multiple osteochondromas

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Backround

Multiple Hereditary Osteochondromas(MHO) previously known as Multiple Hereditary Exostoses(MHE) is characterized by growth of multiple osteochomdromas. These are benign bone growths that typically form at the ends of long bones, particularly in the metaphyseal areas, and grow outward covered by cartilage. We report a patient with a novel pathogenic *EXT1* gene mutation inherited paternally, who presented with multiple osteochondromas.

Material and Methods

Genomic DNA materials were isolated from the peripheral blood samples of the family members which were obtained after informed consent was taken. Conventional karyotyping and whole-exome sequencing (WES) were performed concurrently. To confirm the findings and perform segregation analysis, Sanger sequencing was utilized.

Results

A 4-year and 2-month-old male child, born to unrelated parents, was referred to our clinic due to the presence of multiple painless palpable bone masses, which were first noticed by the parents six months earlier. The lesions progressively grew in number and size. Axial radiography revealed multiple osteochondromas on the long bones. Conventional karyotyping revealed a normal 46,XY karyotype. WES identified a novel paternally inherited mutation in the *EXT1* gene [c.640_659del]. The father of the patient also exhibited multiple exostoses, along with a limb length discrepancy.

Conclusion

We report a novel pathogenic *EXT1* mutation that causes multiple hereditary exostoses in both our patient and his father. This mutation is expected to cause a frameshift in the ribosome reading frame leading to premature termination of the *EXT1* protein.

PP16- Williams syndrome: Phenotypic features of 10 Turkish patients

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Introduction:

Williams Syndrome (WS, OMIM194050) is a multisystemic genetic disorder characterized by developmental delay, intellectual disability, distinctive facial features, cardiovascular disease and renal, endocrinological, ocular, auditory, connective tissue anomalies. It is usually caused by a de novo microdeletion in the Williams-Beuren Syndrome Critical Region at 7q11.23, which includes *ELN, CLIP2, GTF2I, GTF2IRD1, LIMK1* genes. In this study, we examined the phenotypic features of 10 patients presenting with dysmorphic facial features and developmental delays.

Materials and Methods:

Ten patients, who were followed in our outpatient clinic with a diagnosis of Williams Syndrome, were included in the study. Phenotypic features were obtained from patient records retrospectively.

Results:
Patients median ages of the patients was 37.5 months (70 days and 12 years). Two patients were male, eight were female. All patients exhibited common dysmorphic features including broad forehead, periorbital fullness, long philtrum, thick lips, wide mouth and developmental delay. Nine patients had cardiovascular disease, three had hypothyroidism, two had nephrolithiasis and one had hypercalcemia. The most common cardiac anomalies were supravalvular aortic stenosis (4/9), mitral valve insufficiency (4/9). Diagnosis was confirmed in all patients by fluorescence in situ hybridization.
Conclusion:
Morbidity and mortality are increased 25- to 100-fold due to complications. Awareness of the typical facial features is crucial for early diagnosis and treatment. Microarray analysis can define the extent of deletions. Deletion of the *ELN* gene is responsible for arteriopathy and connective tissue abnormalities. Further studies are needed to elucidate the clinical outcomes of the deletions.
Keywords: Williams syndrome, 7q11.23, ELN

PP17- The role of high-resolution testing in rare disease diagnosis: case presentation
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Introduction
Advancements in technology have significantly improved the ability to diagnose rare diseases. Genetic tests are usually performed once in a lifetime. However, with an increased resolution test, it is advisable to take the test again.
Case presentation
We report a case of an 8-year-old girl with hydrocephalus and dysmorphic features, including hypertelorism, ptosis, downturned palpebral fissures, brachydactyly, clinodactyly, high-arched palate, and caudal appendage. She was referred due to developmental delays, including delayed walking (at 4 years) and speech development. Additionally, a hearing test revealed left-sided hearing loss. Her parents are first cousins, and her family history was unremarkable. Growth parameters were notably below average, with a height of 111 cm (SDS: -3.49). Cardiac evaluation showed ASD and PDA, and abdominal ultrasound revealed horseshoe kidneys.
Result
Genetic testing (Array CGH 8x60K ISCA) revealed a 4.2 MB interstitial deletion at 4p16.3 in 2017. In addition to the previous array analysis, higher-resolution microarray (SNP 6.0 Cytogenetics (Affymetrix) testing identified a 16 kilobase homozygous deletion in the *MASP1* gene (exons 1 and 2). CES (Clinical Exome Sequencing) in which Copy Number Variation (CNV) analyses were integrated also confirmed this homozygous deletion.
Discussion
This case highlights the utility of advanced genetic technologies, such as microarray and CNV analysis, in detecting small genomic changes that were previously undetectable, offering a more accurate diagnosis of rare genetic disorders and potential for targeted interventions. If a genetic alteration found does not deeply explain the patient's clinical findings, the patient should be reevaluated for higher-resolution test.
Keyword: High-resolution testing, Dysmorphic feature, *MASP1* gene deletion

