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Oral Presentations

ORAL PRESENTATIONS

[OP-01]

Combined Implementation of Local Outlier Factor Analysis and Extremely Randomized Trees Classifier on *MEFV* Gene Variants Display Outstanding Classification Performance

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Abstract

Introduction: More than half of the familial Mediterranean fever gene *(MEFV)* gene variants pathogenicity is unknown. The extremely randomized tree classifier (ETC), a type of ensemble learning, employs the outcomes of numerous unrelated decision trees arranged in a "forest" pattern to make a classification decision. ETC is applicable to the prediction of variants of uncertain significance variants of the *MEFV* gene.

Methods: We extracted more than 11,000 variants of the *MEFV* gene from the ensembl database. For most of the *in-silico* tools previously trained on the missense dataset, we selected 6,034 *MEFV* gene missense gene variants for our model. We excluded eight highly known *MEFV* gene pathogenic variants and 10 benign *MEFV* gene variants from the study. In the feature engineering step, we implemented local outlier factor analysis, and overall, 370 variants included our machine learning analysis. In the feature selection step, we determined the optimal number of *in-silico* tools for our model. After establishing our model on the training and test datasets, we deployed it into unknown variants.

Results: After hyperparameter tuning, our model obtained 100% accuracy on our training dataset and 98% accuracy on a 5-fold cross-validated dataset. After this step, we deployed our model on 8 *MEFV* gene pathogenic variants and 10 benign *MEFV* gene variants. Our model accurately classified all 18 (100%) known variants.

Conclusion: Many *in-silico* tools are trained on many genes. However, ClinGen recommended that gene-specific evaluation is necessary to improve the classification of *in-silico* tools. Re-evaluation of *in-silico* tools can improve the accuracy of *MEFV* gene variants.

[OP-02]

Two Different Cytogenetic Anomalies in a Case: Ring-(13) and Dup22q11

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Abstract

Introduction: Ring chromosome 13 [r(13)] is a rare chromosomal disorder characterized by missing genetic material from one or both ends of chromosome 13, resulting in the formation of a ring structure. Patients with r(13) have various phenotypic abnormalities that correspond to the amount of genetic material lost. Deletions of the distal locus 13q34 have been shown to be involved in symptoms such as growth and developmental retardation, microcephaly, facial dysmorphism, hand-feet anomalies and ambiguous genitalia. 22q11.2 duplication syndrome is an extremely variable disorder with a phenotype ranging from normal to learning disability and congenital defects. In this report, we described an r(13) patient who has distinct phenotypic traits and duplication of 22q11 besides deletion 13q34.

Methods: A 12-year-old female was referred to our genetics clinic for short stature, developmental delay, cardiac defect, and foot deformity. Karyotyping from peripheral blood culture were performed, following fluorescence *in situ* hybridization (FISH) and microarray analysis were planned.

Results: The karyotype imaging revealed 46, XX, r(13). FISH analysis was performed by using a 13qter specific subtelomeric probe (Cytocell, LPT13 QR/G), showing a one red signals in that region. Acro-p-arm FISH probe (Cytocell, LPENOR) had two signal. Microarray analysis (GenetiSureCyto8x60K) showed a deletion containing 17 *OMIM* genes (1.4 Mb) in the 13q34 and duplication containing 30 genes (2.4 Mb) in the 22q11.21q11.22. The parents' karyotypes revealed as normal and microarray analysis is ongoing for them.

Conclusion: To our knowledge, there is no previous report of a r(13) who has del13q34 and concomitant dup22q11. 21q11.22. The characterization of the structure and the additional genomic aberrations of the r(13) are valuable for future researchers to better understanding of the genotype-phenotype correlation.

Keywords: r(13), del13q34, dup22q11

ORAL PRESENTATIONS

[OP-03]

A Rare Syndrome from Physical Examination to Diagnosis: Short-Rib-Thoracic Dysplasia-3

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Introduction

Skeletal dysplasia is a heterogeneous group of genetic disorders affecting bones and cartilages. Short rib thoracic dysplasia-3 is a ciliopathy characterised by a narrow rib cage, short ribs, short tubular bones and a "trident" appearance of the acetabular roof. This condition is lethal in the perinatal period. The prevalence of DYNC2H1-associated short rib thoracic dysplasia-3 is currently unknown.

Case Report

Amniotic fluid was obtained from a 23-year-old gravida 2, para 0, abortus 1 mother due to the presence of skeletal dysplasia in the fetus. The chromosome analysis was normal. The case was born by C/S at 36+5 weeks, followed up in the intensive care unit due to respiratory distress and prematurity and died at the age of 1 day. The examination of the dead foetus revealed a narrow thorax, horizontal ribs, shortness and curvature of the long bones and brachydactyly. The radiological imaging revealed the presence of handlebar clavicle, trident acetabulum, and shortening of long bones. The parents were from the same village. In the next generation sequencing analysis, the c.7606C>T variant was identified as homozygous in the *DYNC2H1* gene. This variant was classified as a variant of unknown significance or possibly pathogenic according to the American College of Medical Genetics and Genomics criteria. The parents were included in the segregation analysis.

