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Poster Presentations

POSTER PRESENTATIONS

[P-01]

Exploring and Expanding Secondary Findings Through Exome Sequencing in the Çanakkale/ Türkiye Population

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Introduction: Exome-sequencing (ES) methods enable accurate diagnosis in challenging cases, and uncover secondary findings (SFs) potentially linked to life-threatening or preventable diseases. The American College of Medical Genetics and Genomics (ACMG) publishes a list detailing which SFs should be reported and regulaly updates it. This study aims to compare results across different SF versions in patients and explore additional SFs to identify potential new recommendations for SF reporting.

Methods: We conducted a retrospective analysis of 724 patients who had previously undergone ES, utilizing the QIAGEN clinical insight interpret database to identify ACMG SFs. Furthermore, we investigated pathogenic/likely pathogenic variants in cancer and cardiovascular disease genes not listed in ACMG SFs, as well as genes associated with common diseases prevalent in our country (e.g., PKU, HBB, SMA, FMF, and G6PD deficiency).

Results: ACMG SF v3.2 variants were identified in 60 patients (8.2%), with no observed differences between ACMG v3.1 and v3.2. However, 51 patients (7%) had variants from ACMG SF v2.0. Additionally, our analysis revealed that 208 patients harbored non-ACMG SF variants. Among these, 67 variants in MEFV, 10 variants in CHEK2, 9 variants in G6PD are particularly noteworthy.

Conclusion: In this study, we focused on known SFs and identified additional variants that could be considered as new recommendations. While expanding the list of SFs can pose challenges during analyses and genetic counseling, a thoughtfully curated SF list has the potential to enhance patient care and improve clinical outcomes.

[P-02]

Multiple Congenital Anomalies-Hypotonia-Seizure Syndrome 1: A First Case from Türkiye

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Introduction

Mutations in the *PIGN* gene result in a condition characterized by severe developmental delay, hypotonia, and early-onset seizures, associated with multiple congenital anomalies, termed "Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1." Its prevalence is estimated to be <1/1,000,000 (ORPHA: 280633). Genitourinary and gastrointestinal abnormalities can be observed. Here, we present a case of "multiple congenital anomalies-hypotonia-seizures syndrome 1".

Case Report

The patient, referred to us due to the manifestations of epilepsy and hypotonia, underwent an evaluation revealing hypotonia, a history of macrosomic birth, bitemporal narrowing, nystagmus, hypertelorism, bilateral hypoplastic distal fingers and toes. A contrast-enhanced brain magnetic resonance imaging examination indicated cerebral parenchymal and corpus callosum atrophy. Echocardiography showed a persistent foramen ovale. There was a first-degree cousin marriage between the parents. A similar clinical history of a deceased male sibling with comparable clinical features and a family history were present. The patient who applied to the Medical Genetics Clinic of Necmettin Erbakan University Faculty of Medicine for the investigation of the etiology of hypotonia were evaluated with their medical history, physical examination, and pedigree. Peripheral blood sample from the patient was examined using clinical exome sequencing. Variants were classified according to ACMG standards. CES analysis of the patient revealed a homozygous missense variant in the *PIGN* gene (ENST00000357637,c.996T>G,rs1060499763), classified as "likely pathogenic".

Discussion

The presentation of this case aims to guide clinicians and medical geneticists in considering rare clinical associations with the *PIGN* gene in patients presenting with hypotonia, macrosomia, and epilepsy, and to present the first Turkish case in the literature.

Keywords: *PIGN* gene, hypotonia, seizure

POSTER PRESENTATIONS

[P-03]

The Unusual Cause of a Common Association: Neuroocular Syndrome

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Introduction

Neuroocular syndrome (NOS) is an autosomal dominant syndrome that encompasses a wide range of systemic features. The type and severity of neuropsychiatric problems (developmental delay, intellectual disability, isolated speech delay, autism spectrum disorder) and eye anomalies (ptosis, coloboma, microphthalmia, retinal dysplasia, cataract, strabismus) exhibit marked variability. We present this rare NOS diagnosis found in a patient aiming to contribute to genotype-phenotype correlation studies.