PP18- Investigation of molecular prevalence and molecular characterization of zoonotic Cryptosporidium species in human and animal hosts
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Abstract
Introduction: Cryptosporidiosis is an infectious disease caused by Cryptosporidium species. In general, it was aimed to reveal the prevalence and genotypic diversity of the parasite against cyriptosporodiosis caused by Criptosporidium species by investigating the transmission between animal and human hosts at the molecular level. Therefore, the project titled "Investigation of Molecular Prevalence and Molecular Characterization of Zoonotic Criptosporidium Species in Human and Animal Hosts" was designed.
Materials and Methods: For this purpose, PCR and QPCR tests were performed after DNA isolation of stool samples collected from human and animal hosts and the samples detected to be positive for Criptosporidium species were purified and sent to the company from which the service was purchased for sequence analysis. The obtained sequence information was analyzed using phylogenetic tools.
Discussion: As a result of the phylogenetic examination of the samples detected positive in cat, dog and calf samples together with their breeders, it was determined that animal isolates and human isolates - within each group - had similar sequences and phylogenetic characters. It was found to be similar. The study is unique in that it is the first study to show the molecular level of transmission among dog, cat, horse, cattle and poultry groups and among those who raise them.
Results: Therefore, it is thought that examining the symptoms and elucidating the relationship between symptoms and parasite genotypes will contribute to diagnostic studies as well as epidemiological studies. The data obtained will form the basis

of various studies to be conducted in the future.

Keywords: Cryptosporidium, Zoonosis, Molecular characterization, PCR

PP19- Molecular prevalence and molecular characterızatıon of dıentamoeba fragılıs ın patıents dıagnosıs of cancer

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Abstract

Introduction: Dientamoebiasis is an infection caused by Dientamoeba fragilis. Data on the relationship between the molecular types of this parasitosis, which is of increasing importance especially in cancer patients, and cancer diseases are limited. This study aimed to obtain new data on the relationship between its molecular characteristics and the disease.

Materials and Methods: The study included stool samples collected from patients and healthy volunteers who would form the control group. In the study, PCR and qPCR tests were performed after total genomic DNA isolation of the collected samples, and phylogenetic characterization was performed by obtaining sequence analysis of the samples found to be positive for *Dientamoeba fragilis*.

Discussion: Accordingly, 6 patient was detected as positive with standard PCR, while 11 patient was detected as positive with qPCR. It was shown that there was no significant difference in the distribution of the parasite between male and female patients diagnosed with cancer. The different genotype was detected in cases infected with *D. fragilis*.

Results: In conclusion, this study has shown that there may be a molecular relationship between patients diagnosed with cancer and the genotypes detected in this parasite, which is thought to affect clinical findings. It is a study that sheds light on the effect of the genotypes of the parasite on clinical symptoms in the cases included in the study. It is thought that this study will contribute to diagnostic studies as well as epidemiological studies.

Keywords: *Dientamoeba fragilis*, Cancer, Genotyping

PP20- Expanding the Genotypic Spectrum of DNM1L-Associated EMPF1: A Case Report of a Novel Variant

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Abstract

DNM1L encodes dynamin-related protein 1 (DRP1), a large GTPase essential for mitochondrial and peroxisomal fission. Heterozygous, mostly de novo pathogenic variants in *DNM1L* cause Encephalopathy, lethal, due to defective mitochondrial and peroxisomal fission 1 (EMPF1), an autosomal dominant disorder characterized by developmental delay, refractory seizures, neurologic regression, and cerebral atrophy.