Discussion

Currently, there is no definitive treatment for short costal-thoracic dysplasia; therefore, the best strategy in the management of the disease is to determine the carrier status of the parents. Families in which the variant is identified have a chance of having a healthy child with preimplantation genetic diagnosis.

[OP-04]

Investigation of Innate Lymphoid Cells in Patients with Familial Mediterranean Fever and Spondyloarthritis

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Abstract

Introduction: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease characterized by recurrent and self-limiting attacks of fever and serositis. FMF is the prototypical example of autoinflammatory diseases. Spontaneous activation of the innate immune system results in the release of IL-1B and typical clinical attacks occur. Musculoskeletal involvement of abdominal aortic aneurysm (AAA) includes acute arthritis, chronic arthritis, sacroiliitis, and spondyloarthropathy (SpA). In this study, changes in innate lymphoid cells (ILC) cells were examined to understand how AAA, an autoinflammatory disease, and SpA come together.

Methods: Ficoll-Hypaque density gradient was used to isolate peripheral blood mononuclear cells (PBMCs) from blood samples taken from healthy volunteers (n=6), FMF patients (n=17), SpA patients (n=12) and FMF patients with SpA (n=14). PBMCs were were counted with Tyrpan Blue staining, and stained with appropriate surface markers for ILCs examined on FACSAria III and all data was analyzed using FlowJo and Graphpad 9.

Results: In analyzes made from peripheral blood, it was observed that the frequency of the ILC2 subtype was significantly reduced in patients with SpA compared to patients with AAA. In patients with SpA + AAA, despite the increasing trend, statistical significance was not reached. It was observed that ILC3 cell frequencies and numbers tended to increase compared to the FMF group, although it did not reach statistical significance. Supported by ERÜ BAP unit with TDK-2022-11916 procect code.

Conclusion: Quantitative and phenotypic changes in ILCs in FMF patients with SpA may contribute to disease pathogenesis.

Keywords: Familial mediterranean fever, spondyloarthritis, innate lymphoid cells

ORAL PRESENTATIONS

[OP-05]

FBN2 Related Fibrillinopathy with New Phenotypic Findings in an Affected Family

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Abstract

Fibrilinopathies represent a group of diseases that microfibrils are disrupted by genetic variants in one of the genes encoding fibrillin molecules, large glycoproteins of the extracellular matrix. There are three isoforms of fibrillin molecules identified in mammals: fibrillin 1, fibrillin 2 (FBN2), and fibrillin 3. FBN2 is an important component of microfibers involved in the formation of elastic fibers in connective tissue throughout the human body. FBN2-associated fibrillinopathies have been associated with different connective tissue diseases such as congenital contractural arachnodactyl (CCA), macular degeneration, and myopathy. Congenital CCA is an autosomal dominant disorder caused by heterozygous disease-causing variants on the gene encoding FBN2. FBN2 is located on chromosome 5q23-q31, and it is the only gene known to be associated with CCA, which has similar features with Marfan syndrome. CCA is characterized by a marfanoid habitus (a long and slender build), dolichostenomelia, crumpled ear, arachnodactyly, flexion contractures of multiple joints, kyphoscoliosis. Some patients also have cardiovascular and ocular complications. Here we report 4 affected individuals in a family who were referred to us with findings such as marfanoid habitus, Chiari malformation, aortic dilatation, glaucoma, scoliosis and arachnodactyly. We detected the same heterozygous missense variant on FBN2 [NM_001999 c.680G>A p.(Gly227Glu)] in all affected individuals. We classified this variant as a likely pathogenic according to American College of Medical Genetics and Genomics Critierias. Our study broadens the phenotypic spectrum of CCA with findings that have not been reported before, including glaucoma and Chiari malformation. We emphasize the importance of understanding the phenotypic spectrum of the disease and genetic counseling.

Keywords: FBN2, fibrillinopathy, glaucoma, Chiari malformation

[OP-06]

Impact of Polymorphisms on Clinical Management

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Abstract

Genetics have been impacting healthcare and patient management for many years. The impact of genetics on healthcare is becoming more and more profound. Most of this management is based on the identification of pathogenic, likely pathogenic and even VUS variants. Precision Health Group (PHG), is the world's first healthcare and wellness provider that integrates genetics, functional and regenerative medicine, naturopathy, nutrition, fitness and healing under one roof to provide a unique "system of care" for patients and clients, with a stated mission of "from illness to wellness and beyond", PHG is set to change medicine and healthcare as we know it! This means going beyond the simple variant reporting, we go deeper to search the literature, investigating all variants and their clinical correlations, guided by and working with the patient's physician and the care team, we don't stop until we get the right answers to help the patients. Here we present to you with a case to demonstrate this concept of care, a 76 year old male presented to our care team asking for guidance to help him understand his mysterious post surgical bleeding following eye surgery. This case is a great example of how even a polymorphism may have profound impact on patient management.