Case Report

A 7-month-old male with a Noonan syndrome-like phenotype (ventricular septal defect, bilateral ptosis) was referred to the genetic diseases evaluation center. He was delivered by C/S at 31 weeks of gestation, with a weight of 1370 grams, from a 38-year-old G3P1 mother. No family history of similar conditions. The examination revealed various dysmorphic features (cryptorchidism, partial syndactyly on right foot, frontal bossing, ptosis, downslanting palpebral fissures, wide-set eyes, long philtrum, tented mouth, retrognathia) along with failure to thrive. Abdominal ultrasonography and brain MRI were normal. CES analysis (KAPA HyperCap Heredity Panel) uncovered a heterozygous nonsense variant (ENST00000418929.7:c.2545C>T/p.Gln849Ter) in exon 4 of the *PRR12* gene.

Discussion

In the ClinVar database, the majority of pathogenic variants identified in this gene consist of variants causing loss of function (54% frameshift, 23% nonsense). A stop-gain variant in a gene, where loss of function is the primary pathogenic mechanism, and its absence in population databases, along with clear clinical correlation, led to the likely pathogenic classification of this novel variant based on ACMG standards (PVS1, PM2). In the differential diagnosis of Noonan syndrome, considering NOS is recommended.

[P-04]

A Novel Variant in *CACNA1H* Gene in Childhood Absence Epilepsy

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Introduction

Absence seizures are characterized by a brief loss of consciousness and seen 4.6 per 100,00 in the general and 6 per 100,000 in children younger than 15 years. CACNA1H encodes a T-type calcium channel and associated with epilepsy susceptibility. With this case we aimed to enlighten a novel variants of *CACNA1H* gene.

Case Report

A 6-year-old patient with no additional disease history was referred to our outpatient clinic with a complain of loss of awareness, unresponsiveness and occasional incontinence. It was stated that symptoms were lasting about 10 seconds, were usually seen once a day. Generalized epileptiform anomaly was reported in electroencephalography. DNA isolation from patient's peripheral blood and clinical exome sequencing containing 3300 genes was performed for epilepsy, then analyzed on SEQ NGS analyze platform. Molecular analysis revealed two different heterozygous missense variants [c.5024G>A,p.Arg1675Gln (rs149367557) and c.4462G>T,p.Asp1488Tyr] in *CACNA1H* gene. Variants are classified as "Variant of Uncertain Significance" according to ACMG criteria. To identify the clinical importance, segregation analysis was also performed with Sanger sequencing. The former variant was found in patient's mother who has no related symptom and the latter variant was not detected in both parents. The variant was evaluated as *de novo* and thought to be responsible for complaints of the patient.

Discussion: Here we conclude that missense c.4462G>T:p.Asp1488Tyr variant which has never been encountered before may be responsible for childhood absence epilepsy. With this case report, we hope to make contribution to the literature.

Keywords: Absence seizure, epilepsy, *CACNA1H* gene

POSTER PRESENTATIONS

[P-05]

Pathogenic Variant in CBL Causing Juvenile Myelomonocytic Leukemia: A Case Report

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Introduction: Pathogenic variants altering RAS/MAPK pathway cause wide spectrum of diseases including developmental abnormalities, growth delay, various neoplasms and hematologic diseases. Juvenile myelomonocytic leukemia (JMML) is a rare and aggressive myelodysplastic disorder of early childhood. Somatic or germline pathogenic variants in 5 genes (*NF1*, *PTPN11*, *KRAS*, *NRAS*, *CBL*) affecting this pathway account for 90% of JMML cases. We report a patient diagnosed with Noonan syndrome-like disorder and CBL-mutated JMML (NS-JMML).

Methods: A 41-month-old female, the first child of a healthy unconsanguineous-couple, with growth and neurodevelopmental delay, absent speech, microcephaly and open-fontanel initially applied to hospital with abdominal distention and splenomegaly. After the detailed work-up, she was diagnosed with NS-JMML. Following consultation to our department, she was tested with next generation sequencing RASopathy panel from peripheral blood sample as well as cytogenetics and molecular tests from bone marrow biopsy.