We present the case of an 11-year-old girl referred to our clinic with refractory status epilepticus lasting 15 hours. Seizures began with numbness in the left arm and progressed to generalized tonic-clonic convulsions. At admission, she was unconscious, intubated, and receiving multiple antiepileptic medications. Her medical history included bilateral ptosis since the age of five, attention deficit, learning difficulties, and episodes of aggressive behavior. No dysmorphic features or parental consanguinity were noted. Brain imaging revealed cerebral atrophy. Initial differential diagnoses included infectious or autoimmune encephalitis, mitochondrial disorders, and GLUT1 deficiency.

Whole exome sequencing revealed a novel heterozygous in-frame deletion in exon 14 of the *DNM1L* gene. We classified the variant as likely pathogenic according to the ACMG criteria. The clinical presentation was consistent with previously reported cases of *DNM1L*-related encephalopathy. No biochemical abnormalities indicating mitochondrial or peroxisomal dysfunction were detected, underscoring the diagnostic value of genomic analysis. This variant has not been previously reported in the literature and was confirmed as de novo.

Keywords: *DNM1L*, mitochondrial fission, in-frame deletion, status epilepticus, cerebral atrophy.

PP21- Clinical and laboratory comparison of patients with compound heterozygous MEFV P369S-R408Q variants and M694V mutations

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Introduction:

Familial Mediterranean Fever (FMF) is the most common hereditary autoinflammatory disorder, characterized by recurrent febrile attacks and serosal inflammation. While MEFV:p.P369S and p.R408Q variants are classified as variants of uncertain significance (VUS), recent studies suggest that their compound heterozygosity may be associated with autoinflammatory phenotypes. This study compares the clinical and laboratory features of patients carrying compound heterozygous

P369S-R408Q with those carrying M694V mutations.
Methods:
We retrospectively evaluated 86 patients with MEFV mutations and complete clinical/laboratory data. Genetic analyses were performed at Çanakkale Onsekiz Mart University. Patients were grouped as follows: Group A (n=28) – compound heterozygous P369S-R408Q; Group B (n=43) – heterozygous or compound heterozygous M694V; Group C (n=15) – homozygous M694V.
Results:
Group C exhibited higher levels of serum amyloid A, CRP, and ESR compared to Groups A and B, indicating a more pronounced inflammatory response. Group C also fulfilled the Tel-Hashomer criteria more frequently. While overall inflammation markers were comparable between Groups A and B, clinical features such as pleuritis and erysipelas-like erythema were less common in Group A. Colchicine treatment response was observed in all groups, with no significant differences.
Conclusion:
Although P369S and R408Q are VUS, their compound heterozygosity may be associated with FMF-like symptoms. Despite the milder clinical course and lower frequency of key diagnostic findings, colchicine therapy appears effective. FMF should be considered in such patients, and colchicine should be initiated when clinically indicated.
Keywords: FMF, M694V, P369S, R408Q

PP22- 22q11.2 Deletion Syndrome Presenting with Multisystemic Findings: A Case Report of a 19-Year-Old Male
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Introduction:
22q11.2 deletion syndrome (DiGeorge syndrome) is a genetic disorder caused by a microdeletion in the 22q11.2 region, characterized by multisystem involvement. Developmental delay, immunodeficiency, congenital heart defects, palatal anomalies, and neuropsychiatric manifestations are among the most frequently observed features.
Case Presentation:
We present a 19-year-old male with a history of cerebral palsy, epilepsy, diabetes mellitus, and recurrent pneumonia. Hypotonia was identified during infancy, generalized tonic-clonic seizures began at the age of six, and diabetes mellitus was diagnosed one year ago. The patient also had a history of deep vein thrombosis secondary to immobilization following pneumonia. Cranial imaging revealed polymicrogyria and calcifications. Array comparative genomic hybridization (aCGH) analysis identified an approximately 2.5 Mb heterozygous deletion in the 22q11.2 region (chr22:18,893,637–21,415,067), including critical genes such as *TBX1* and *CRKL*, and this finding was confirmed by FISH analysis.
Discussion:
This case demonstrates the broad phenotypic spectrum of 22q11.2 deletion syndrome, involving neurological, endocrine, and immune systems. Interestingly, the absence of cardiac findings in our patient indicates an atypical presentation of the syndrome. Early implementation of molecular and cytogenetic analyses is crucial for accurate diagnosis and appropriate clinical management.
Conclusion:
This case highlights the importance of early genetic testing in patients with multisystemic manifestations and clinical suspicion of 22q11.2 deletion syndrome. Timely diagnosis enables appropriate treatment planning and facilitates effective genetic counseling for affected families.
Keywords: 22q11.2 deletion syndrome, cerebral palsy, epilepsy, genetic counseling