ORAL PRESENTATIONS

[OP-07]

Hypoparathyroidism, Short Stature, Glaucoma, Epilepsy and Thalassemia: A Case with Blend Phenotype

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Introduction

Next generation sequencing technologies have the capacity to sequence the entire genome or many DNA fragments in small targeted regions. These technologies are an important tool for determining the etiology of diseases with genetic heterogeneity. Once the root cause of the disease is identified, more precise genetic counseling can be provided to patients and family members at risk can be rapidly screened. Especially in cases where various clinical findings coexist, more comprehensive gene panel tests can be preferred and diagnostic superiority can be achieved.

Case Report

A 10-year-old girl with congenital glaucoma, hypoparathyroidism, history of epilepsy starting at 2 months of age, profound anemia and short stature was referred to us from the pediatric endocrinology department. Physical examination revealed buphthalmos in the left eye, prominent ear and mild microcephaly. Clinical exome sequencing was performed to elucidate the etiology of the patient's current clinical findings. In the study, c.1336 C>T p.(Arg446*) non-sense homozygous pathogenic variant in *ABCG5* gene, c.868dup p.(Arg290Profs*37) frameshift homozygous pathogenic variant in *CYP1B1* gene and c.25_26del p. (Lys9Valfs*14) frameshift heterozygous pathogenic variant in *HBB* gene were detected.

Discussion

In this study, we emphasize that the presence of different clinical findings is not always associated with a single syndrome, that more than one gene alteration may cause clinical manifestations, and therefore, the superiority of studying broad panels instead of narrowly targeted panels in patients with complex phenotypes in making a diagnosis.

Keywords: Next generation sequencing, blended phenotype, sitosterolemia, congenital glaucoma

[OP-08]

Novel LRP5 Variant in a Patient with Multiple Fractures, Retinal Detachment and Epilepsy

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Introduction

Low-density lipoprotein receptor-related protein 5 (LRP5) is a 1,615 amino acid transmembrane receptor for the conserved Wnt-β-catenin signaling pathway, a pathway known to regulate bone metabolism in humans. Specific human polymorphisms in LRP5 have been hypothesized to affect bone density, in part by altering the anabolic response of bone to mechanical loading. Recessive loss-of-function mutations in LRP5 cause osteoporosis-pseudoglioma syndrome, a condition characterized by severe osteoporosis and occasional ocular abnormalities.

Case Report

A 17-year-old female patient was referred to us from pediatric endocrinology for osteogenesis imperfecta due to multiple fractures. She had a history of nearly 30 fractures. She was followed up with epilepsy but no active seizure was observed. There is bilateral visual loss due to retinal detachment. There was no pathology in prenatal follow-up and birth history. Physical examination revealed curved legs and inability to stand bilateral ptosis, large auricle, underdeveloped helix structure, bulbous nasal tip, faint filtrum, and scoliosis. Our patient's maternal and paternal grandparents are siblings. Eletroencephalogram shows the presence of epileptiform discharges. Vertebral radiography showed trocholumbar scoliosis.

Discussion

Clinical exome sequencing was performed. As a result of the analysis, we detected a homozygous c.2645T>A p.(Ile882Asn) variant in the exon 12 of the *LRP5* gene. When we examined the databases, we found that this variant has not been reported before. We hope that our case will contribute to the literature with this report.

Keywords: LRP5, osteoporosis-pseudoglioma syndrome, rare disease

ORAL PRESENTATIONS

[OP-09]

Comparative Analysis of Sickle Cell Trait Distribution Among Nigerian and Zimbabwean Students in Northern Cyprus

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Abstract

Sickle cell disease (SCD) is a genetic disorder caused by abnormalities in the *HBB* gene, which codes for the hemoglobin component. This research paper investigates the distribution of SCD among Nigerians and Zimbabweans in Northern Cyprus. The study found that in Nigerians with a sample size of 50 males (50%), and 50 females (50%), about 51% of individuals had normal hemoglobin, 47% had AS, and 1% had carrier individuals, with the observed values for A and SS being 0.75% and 0.25%, respectively, indicating a lower prevalence of the disease. In contrast, the study analyzed 108 Zimbabwean students studying in Northern Cyprus, with a sample size of 56 males (52%), and 52 females (48%). Polymerase chain reaction genotyping revealed that 27% had SCD features. The A allele frequency was 0.87%, while the S allele frequency was 0.12%. The genotype distributions were calculated using the gene- counting method, in addition, the Hardy-Weinberg equilibrium was observed in the *HBB 20A>T* gene. As a result, Nigerians have a higher prevalence of SCD compared to Zimbabweans. The allele frequencies also differ slightly between the two populations in Northern Cyprus.