Results: RASopathy panel revealed a c.1112A>C(pTyr371Ser) heterozygous likely pathogenic missense variant in *CBL(NM_005188.3)* gene with the allele frequency of 56% (reading depth: 375). Variants affecting Tyr371Ser has been reported several times in both isolated JMML and NS-JMML. Chromosomal analysis, monosomy 7 FISH and t(9;22) RT-PCR tests from bone marrow biopsy were all normal.

Conclusion: We present a heterozygous variant in the *CBL* gene detected in a female with NS-JMML. Considering that transplantation is not recommended in germline CBL mutations, it is valuable to detect these mutations for patients' follow-up and treatment. In addition, we aim to demonstrate that genetic counseling and monitoring for hematologic malignancies is crucial for Noonan syndrome-like phenotype.

Keywords: CBL, JMML, RASopathy, Noonan syndrome-like

[P-06]

A Rare Li-Fraumeni Syndrome Caused by a Homozygous TP53 Pathogenic Variant

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Introduction

Li-Fraumeni syndrome (LFS) inherited in an autosomal dominant manner, is a hereditary cancer predisposition syndrome, resulting from pathogenic variants in the *TP53* gene. TP53 is a tumor suppressor gene encoding the p53 transcription factor involved in the cell cycle regulation.

Case Report

A 3-year-old female patient was consulted with relapsed refractory choroid plexus carcinoma (CPC) and surrenal mass. An abdominal wall defect was detected prenatally at 24 weeks and the patient was operated twice for omphalocele. Cranial magnetic resonance imaging (MRI) revealed a mass almost completely filling the left cerebral hemisphere, causing midline shift and hydrocephalus. Pathological examination of the excised tumor tissue revealed a diagnosis of grade 3 CPC. Abdominal MRI was performed due to high androgen levels. A 38x23mm lesion was observed in the right adrenal gland. It was found compatible with adrenocortical carcinoma (ACC). Next generation sequencing revealed a homozygous c.375G>A (p.Thr125Thr) variant in the 4th exon of the TP53. This variant was evaluated as "Pathogenic Variant" according to the The American College of Medical Genetics and Genomics 2015 variant classification guide.

Conclusion

Although TP53 is the most frequently mutated gene in cancer patients, homozygous germline variants are very rare. In our case, two LFS-associated tumors (CPC and ACC) were seen at a very early age. CPC recurred multiple times and our patient died due to a severe clinical course. This prognosis indicates that the homozygous status, may have brought the age of tumor emergence earlier and aggravated the clinical course.

Keyword: TP53

POSTER PRESENTATIONS

[P-07]

Smith-Kingsmore Syndrome: A Rare Case of Intellectual Disability from Çanakkale

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Introduction

Smith-Kingsmore syndrome is a rare neurological disorder characterized by a macrocephaly, intellectual disability, seizures. It is caused by pathogenic mutations in the *MTOR* gene. We aimed to present a case of Smith-Kingsmore syndrome with a rare MTOR mutation.

Case Report

A 30-year-old male patient applied to the outpatient clinic with his family with the diagnosis of mental retardation. The patient additionally had newly diagnosed hypothyroidism and congenital macrocephaly. There was no other patient with intellectual disability in the family. We performed clinical exom analysis to the patient and detected heterozygous c.5395G>Ap. E1799K(NM_004958.4) variant in MTOR. *MTOR* gene is associated with autosomal dominant "Smith-Kingsmore syndrome" in Online Mendelian Inheritance in Man which shows compatibility with the case.