PP23- A Novel KRT6A Variant in Pachyonychia Congenita
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Introduction:
Pachyonychia congenita (PC) (OMIM #615726) is a rare genodermatosis characterised by hypertrophic nail dystrophy, painful palmoplantar keratoderma, oral leukokeratosis, pachyonychia, pilosebaceous cysts, palmoplantar hyperhidrosis, and follicular keratosis on the trunk and extremities. It is inherited in an autosomal dominant pattern, and approximately 30% of cases arise *de novo*. PC is caused by mutations in keratin genes (*KRT6A, KRT6B, KRT16, KRT17*). The *KRT6A* gene, associated with PC type 3, is located on chromosome 12q13.13 and encodes keratin 6A, a type II cytokeratin essential for maintaining epithelial structural integrity.
Case Report:
A 20-year-old male was referred by dermatology for palmoplantar keratoderma manifested at birth. Palmoplantar keratoderma, painful plantar keratosis, oral leukokeratosis, onychogryphosis of the toenails and pachyonychia of the fingernails were observed on physical examination. There was no parental consanguinity, but similar findings were observed in four siblings, the father, grandfather, uncle, and the uncle's four children. A genetic panel for suspected PC identified a heterozygous c.1384A>T (p.Ile462Phe) variant in *KRT6A*.
According to ACMG guidelines, this variant was classified as likely pathogenic. Segregation analysis was planned for the patient's parennjujts and siblings.
Conclusion:
This case presentation highlights a previously unreported *KRT6A* variant associated with PC, expanding the known mutational spectrum of the disease. Recognition of clinical features

alongside genetic confirmation is essential for accurate diagnosis and appropriate management. Furthermore, identifying pathogenic variants allows for effective genetic counselling and family screening in inherited genodermatoses.

Keywords: Pachyonychia congenita, *KRT6A*, keratin

PP24- Robinow syndrome in a family: Two cases with variable penetrance

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Introduction: Robinow syndrome is a rare genetic disorder that affects the development of the skeletal system and various structures of the body. In Robinow syndrome, shortening of the long bones in the arms and legs, braidactyly, vertebral anomaly, short stature, fetal face and ambiguous genitalia are common symptoms. The autosomal recessive Robinow syndrome with more severe clinical course has been described in less than 200 individuals in the literature. The autosomal dominant form has been diagnosed in approximately 50 families.

Materials and Methods: An infant aged 7 months male patient was referred to us from the pediatric endocrinology outpatient clinic with a prediagnosis of sexuel development disorder. Detailed anamnesis revealed micropenis and fetal face. The patient underwent conventional cytogenetic analysis and sexual development disorder panel by NGS method.

Conclusion: Conventional cytogenetic analysis showed a normal 46,XY karyotype with no sex chromosome abnormalities. DNA sequencing identified a heterozygous pathogenic variant in the DVL1 gene, associated with autosomal dominant Robinow syndrome. Segregation analysis confirmed the variant in the heterozygous state in the father.

Discussion: Robinow syndrome is a rare genetic disorder that occurs in approximately 1/1,500,000 live births worldwide. This case was diagnosed as Robinow syndrome with an autosomal dominant inheritance pattern. Since complete penetrance is not observed in this inheritance pattern, the variant observed in the index patient was also detected in the father, but no clinical findings were observed in the father.