Keywords: HBB, sickle cell trait, sickling, sickle cell anemia, sickle cell

[OP-10]

5q35.2q35.3 Microduplication with Xp22.3 Microdeletion: A Rare "Reverse" Sotos Syndrome with A New Chromosomal Rearrangement

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Abstract

In the genetic approach to short stature and developmental delay, microarray testing plays an important role. Microduplication of 5q35.2q35.3 region is associated with commonly including short stature, microcephaly, delayed bone age, and mild developmental delay. A 10-year-old female patient with short stature is referred to our clinic by pediatric endocrinology. The patient was found to have short limbs during prenatal follow-up. Her height was 112.5 cm (<3p), weight was 20.7 kg (<3p), head circumference was 48 cm (<3p). Her physical examination revealed disproportionate short stature (rhizomelic shortness in the upper limbs), microcephaly, low weight, upslanting palpebral fissure, periorbital fullness, hypotelorism, prominent broad nasal tip, low hanging columella, thin upper lip, cubitus valgus and pectus excavatum deformity. She had surgery due to strabismus. Karyotype analysis from the patient's peripheral blood was found to be 46,XX. In microarray analysis, 1.8 Mb heterozygous duplication was detected in the 5q35.2-35.3 chromosome region including *NSD1* gene and 1.1 Mb heterozygous deletion was detected in the Xp22.31 chromosome region. Although the phenotype of our index patient is similar to the phenotype of previously published patients, some dysmorphic findings observed in our patient have not been previously reported in the literature. Fewer than 50 cases have been reported in the literature. To the best of our knowledge, this is the first case report of 5q35.2q35.3 microduplication and Xp22.3 microdeletion together seen. We also present the first 5q35.2q35.3 microduplication syndrome from Türkiye. For these reasons, it is thought that this case report will contribute to the literature.

Keywords: 5q35.2q35.3 microduplication, reverse Sotos syndrome, NSD1, aCGH

ORAL PRESENTATIONS

[OP-11]

Case Presentation: Dravet Syndrome Patient with SCN1A Homozygous Mutation, Which Has Been Rarely Reported Worldwide

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Introduction

Mutations affecting the alpha subunit of the *SCN1A* gene can cause various clinical pictures including simple febrile seizures, febrile seizures plus, Dravet syndrome, generalized tonic-clonic seizures, intractable childhood epilepsy and developmental and epileptic encephalopathy. The varying severity of mutations appears to correlate with the clinical spectrum of epileptic disorders. The SCN1A related phenotypes typically have autosomal dominant inheritance, usually occurring *de novo*. In this case report, we report one of the few cases with a homozygous disease-causing variant in SCN1A.

Case Report

A 3-year-old male patient with consanguineous parents had his first seizure as a myoclonic seizure after routine vaccination in the infantile period. His seizures, which started febrile and continued non-febrile, were attenuated with multiple antiepileptic treatments but could not be completely controlled. The patient was referred with a prediagnosis of Dravet syndrome. Molecular analysis revealed a homozygous missense likely pathogenic variant in exon 29 of SCN1A (NM_001165963 : c.5053G>A : p.(Ala1685Thr).

Conclusion

We present a patient with a homozygous mutation of the *SCN1A* gene and a clinical presentation of Dravet syndrome. There are very few reported cases with biallelic pathogenic variants in SCN1A. Our report helps enlighten the clinical course of Dravet syndrome with recessive inheritance.

Keywords: Dravet syndrome, SCN1A, recessive inheritance

[OP-12]

Identification of Novel Variants in *HPRT1* and *OTOG* Genes

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Introduction

The *HPRT1* gene, located on the X-chromosome at Xq26.3, produces a crucial enzyme, hypoxanthine-guanine phosphoribosyltransferase, essential for purine synthesis. HPRT1 disorders, stemming from enzyme deficiency, present with clinical symptoms such as elevated uric acid levels, kidney stones, and neurological and/or behavioral issues. Three distinct phenotypes have been identified: Lesch-Nyhan disease, HPRT1-related neurologic dysfunction, and HPRT1-related hyperuricemia, ranging from severe to mild. Hearing loss is one of the most common deficiencies of the neural-sensory system and has a significant impact on the quality of life. The *OTOG* gene encodes otogelin protein, a non-collagenous component of the acellular gelatinous structures that cover the sensory epithelia of the inner ear. Mutations in OTOG are known to cause DFNB18B (OMIM 614945).

Case Report

In this study, we present a case of a 17-year-old male patient with elevated uric acid levels and bilateral sensorineural hearing loss. He was referred from the pediatric nephrology rheumatology service service for evaluation of hearing loss, gut, and learning difficulties. Whole exome sequencing revealed a novel missense variant, c.431A>C p.(Gln144Pro), of uncertain significance in the *HPRT1* gene, and a frameshift likely pathogenic novel variant, c.1366_1369del p.(Tyr456Alafs*33), in the *OTOG* gene. These variants detected in the patient were evaluated as a compound phenotype. The identification of novel variants contributes to the variant spectrum.