Conclusion

The *MTOR* gene affects the PI3k/Akt/mTor pathway and plays a role in the extracellular communication, growth and proliferation of cells. MTOR mutations that cause Smith-Kingsmore syndrome cause hyperactivation of this pathway, causing symptoms such as megaloencephaly, macrocephaly, intellectual disability and epilepsy. To date, 56 patients with a missense mutation in the *MTOR* gene that causes Smith-Kingsmore syndrome have been reported and 30 of these patients have the same mutation as our patient. Currently, there is no treatment for this disease and it has been reported that patients with gain-of-function mutations in the *MTOR* gene may benefit from MTOR inhibitors such as rapamycin. Therefore, functional studies are required for patients diagnosed with Smith-Kingsmore syndrome. Although there are not enough publications in the literature regarding the treatment of this disease, we think that the increase in the number of published cases will be beneficial in finding a treatment for the disease.

[P-08]

The Role of Array-CGH Analysis in the Diagnosis of Rare Diseases: A Single-Center Experience

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Abstract

Array-CGH analysis is an important tool in the diagnosis of rare diseases due to its ability to identify defined microdeletion-duplication syndromes, unique copy number variations in individuals, major chromosomal abnormalities, chromosomal numerical anomalies, single gene disorders, imprinting disorders; providing insight into mosaicism, and detecting loss of heterozigosity. Rare diseases were diagnosed in 47 out of the 695 patients we analyzed (6.7%). Copy number variations were detected in 10 patients, with a single gene (*SHANK3*, *CHRNA7*, *GLI3*, *HNF1B*, *NRXN1*, *ABCG2*, *NF1*, *HBA1*, *BHLHA9*) responsible for the clinical manifestations. Copy number variations were detected in rare regions among 14 patients, with sizes ranging from 145 KB to 7.7 MB, along with identified variations in microdeletion/duplication syndrome regions including 22q11.2 microdeletion syndrome in 4 patients, Prader-Willi/Angelman syndrome in 3 patients, 3q29 microduplication syndrome in 4 patients, and other syndromes found in 1 patient each such as Phelan McDermid syndrome, 1q21.1 duplication syndrome, 9q31.1q31.3 microdeletion syndrome, cat eye syndrome, 6q25 microdeletion syndrome, and 8q21.11 microdeletion syndrome. Additionally, major numerical and structural chromosomal anomalies, such as trisomy 9p, partial monosomy 11q, 6q25 microdeletion syndrome, Turner syndrome, and derivative Y chromosome, were detected in 7 of these patients, which also identified through chromosome analysis. In today's context where sequencing technologies have emerged as prominent tools for diagnosing rare diseases, the significance of array CGH technology remains crucial in the diagnosis of rare diseases due to its ability to diagnose genetic disorders arising from various mechanisms.

POSTER PRESENTATIONS

[P-09]

DeSanto-Shinawi Syndrome with *De Novo* WAC Variant in Çanakkale: A Case Report with Dysmorphic Face, Congenital Heart Disease, and Neonatal Convulsion

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Introduction: WAC-related intellectual disability, known as DeSanto-Shinawi syndrome (Online Mendelian Inheritance in Man #616708), is an autosomal dominant disorder caused by pathogenic variants in the WW domain-containing adapter with coiled-coil (*WAC)* gene, located on 10p12.1. This syndrome is characterized by global developmental delay, dysmorphic facial features, intellectual disability, and behavioral problems. We present the clinical findings and genetic analysis results of a newborn female patient with DeSanto-Shinawi syndrome.

Methods: A newborn female patient was referred to us due to congenital heart disease, hypotonia, respiratory distress, neonatal convulsion, and dysmorphic face (deep-seated eyes, bulbous nasal type, prominent ear). The patient was born via cesarean section at 34 weeks in a twin pregnancy, with her twin sibling showing no health issues. Transfontanellar ultrasound revealed multiple corticothalamic cysts. There was no consanguinity between the parents. The father, aged 28, exhibited a similar dysmorphic facial phenotype, mild ID and congenital heart disease.

Results: Since no pathogenic/likely pathogenic variant that could explain the clinic was detected in chromosome and microarray analyzes, we detected a heterozygous likely pathogenic *de novo* c.920-5delTTTAGinsTTAA variant in the *WAC* gene in the patient and his father in the clinical exom analysis.