Keywords: *DVL1* gene, *Robinow Syndrome, Next-generation sequencing (NGS)*

PP25- The role of type 3 immunity in Pediatric Cystic Fibrosis

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Abstract

Background: Cystic Fibrosis (CF) is an autosomal recessive disease affecting the respiratory tract, pancreas, intestine, exocrine, male genital system, hepatobiliary system and exocrine sweat glands due to dysfunction of exocrine glands as a result of mutations in the Cystic Fibrosis Transmembrane Regulator (CFTR) gene. The defective CFTR gene causes protein degradation, leading to dehydration of the airway surface and thick mucus accumulation. Although the levels of IL-17A, IL-23, IL-22 cytokines have been shown to increase in CF, the relationship between type 3 immunity and CF is still controversial.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from blood samples of control (n = 20), patient (n = 20) and attack groups (n = 8) by creating a density gradient with Ficoll-Hypaque and serum was collected. In order to determine the amounts of intracellular cytokines, cells were stimulated with PMA-ionomycin and Golgi stop. Cytokine staining was performed for IL-17, IL-22, IL-10 using Cytofix/Cytoperm™ kit. ELISA was performed for IL-17A, IL-22 and GM-CSF from the serum.

Results: When the percentages and absolute numbers of CD3+IL-17+ and CD3-IL-17- cells were compared between the groups, no statistically significant difference was found. However, the absolute number and percentage of CD3+IL-22+ cells had a significant difference between the groups. In addition to these results, increased IL-17A levels were shown in plasma by ELISA.

Conclusions: These results indicate that Th17-related cytokines have significant effects in CF patients and affect the prognosis of the disease.

Keywords: Cystic Fibrosis, IL-10, IL-17, IL-22, GM-CSF

PP26- SYNE1 Gene De-Novo Variant In Autosomal Recessive Spinocerebellar Ataxia Type 8

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Introduction: Cases presenting with a clinical prediagnosis of SCA are diagnosed with molecular genetic tests.The estimated worldwide prevalence of SCAR8 disease due to SYNE1 variants is less than 1 million.

Materials and Methods: In this study, we report a 29-year-old woman who presented with stiff neck, tinnitus, weakness in arms and inability to walk unassisted. Neurological examination of the patient revealed significant cerebral findings and MRI performed at an external center revealed brain shrinkage. After detailed anamnesis of the patient, pedigree was obtained.
Discussion: While the parents had a complaint of staggering, the older sister had staggering since she was young but did not need any help. Similar indications were also found in previous generations. The patient was included in the ataxia panel using the NGS method. The SYNE1 gene was found to be a de novo frameshift variant. In line with the molecular genetic results for this patient, their parents and a sibling with similar clinical findings were invited to our department for screening for the variant detected in the SYNE1 gene.
Results: The patient's clinical and genetic diagnosis was consistent with autosomal recessive spinocerebellar ataxia type 8. In addition to the autosomal recessive inheritance of the highly pathogenic variant in the SYNE1 gene, the patient's homozygosity indicates that we made a molecular genetic diagnosis that supports the clinical findings. In conclusion, our aim in presenting this case was to contribute to the literature by adding a de novo variant.
Keywords: Ataxia, SCA type 8, SYNE1/SCAR8, prevalence

PP27- A late-diagnosed case of cornelia de lange syndrome with a BRD4 variant
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Introduction:
Cornelia de Lange syndrome (CdLS) is a genetically heterogeneous condition with distinctive facial features, growth delay, intellectual disability, and multiple congenital anomalies. Variants in **NIPBL** are most common, followed by **HDAC8** and **SMC1A**, with less frequent involvement of **RAD21**, **SMC3**, and **BRD4**. Since the CdLS phenotype may evolve, diagnosis can be delayed—especially in adolescents. Early childhood features can therefore aid recognition. This report presents a late-diagnosed CdLS case with a **BRD4** variant.
Case Presentation:
A 17-year-old male was referred to the genetics clinic for choanal atresia, short stature, and borderline intellectual disability. He was born at 36 weeks by cesarean section with a birth weight of 1500 grams and required neonatal intensive care due to cyanosis and absent crying. He had been followed by endocrinology for short stature (–3.81 SDS). Physical exam showed microcephaly, scoliosis, unilateral gynecomastia, and clinodactyly. Karyotype was normal. Due to the combination of clinical findings, a broad next-generation sequencing panel was planned. It identified a heterozygous missense variant in the **BRD4** gene (c.1289A>G, p.Tyr430Cys), classified as likely pathogenic.
Conclusion:
CdLS was not initially suspected due to a non-classic facial appearance. However, multiple clinical features prompted comprehensive genetic testing, which confirmed the diagnosis. Later review of childhood photographs revealed facial traits consistent with CdLS. This case illustrates how evolving phenotypes can complicate recognition and underscores the value of broad molecular testing. Reporting BRD4-related cases also contributes to expanding the CdLS genetic spectrum.
Keywords: Cornelia de lange syndrome, CdLS, BRD4, NGS