Discussion: The detected variants were evaluated as a compound phenotype, and the identification of novel variants contributes to the variant spectrum.

Keywords: HPRT1, Lesch-Nyhan, OTOG, hearing loss

ORAL PRESENTATIONS

[OP-13]

Case Report: A Derivative Chromosome Involving a Large Duplication in Distal Arm of Chromosome 15

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Abstract

Duplications in the distal arm of chromosome 15 reported in the literature so far have been associated with prenatal and postnatal overgrowth, mental retardation, and craniofacial malformations. The prevalence and severity of symptoms and physical findings may vary from case to case depending on the length and location of the duplication of chromosome 15q. Here we report a 21-month-old male patient with dysmorphic facial features, craniosynostosis, undescended testis, and afebrile seizures. The patient had intrauterine restriction of movement, and developmental delay due to the history of SGA, secundum autism spectrum disorder, and electroencephalography abnormality. The prominent dysmorphic features were scaphocephaly, epicanthal folds, low-set ears, wide nasal root, thin upper and lower lip, high palate, and abnormal teeth. We performed a series of genetic tests including conventional karyotyping, fluorescence in situ hybridization (FISH), and array comparative genomic hybridization (CGH). The karyotype result of the patient was 46,XY, der(15)(qter-->q23: :pter-->qter). FISH analysis using probes designed for 15qter and 15q11.2 revealed an additional signal from the 15qter probe proximal to the 15q11.2 signal. Array CGH result of the proband was Arr[GRCh37] 15q23q26.3(68487617_102465355)x3, revealing a 34 mb copy number gain. Previous reports of cases with 15q duplications including the terminal region presented with some overlapping clinical features such as hypotonia and craniosynostosis and carried smaller duplications. On the other hand, our case harbors a previously unreported larger duplication and an interesting chromosomal rearrangement. Our study reports a unique case of a derivative chromosome 15 broadening the clinical and genetic spectrum of 15q terminal duplications.

Keywords: Duplication 15q, array CGH, FISH, derivative chromosome

[OP-14]

ATP8A2 Homozygous Deletion: A Novel Presentation in Cerebellar Ataxia and Intellectual Impairment Syndrome

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Abstract

Cerebellar ataxia, impaired intellectual development, and dysequilibrium syndrome denote a genetically heterogeneous rare disorder characterized by congenital cerebellar ataxia and impaired intellectual development. *ATP8A2* is one of the responsible genes for the disorder. Furthermore, some patients with biallelic *ATP8A2* pathogenic variants have a slightly different clinical presentation with intellectual disability, hypotonia, hyperkinetic movements, and optic atrophy. In this instance, a 40-year-old mother, presenting with hypotonia, referred her 2-year-old daughter, who was born at 39 weeks weighing 2,700 grams. The physical examination unveiled low weight percentiles, low height percentiles, low head circumference percentiles, bilateral strabismus, overlapping 4th toes, Mongolian spots on the back, high-arched palate, and a tented mouth. Neurological examination indicated absent deep tendon reflexes, no pathological reflexes, a negative Babinski sign, negative clonus, and no fasciculations. Subsequent analysis of copy number variations from Next-Generation Sequencing data delineated a suspected homozygous deletion in exons 2, 3, 4, and 5 of the *ATP8A2* gene. Primers were tailored for the 2nd and 4th exons, and polymerase chain reaction (PCR) and gel electrophoresis were executed on both healthy controls and the patient. For the proband's sample, gel electrophoresis revealed no PCR product for either exon, contrary to the control samples with normal PCR products, confirming the suspected deletion. Consequently, our patient emerges as the first documented case in the literature with ATP8A2 homozygous deletion, thereby broadening the mutational spectrum of ATP8A2- linked disorders.

Keywords: Homozygous deletion, dystonia, hypotonia

ORAL PRESENTATIONS

[OP-15]

A Case of Beta Thalassaemia Major with Joubert Syndrome

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Abstract

Beta-thalassemia is an autosomal recessive disease that occurs as a result of a disorder in the β-globin chains synthesis.Hemoglobinopathies such as beta thalassaemia are highly prevalent along a belt stretching from the Middle East to the Far East, especially in Mediterranean countries such as Italy, Greece, Cyprus and Türkiye. The severity of disease expression is mainly related to the degree of alpha-globin chain excess that precipitates in red blood cell precursors, causing both mechanical and oxidative damage (ineffective erythropoiesis). Homozygous cases progress to severe anaemia requiring regular blood transfusions. Joubert syndrome is a rare autosomal recessive neurological disorder characterised by neurological findings such as hypotonia, abnormal respiratory pattern and eye movements, ataxia and psychomotor developmental delay. A hypoplastic cerebellar pedicle and complete or partial absence of the vermis are basic radiological findings and the cause of fourth ventricle deformity. These findings cause "molar tooth signs" on magnetic resonance. First described by the paediatric neurologist Marie Joubert in 1969, the prevalence of this condition is estimated to be 1/80,000-1/100,000 live births. Awareness of the characteristic clinical and radiological findings of Joubert syndrome will facilitate early diagnosis, appropriate counselling and rehabilitation. A case of Joubert syndrome associated with beta thalassaemia is presented in people with epilepsy and mental retardation.