Conclusion: DeSanto-Shinawi syndrome is an exceedingly rare genetic disorder, with only a limited number of cases reported in the medical literature. As far as we know, this is the first DeSanto-Shinawi syndrome reported in Türkiye. Our case contributes to the current literature by emphasizing the importance of advanced genetic testing methods such as CES in rare diseases.

Keywords: DeSanto-Shinawi Syndrome, *WAC* gene, CES

[P-10]

Dual Phenotype Patient with Congenital Hypothyroidism and Family History of Common Hearing Loss

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Introduction

Thyroid disorders and hearing loss may coexist in diseases such as Pendred syndrome, but they may also be present independently of each other. Numerous genetic aetiologies have been described for these two clinical conditions.

Case Report

A 2-year and 6-month-old male patient was consulted to us from pediatric endocrinology with a prediagnosis of Pendred syndrome because of congenital hypothyroidism and diffuse hearing loss in the family. There were no significant findings in prenatal follow- up and hypothyroidism was detected on heel prick screening. His parents were not related and he had a healthy sibling. In the family history, the mother had mild hearing loss. His father and some relatives on the paternal side had a history of hypothyroidism and hearing loss. The patient's neuromotor developmental milestones were normal. There were no significant dysmorphic findings on physical examination.

Discussion

The patient underwent clinical exome sequencing and the analysis revealed a heterozygous pathogenic variant c.167del in exon 2 of the *GJB2* gene. In the *TG* gene, c.7111C>T non-sense heterozygous probable pathogenic variant and intronic c.638+5G>A heterozygous probable pathogenic variant were detected in exon 41. Variants were detected in two different genes explaining the clinical status of the patient. We hope that this rare case will contribute to the literature.

Keywords: Hypothyroidism, hearing loss, dual phenotype

POSTER PRESENTATIONS

[P-11]

A Case with Kaufman Oculocerebrofacial Syndrome with an UBE3B Variant

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Abstract

Kaufman Oculocerebrofacial syndrome (KOS) or Blepharophimosis-Ptosis-Intellectual Disability Syndrome is an autosomal recessive developmental disorder characterized by reduced growth, microcephaly, ocular anomalies (microcornea, strabismus, myopia, and pale optic disc), distinctive facial features (narrow palpebral fissures, telecanthus, sparse and laterally broad eyebrows, preauricular tags, and micrognathia), mental retardation, and generalized hypotonia. Inactivating mutations in *UBE3B*, an *E3* ubiquitin ligase gene, are causative for KOS. At least 46 cases have been reported in the literature. Here, we report an infant with dysmorphic features, growth delay, cleft palate, laryngomalacia, respiratory distress, atrial septal defect, pectus carinatum, and talipes equinovarus. Dysmorphic facial features included low-set ears, dysplastic ears, bilateral preauricular skin tags, microphthalmia, blepharophimosis, hypertelorism, wide nasal bridge, anteverted nares, microretrognathia, and small mouth. Whole Exome Sequencing detected a homozygous splice acceptor variant in intron 1 of *UBE3B* (NM_130466.3 c.1623-1G>T). We classified the variant as likely pathogenic according to the ACMG criteria. KOS should be considered among the autosomal recessive causes of blepharophimosis-mental retardation syndromes, particularly in populations with a high rate of consanguineous marriages, even if there are dysmorphic facial features that are not typically associated with the phenotype. Our report contributes to the literature on this ultra-rare syndrome.

Keywords: Kaufman oculocerebrofacial syndrome, *UBE3B*, blepharophimosis, intellectual disability

Case Report: Patient with Blepharophimosis Ptosis Epicanthus Inversus Syndrome

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Abstract

Blepharophimosis, ptosis, and epicanthus inversus syndrome [(BPES), OMIM #110100] is a rare autosomal dominant disease of the eyelids and mid-face structures. There are two main types of BPES. Each type harbors the four classic clinical signs: PBE inversus, and telecanthus. Type 1 is associated with premature ovarian failure. Type 2 is characterized by the classic facial features alone. Here we present a family with multiple cases that prediagnosed with BPES due to their midface and eye features. Molecular analysis of the patients with whole exome sedquencing revealed *FOXL2* gene heterozygous frameshift likely pathogenic variant (c.11_12insGG p.(Ser4Argfs*147)) in exon 1. With respect to clinical and molecular data, patient's diagnosis is confirmed as BPES.