PP28- Freeman-Sheldon Sendromlu Olguda Prenatal Genetik Danışmanlık Önemi
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Giriş: Freeman-Sheldon sendromu (FSS), distal artrogripozis tip 2A (DA2A) olarak da bilinen, *embryonic myosin, heavy chain 3, skeletal muscle* (*MYH3*, OMIM no * 160720) genindeki patojenik varyantlara bağlı nadir, otozomal dominant geçişli konjenital bir kontraktür bozukluğudur. Burada otozomal dominant kalıtımlı nadir hastalıklara sahip bireylerde prenatal genetik tanı ve genetik danışmanlığın öneminden bahsedilecektir.
Yöntem: Prenatal ultrasonografide artmış nazal kemik kalınlığı, iskelet anomalileri saptanan 29 yaşındaki gebe hasta değerlendirildi. Hastanın yapılan ayrıntılı dismorfik muayenesinde kısa boy, kısa boyun, uzun filtrum, küçük ağız, H-şeklinde çene çukuru, pitoz, strabismus, kamptodaktili, ve kifoskolyos yer almaktaydı. Hastaya tüm ekzom sekanslama yapıldı.
Bulgular: Hastada, yeni nesil dizileme ile *MYH3* geninde c.533C>T (p.Thr178Ile) heterozigot varyantı tanımlandı. Bu mutasyon, Freeman-Sheldon sendromu ile ilişkilidir.
Tartışma: Otozomal dominant kalıtım nedeniyle, her gebelikte %50 geçiş riski bulunmaktadır. Prenatal görüntülemede şüpheli bulgular (örneğin, artmış nazal kemik kalınlığı, ekstremite kontraktürleri) saptandığında hastanın gebelik haftası ile uyumlu olarak prenatal invaziv test önerilebilir. Bu vaka, özellikle aile temelli mutasyon taramasının dominant geçişli hastalıklardaki rolü, prenatal ultrason bulgularının tanı koymada yol göstericiliği, genotip-fenotip korelasyonunun kişiye özgü yönetim planlamasındaki katkısı gibi yönlerden önem

taşımaktadır. Ayrıca ebeveyn genotipinin bilinmesi, prenatal danışmanlık ve fetal risk değerlendirmesi açısından kritik önemdedir. Tıbbi Genetik ve Perinatoloji gibi disiplinlerin iş birliği, prenatal ve postnatal dönemde komplikasyonları önlemek açısından büyük önem taşır.

Anahtar Kelimeler: Freeman-Sheldon sendromu, MYH3, p.Thr178Ile, distal artrogripozis, prenatal tanı, konjenital kontraktür, genetik danışmanlık

PP29- Clinical And Molecular Evaluation of *ASXL3* and *KCNK4* Gene Variants in A Patient With Drug-Resistant Epilepsy, Psychomotor Regression, and Dysmorphic Features

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Introduction: Next-generation sequencing often reveals variants in complex cases. We report a 15-year-old female with drug-resistant epilepsy, psychomotor regression, fluctuating neutrophils, and white matter abnormalities. Genetic evaluation identified *ASXL3* and *KCNK4* variants, linked to Bainbridge-Ropers (BRPS) and FHEIG Syndromes. This report details her phenotype, evaluates these variants, and highlights diagnostic challenges.

Case Presentation: A 15-year-old female, born to consanguineous parents, experienced early-onset drug-resistant epilepsy and severe psychomotor regression after an 8-year-old seizure. She presents with microcephaly, balance disorder, involuntary movements, and dysmorphic features (e.g., facial asymmetry, long thumbs, prominent ears).

Findings: Profound developmental delay, severe microcephaly, and growth retardation were observed. Brain MRI showed non-specific FLAIR hyperintense lesions. WES revealed heterozygous *ASXL3* c.4966C>T p.His1656Tyr and KCNK4 c.660C>T p.Ala220= variants. Her complex phenotype overlaps significantly with core features of both BRPS (*ASXL3*-related) and FHEIG syndrome (*KCNK4*-related), including epilepsy and intellectual disability.