Keywords: Thalassemia, joubert, mental retardation

[OP-16]

A Blended Phenotype of AChromatopsia and Conjenital Myotonia with Germline Novel ATF6 and Rare CLCN1 Variant

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Abstract

ATF6 is an endoplasmic reticulum stress-regulated transmembrane transcription factor that activates transcription of endoplasmic reticulum molecules. Studies have shown that mutations in ATF6 are one of the rare causes of achromatopsia. *CLCN1* is a muscle chloride channel and regulates striated muscle cell membrane excitability. Defects in *CLCN1* cause disturbances in electrical activity and myotonia. A 4-year-old male patient was admitted to our clinic with complaints of nystagmus, photophobia and myotonia. Physical examination revealed frontal bossing, flattened nasal root, hypertelorism, retrognathia, photophobia and peripheral nystagmus. Electromyelography revealed myotonic discharges in the muscles and the patient's findings were consistent with myotonia. Clinical exome sequencing was performed. Clinical exome sequencing was performed. As a result of the analysis, homozygous probable pathogenic variant in exon 15 of *ATF6* gene and homozygous probable pathogenic variant in exon 12 of *CLCN1* gene were detected. The variant in the *ATF6* gene was associated with the patient's nystagmus and photophobia clinic and the variant in the *CLCN1* gene was associated with the patient's myotonia findings and led to a blend phenotype. To the best of our knowledge, the variant in the *ATF6* gene was considered novel because it has not been reported before. We hope that this case will contribute to the literature because it has a blended phenotype and novel variant.

Keywords: ATF6, nystagmus, myotonia, photophobia

ORAL PRESENTATIONS

[OP-17]

Analysis of Methylation of Individuals with a History of COVID-19

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Abstract

Introduction: The coronavirus disease-2019 (COVID-19) pandemic has led to a global health situation due to severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). This study provides clinical examination of methylations in COVID-19 patients infected with SARS-CoV-2.

Methods: Patients, survival and diseases, had chronic diseases, were divided into 4 groups, and N6-methyladenosine (m6A) pathway genes *METTL3*, *WTAP*, *FTO*, *ALKBH5* and *YTHDF2* gene expressions were measured by quantitative real-time polymerase chain reaction (RT-qPCR) method and global m6A methylation levels were evaluated with ELISA tests. Additionally, genes and intergroup details were evaluated.

Results: There are few studies in the literature on recorded *m6A* genes in patients infected with SARS-CoV-2 and showing chronic disease. There is a significant decrease in the *ALKBH5* gene between group 1a, b chronic, which contain mild protection at the level of gene expression. According to our findings, the *ALKBH5* gene stands out for its powers in growth in patients with mild COVID-19 and chronic disease. It is the common chronic pathogen DM and asthma virus that lives in group 1b. Especially in asthma patients, an improvement is achieved by the emergence of mRNA and protein of ALKBH5, and the growth is significantly reduced compared to the control group.

Conclusion: Findings show that with increasing disease changes, global m6A methylation increases and there are changes in *m6A* gene expressions. In conclusion, a complex relationship emerges between COVID-19 and m6A methylation and gene expressions. This study is an important step in supporting related mechanisms and disseminating therapy methods.

Keywords: COVID-19, SARS-CoV-2, M6A

[OP-18]

An Acute Myeloid Leukemia Case Transformed from Myelodysplastic Syndrome with Deletion of 6q and Monosomy 7 Cytogenetic Abnormality

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Abstract

Introduction: Myelodysplastic syndrome (MDS) is a clonal bone marrow neoplasm characterized by morphological dysplastic features in hematopoietic cells, peripheral cytopenias, ineffective hematopoiesis, recurring genetic abnormalities, and an increased risk of transformation to acute myeloid leukemia (AML). Detection of specific chromosomal abnormalities helps distinguish MDS from AML in some cases, assists in the classification of MDS, and is a major factor in determining prognostic risk groups and treatment decisions. Here, a 69-year-old female patient diagnosed with transformed acute myeloid leukemia from myelodysplastic syndrome is presented.

Methods: Bone marrow culture was studied for conventional karyotyping. Fluorescence in situ hybridization (FISH) was utilized to examine genomic abnormalities as outlined in the current guidelines for MDS, as well as to confirm the presence of 6q deletion and monosomy 7. Capillary electrophoresis-based fragment analysis method was used for FLT3-ITD mutation screening.