[P-12]

POSTER PRESENTATIONS

[P-13]

New Case with Thauvin-Robinet-Faivre Syndrome: Novel Variant and New Phenotypic Findings

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Abstract

Thauvin-Robinet-Faivre syndrome is an autosomal recessive disease characterized by intellectual disability, delayed psychomotor development, speech delay, macrocephaly, tall stature, large hands and feet, kidney anomalies, congenital heart diseases and dysmorphic facial findings. Biallelic pathogenic variants in the *Fibroblast Growth Factor, Acidic, Intracellular Binding Protein (FIBP)* gene are responsible for this phenotype. In this study, we present a case in which a loss of function variant was detected in this gene. The proband, a 4-year-9-month-old girl, was the fifth child of consanguineous parents. There was congenital heart disease, atrial septal defect (ASD), mitral valve prolapse (MVP) intellectual disability, speech retardation, delayed acquisition of motor developmental stages, abnormal electroencephalography, relative macrocephaly, typical dysmorphic facial findings, large hands and feet, camptodactyly in bilateral third toes, and clinodactyly in 4-5 toes. There was benign neutropenia and non-specific flare hyperintensities in the parenchymal area on cranial magnetic resonance imaging. In the whole exome sequencing performed on the patient, NM_004214.5 c.453dup p.(Arg152Alafs*16) frameshift homozygous novel probable pathogenic variant was detected in the *FIBP* gene. It was the ninth case reported in the literature and the fifth from Türkiye. The findings were consistent with the literature; the case had different ASD, clinodactyly and camptodactyly. This study contributes to the enrichment of the clinical findings and variant distribution of this very rare syndrome. More data are needed for phenotype-genotype correlation.

Keywords: FIBP, Thauvin-Robinet-Faivre syndrome, autosomal recessive

[P-14]

Partial Trisomy 4q Case

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Abstract

Partial trisomy of the long arm of chromosome 4 (distal duplication 4q; ORPHA:96096), is a rare chromosomal anomaly characterized by growth failure, intellectual disability, microcephaly, facial dysmorphism, finger anomalies, cryptorchidism, hearing loss, epilepsy, and heart/kidney malformations. Patients with partial trisomy 4q have highly variable phenotypes, therefore, it is very difficult to establish genotype-phenotype correlation in these cases. The number of cases reported to date is less than 100. Cases most often result from unbalanced inheritance of balanced parental chromosomal translocations. Here, we present an 8-day-old male infant, who was referred to our hospital with respiratory distress and suspicion of choanal atresia. He was born to a non-consanguineous parent, his mother had 9 pregnancies, 7 of which ended in abortion, and he had a healthy brother. In physical examination, he had a broad nasal root, bushy and wide eyebrow, low-set ear, prominent and overfolded ear helices, downslanting palpebral fissures, hypertrichosis, prognathia, high palate, preaxial polydactyly in the right hand, bilateral overlapping toes, sacral hypertrichosis, and bilateral undescended testicles. Based on the patient's findings, karyotype analysis was performed. Upon the detection of a derivative chromosome 15, karyotype analysis was performed from both parents. The mother was found to be a balanced translocation carrier t(4;15)(q21.3;qter), and our patient's karyotype was reported as 46,XY,der(15)t(4;15)(q21.3;qter)mat. To the best of our knowledge, this karyotype has not been published before in the literature. It is important to present such cases to better elucidate the variable phenotype and phenotype-genotype correlation of this disease.