Discussion: Two distinct gene variants linked to severe, overlapping neurodevelopmental disorders suggest complex etiology. *ASXL3* missense variants, though atypical for truncating BRPS, can cause milder phenotypes. *KCNK4* splice region/synonymous variants may disrupt splicing, affecting neuronal excitability and contributing to epilepsy/developmental delay. While no direct digenic inheritance is established for *ASXL3*/*KCNK4*, their combined impact may explain her severe presentation. *HAX1*'s role in neutrophil/neurology adds complexity.

Conclusion: This case underscores diagnostic complexities in severe neurodevelopmental disorders with multiple genetic findings. Her extensive phenotype aligns with key BRPS and FHEIG features. Functional and parental segregation studies are crucial to elucidate precise pathogenicity and combined effects. This case expands the *ASXL3/KCNK4* phenotypic spectrum, emphasizing comprehensive molecular evaluation.

Keywords: *ASXL3, KCNK4*, epilepsy, psychomotor regression, dysmorphic features

PP30- FISH Yöntemi ile Belirlenen FIP1L1-PDGFRA Gen Rearranjmanlarının Retrospektif Olarak Değerlendirilmesi

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Abstract

Hypereosinophilic syndrome (HES) is a rare hematologic disorder characterized by persistent eosinophilia, tissue infiltration, and multi-organ involvement. Genetic abnormalities such as FIP1L1-PDGFRA, PDGFRB, FGFR1, and PCM1-JAK2 are known to play a crucial role in the pathogenesis, especially in myeloproliferative variants. This retrospective study analyzed the genetic and hematological data of 175 patients (87 females, 88 males) diagnosed with HES at Erciyes University between 2017 and 2023. FISH and karyotype analyses were used to identify gene rearrangements including FIP1L1-PDGFRA, t(5;12)(PDGFRB), t(8;13)(FGFR1), and t(9;12)(PCM1-JAK2). Additionally, demographic variables, eosinophil levels, and complete blood count results were evaluated. The findings indicated significantly elevated eosinophil counts in FIP1L1-PDGFRA positive patients and revealed meaningful correlations between mutation types and clinical parameters. This study emphasizes the importance of cytogenetic and molecular analysis in the accurate classification and targeted treatment of HES.

PP31- Exon 7 Matters: A Novel Frameshift Mutation in TALDO1 Expands the Phenotypic Spectrum of Transaldolase Deficiency

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Background:

Transaldolase deficiency is a rare autosomal recessive disorder caused by biallelic pathogenic variants in the TALDO1 gene. It disrupts the non-oxidative branch of the pentose phosphate pathway and manifests as a multisystemic condition involving liver, hematologic, renal, and connective tissues.

Case Description:

We present a 7-year-old girl with consanguineous parents,

evaluated for hepatosplenomegaly, biliary cirrhosis, nephrolithiasis, platelet dysfunction, secundum ASD, and mild skeletal anomalies. Remarkably, the patient exhibited a transient neonatal cutis laxa–like phenotype, a feature not previously reported in TALDO1 deficiency.

Whole-exome sequencing identified a novel homozygous frameshift variant in exon 7 of the TALDO1 gene: c.938del (p.Arg313ProfsTer8), predicted to result in loss of function. This variant is absent from population databases and not previously reported in ClinVar or HGMD. According to the 2020 ClinGen guidelines, the variant was classified as a VUS with PVS1 (moderate), PM2, and PM3 criteria fulfilled. The strong genotype–phenotype concordance supports potential pathogenicity.

Conclusion:

This is the first report of the c.938del variant and one of the few TALDO1 cases presenting with such a constellation of findings. The case contributes to the expanding clinical and mutational spectrum of transaldolase deficiency. In addition to known hepatic and hematologic features, it emphasizes underrecognized manifestations such as renal stones, skeletal anomalies, and reversible cutis laxa. This report reinforces the diagnostic utility of exome sequencing in unexplained multisystem pediatric conditions.

Keywords:

TALDO1, transaldolase deficiency, exome sequencing, cutis laxa, biliary cirrhosis, multisystemic disorder