Results: The patient was referred to our clinic because of low platelet count level. In her bone marrow analyses revealed acute myeloid leukemia transferred from myelodysplastic syndrome diagnosis. Deletion of 6q and monosomy 7 was observed in her bone marrow. Analyzed cytogenetic findings were confirmed using the FISH method.

Conclusion: MDS is a highly heterogeneous disorder. The chromosomal abnormalities most commonly detected in MDS are generally also identified in AML cases. Deletions in the long arm of chromosome 6 (6q del) are a rare occurrence in MDS. To our knowledge, case reports regarding del (6q) in MDS are not commonly encountered, there are very few case reports worldwide.

Keywords: Acute myeloid leukemia, myelodysplastic syndrome, deletion 6q, monosomy 7, chromosomal abnormality

ORAL PRESENTATIONS

[OP-19]

In Vitro Investigation of the Role of Schizophrenia-Associated Potential miRNAs in the Regulation of *COMT* Gene

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Abstract

Introduction: There are potential miRNA-mRNA interactions associated with miRNAs and mRNAs related to schizophrenia. Therefore, our study aimed to biologically validate the association of miR-30a-5p, miR-30e-5p, and miR-34a-5p with the *Catechol-O-methyltransferase (COMT)* gene in the SH-SY5Y cell line for schizophrenia.

Methods: miR-30a-5p, miR-30e-5p and miR-34a-5p mimics were transfected into the SH-SY5Y cell line. Total RNA was isolated from transfected cells, followed by reverse transcription for miRNA and mRNA analysis. Changes in *COMT* gene expression levels were observed using RT-qPCR and western blotting. RNA immunoprecipitation was performed to determine RNA-protein interactions post miRNA mimic transfection.

Results: We observed that higher levels of miR-30a-5p and miR-34a-5p inhibited *COMT* gene expression at both mRNA and protein levels. Higher levels of miR-30e-5p led to an increase in *COMT* gene levels. Our data revealed an enrichment in *COMT* gene transcript post miR-30a-5p and miR-34a-5p transfection. To date, functional studies on the association of miR-30a-5p and miR-34a- 5p with the *COMT* gene have not been reported in the literature.

Conclusion: Following miR-30a-5p and miR-34a-5p mimic transfection, significant decreases in *COMT* gene expression levels were observed, while significant increases were noted post miR-30e-5p mimic transfection. RNA-IP data demonstrated an increase in *COMT* gene quantity post miR-30a-5p and miR-34a-5p mimic transfections, suggesting that these miRNAs directly target the *COMT* gene.

Keywords: Schizophrenia, miRNA, COMT

[OP-20]

Examining the Genotype of the ABO Blood Group System Using Next-Generation Sequencing

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Abstract

Introduction: The ABO blood group system, discovered by Landsteiner in 1901, stands as one of the most crucial blood group systems in transfusion medicine. The human *ABO* gene resides on chromosome 9 at locus 9q34.2, spanning 18 kilobases and consisting of 7 exons. The *ABO* gene encodes enzymes known as glycosyltransferases that produce A and B antigens. Within the ABO locus, three main alleles exist: A, B, and O. Following the sequencing and cloning of the *ABO* gene, variations in these alleles have also been identified, with the ABO blood group system holding particular significance in blood transfusion, forensic medicine, and disease relationships, routinely determined through serological methods. However, resolving certain issues like blood group incompatibility necessitates blood group genotyping.

Methods: We retrospectively analyzed 256 individuals who underwent next-gen sequencing of the *ABO* gene. Bioinformatics analysis of the *ABO* gene was performed using updated databases, *ABO* blood group allele types were determined and allele frequencies were calculated.

Results: In our study, all individuals evaluated demonstrated 100% concordance between serological and molecular blood group results. Among the 256 individuals, 98 (38.28%) were found to have the A blood group, 76 (29.69%) had the O blood group, 58 (22.66%) had the B blood group, and 24 (9.37%) had the AB blood group. We identified 22 alleles, including 4 alleles that are not currently present in the database, forming 56 genotype combinations.

Conclusion: This study is the first to evaluate the *ABO* genotype of the Turkish population using next-generation sequencing method.

Keywords: ABO, next-generation sequencing, allele frequency

ORAL PRESENTATIONS

[OP-21]

Prenatal Diagnosis of Fetal Ventriculomegaly Associated with a *De Novo* Partial Trisomy 13 and Terminal 1q Deletion

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Abstract

Introduction: Trisomy 13, also known as Patau syndrome, affects approximately 1 in 12,000 newborns and is characterized by midline facial defects, holoprosencephaly, and internal organ malformations, often resulting in high antenatal mortality. Early detection with first-trimester screening is possible. Previous studies suggested that partial duplications of 13q present with variable clinical features, with proximal segment duplications typically associated with more severe symptoms than distal ones. This case study aims to emphasize genotype-phenotype correlations in partial Trisomy 13.