POSTER PRESENTATIONS

[P-15]

Adult-Onset Atypical Absence Epilepsy Associated with a Novel MECP2 Variant: A Case Report

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Introduction

Variants in MECP2, located on Xq28 and encoding a methyl CpG binding protein, are well known to be associated with Rett syndrome in female patients. However, it is becoming increasingly clear that variants in the *MECP2* gene may have a wide range of consequences in terms of neurodevelopmental phenotypes beyond Rett syndrome. Here, we report the case of a female patient with adult-onset atypical absence epilepsy carrying a novel truncating variant in the *MECP2* gene.

Case report

A 27-year-old woman was admitted to the neurology department with epilepsy and intellectual disability. She had her first febrile convulsion at the age of 1.5 years and had no further seizures until the age of 25. The patient had mental retardation and was unable to continue her education after primary school due to poor school performance. At the age of 25, the patient commenced to experience treatment-resistant atypical absence seizures and tonic-clonic seizures. Following a comprehensive etiological workup, which yielded negative results, the patient underwent clinical exome sequencing. This revealed an 80 bp deletion in the *MECP2* gene, NM_001110792.2:c.1190_1269del, p.(Pro397Argfs*24).

Discussion

This case was not consistent with Rett syndrome in terms of clinical manifestations. MECP2 variants may result in a spectrum of neurodevelopmental phenotypes and may manifest as epilepsy in adulthood.

Keywords: MECP2, atypical absence epilepsy, adult-onset epilepsy

[P-16]

NGS as an Indispensable Tool in Cancer: An Overview of the Variants Detected in AML Patients

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Abstract

Introduction: Acute myeloid leukemia (AML) is a heterogeneous, aggressive form of cancer caused by clonal proliferation of malignant hematopoietic precursor cells in the bone marrow. Genetic alterations are common in AML, playing a crucial role in diagnosis, prognosis, and treatment. Recent advancements in next generation sequencing (NGS) have emphasized the crucial role of molecular genetics in disease categorization. In this study, we present the molecular findings of AML patients analyzed using the NGS method.

Methods: The findings of 40 AML patients who underwent NGS panel testing between January 2023 and April 2024 were evaluated retrospectively. NGS was performed on the samples using the QIAseq Myeloid Panel, which contains 32 genes. Variant calling and analysis were performed using the Qiagen Clinical Insight (QCI) interface. Reportable variants were classified according to the AMP/ASCO/CAP guidelines.

Results: Among the 40 patients included in the study, 22 (55%) were male and 18 (45%) were female with a median age of 53 years (11-94 years). Twenty four (60%) samples tested positive for one or more pathogenic or likely pathogenic variant(s). A total of 55 pathogenic/likely pathogenic variants were detected. Most of the variants were detected in *FLT3* (13%), *IDH2* (11%), *TET2* (11%), *NRAS* (9%), and *DNMT3A* (9%) genes. The most recurrent variant was detected on the *IDH2* gene {NM_002168.4:c.419G>A p.(Arg140Gln)}.

Conclusion: NGS panel testing is a fast and cost-effective method for genetic screening of myeloid malignancies. Our study illustrates the significant role of genetic profiling in diagnosis and prognosis of AML patients.

Keywords: Acute myeloid leukemia, hemato-oncology, molecular genetics, next generation sequencing

POSTER PRESENTATIONS

[P-17]

Two Siblings with Trisomy 9p and a Novel Finding

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Abstract

Trisomy 9p is one of the most common autosomal abnormality known to be the fourth frequency after full Trisomy 21, 13 and 18. Compatibility with survival can be explained that 9p is relatively gene poor region. In most cases, Trisomic 9p segment was inherited from reciprocal translocation carrier parent and a few of cases were due to *de novo* chromosomal aberrations. This syndrome has been featured by craniofacial dysmorphism, intellectual disability and developmental delay. We describe the case of a 14 years old girl who was referred to our clinic for evaluation of growth retardation and primary amenorhea. Clinical examination of patient revealed short stature and dysmorphic features such as bulbous nose tip, ocular hypertelorism, high arched eyebrows, strabismus and unilateral ptosis, low-set ears, short filtrum, downturned corners of mouth. Her height was 145 cm (<3p) and her secondary sex characters were prepubertal. Also according to evaluation of pediatric endocrinology clinic she diagnosed as central diabetes insipidus. It was noticed that her little sister has same facial dysmorhic features, mild intellectual disability and mild degre of growth retardation. The karyotype in proband and her sister was identified as 46,XX,der(12)t(9;12)(p24.3-p13.1) resulting from a maternal balanced reciprocal translocation t(9;12) (p24.3-p13.1). These two sibligns were diagnosed as Trisomy 9p syndrome. 9p duplication syndromes are particularly heterogenous because of breakpoint heterogenity. But until now, diabetes insipidus hasn't reported as a finding of Trisomy 9p. For detailed genotype-phenotype correlation, whole exome sequencing and copy number variation analysis will perform from our proband.

Keywords: Trisomy 9p, reciprocal translocation, diabetes insipidus

[P-18]

Ectodermal Dysplasia: A Single Medical Center Experience in Central Anatolia

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Abstract

Introduction: Ectodermal dysplasia is an uncommon genetic disorder known for its distinctive physical features. It is a hereditary condition that affects how the sweat glands, teeth, hair, and nails grow or function. Ectodermal dysplasia can also damage the skin, the inner ear, the development of fingers and toes, the retina or lens of the eye, the nerves, and other regions of the body, depending on the specific disease. We aimed to investigate the clinical characteristics of patients with ectodermal dysplasia in our center.

Methods: We conducted a retrospective analysis of 10 patients with ectodermal dysplasia diagnosed in our clinic from 2017 to 2024.

Results: This case series consisted of 6 males and 4 females aged 2 to 33, with a mean age of 10.8 years. The clinical features were as follows: hypodontia/oligodontia (100%), abnormal hair morphology (70%), abnormality of the skin (40%), onychodysplasia/dystrophic nails (30%), and sparse eyebrows (40%).

Conclusion: This study presents the clinical presentation and variant diversity of patients with ectodermal dysplasia as a single-center experience. In addition, the study introduces four novel variants to the literature.

Keywords: Ectodermal dysplasia, oligodontia, hypodontia, onychodysplasia

POSTER PRESENTATIONS

[P-19]

The Molecular Analysis of the Relationship Between the Pharmacogenetics of Slc19a1 and the Response to Methotrexate Therapy in Patients with Juvenile Idiopathic Arthritis: Preliminary Findings

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Introduction: Juvenile idiopathic arthritis (JIA) is a chronic rheumatic disease that affects children. Though its etiology and pathogenesis remain unclear, it is the most common childhood rheumatic disease. In Türkiye, the oligoarticular subtype is the most frequently observed form of JIA. Methotrexate (MTX) is commonly used for treatment of JIA. In cases of insufficient response, MTX is often combined with Biological disease-modifying anti-rheumatic drugs (bDMARDs). The SLC19A1 gene encodes a protein that plays a role in transporting folates into cells. Point mutations and downregulation of the SLC19A1 gene are key factors in antifolate resistance.

Methods: This study aims to investigate the relationships between the response to therapy and the pharmacogenetics of SLC19A1 in JIA patients who are treated with MTX or MTX+bDMARD. Genomic DNA was isolated from peripheral blood samples of 120 JIA patients. 230 bp SLC19A1 amplicon was amplified using conventional PCR with gene specific primers. RFLP analysis using Hha I restriction endonuclease enzyme was performed to genotype (GA, GG, AA) SLC19A1.

Results: The patients were divided into two groups based on the treatment they received: the MTX group (n=59) and MTX+bDMARD group (n=61). The analysis showed that hemoglobin level was a risk factor for the drugs used. However, this did not show significance within the drug groups ($p>0.05$). Additionally, no significant difference was observed among the three different genotypes in patients treated with MTX or MTX+bDMARD based on RFLP results.

Conclusion: It is planned to increase the number of patient volunteers treated with MTX or MTX+bDMARD and conduct re-analysis of the study.

Keywords: Juvenile idiopathic arthritis, pharmacogenetics, SLC19A1, Methotrexate

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