Methods: Genomic DNA isolation performed directly from amnion tissue for quantitative fluorescence polymerase chain reaction (QF-PCR) analyses. Primary human amnion cell culture is studied for conventional karyotyping and SNP microarray. Metaphase fluorescence *in situ* hybridization (M-FISH) 13qter and 1qter used for confirmation of partial Trisomy 13. Conventional karyotyping is performed from peripheric blood leukocytes of parents to identify possible reciprocal translocations.

Results: QF-PCR analysis of chromosome 13 indicates grey zone for Trisomy 13. Conventional karyotyping of amnion cell culture identified additional chromosomal segment in terminal part of chromosome 1. Additionally, SNP-microarray identified 1q44 microdeletion and 13q31.3q34 duplication which explains derivative chromosome 1. M-FISH analysis showed three hybridization signals with 13qter locus. Parental karyotype analysis showed that this aberration occurred *de novo*.

Conclusion: Fetal ventriculomegaly and lemon sign were detected during ultrasound examination in a 29-year-old primigravida, at 22 weeks of pregnancy. First trimester screening tests indicated low risk pregnancy. Selective termination of pregnancy was performed upon parents' request. Compared with other studies, this case report will contribute knowledge about genotype-phenotype correlation in partial Trisomy 13.

[OP-22]

Investigation of Polycystic Kidney Disease by Molecular Methods

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Abstract

Introduction: Polycystic kidney disease (PKD) affects millions of people worldwide and is known as the most common cause of end- stage renal failure. In our study, we aimed to investigate mutations in *PKD1*, *PKD2* and *PKHD1* genes in patients with PKD using the next generation sequencing (NGS) method and to compare the phenotype-genotype relationship.

Methods: In the study, pedigrees of 31 patients were drawn, their inheritance types were determined, and clinical data and blood samples were collected. DNA isolated samples were analyzed on the NGS device after library preparation and target enrichment. Bioinformatics analysis was performed using databases. The phenotype-genotype relationship of the patients was evaluated.

Results: Variants detected were evaluated as: *PKD1* gene 3.53% pathogenic (P), 5.88% likely pathogenic (LP), 24.71% unknown clinical significance (VUS), 51.76% benign (B), 14.12% likely benign (LB); *PKD2* gene 20% P, 10% VUS, 50% B, 20% LB; *PKDH1* gene 1.79% LP, 30.36% VUS, 67.85% B. Ten variants detected in the *PKD1* gene and six variants detected in the *PKHD1* gene were evaluated as Novel. The variants detected in the genes, phenotype-genotype relationships were evaluated, were found to be compatible with the literature.

Conclusion: Our original results, obtained for the first time in Manisa province in the Aegean region, may contribute to future research focusing on diagnosis, prognosis and potential therapeutic interventions in PKD, and the variants considered as Novel will be included in the databases and may be a reference for researchers who will work on this subject.

Keywords: PKD1, PKD2, PKHD1

ORAL PRESENTATIONS

[OP-23]

The Importance of Further Examinations in Rare Cases

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Abstract

Growth is the most important indicator of a child's health. Short stature is a common clinical picture in children. However, in most children with short stature, a cause cannot be determined with routine screening. In this study, a case with a preliminary diagnosis of short stature and his family were examined. Chromosome, FISH and array-CGH analysis were performed on the peripheral blood sample taken from our case. After cell culture with peripheral blood, chromosome analysis, FISH analysis using SHOX Xp22.33 probe and array-CGH using Agilent CytoGenomics v5.3.0.14 program were performed. Chromosome and FISH analysis were performed on the entire family to examine familial segregation. In the patient's chromosome analysis, 46,X,der(X)(pter?)[50], *SHOX* gene deletion in the FISH analysis, and heterozygous deletion in the Xp22.33 in array-CGH analysis. In this regard, while the same deletion was detected in the mother and daughter whose family segregation was examined, it was not detected in the father and brother. In our case, chromosome analysis initially revealed a suspicion of a break in the X chromosome. After further examination, it was determined that there was a deletion in the Xp22.33 region and the same result was seen in all women of the family, but not in the men. This study shows that laboratory tests alone are not sufficient and that one should not jump to conclusions based on initial tests, and contributes to the literature by emphasizing the importance of conducting further tests by carefully examining clinical findings.

Keywords: Short stature, chromosome analysis, further examination

[OP-24]

A Rare Chromosome Anomaly, Isodicentric Chromosome 15: Case Report

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Abstract

It is known that eighty percent of marker chromosomes originate from acrocentric chromosomes. In particular, the 15th chromosome was found to be the chromosome that forms the most marker chromosomes, with a share of fifty percent. Isodicentric chromosome 15 [idic(15)], also known as marker chromosome 15 syndrome, is found at a rate of 1 in 30000. It is a rare chromosomal anomaly syndrome that causes epilepsy, psychomotor developmental delay, autism and hypotonia. In this report, we present a two-year-old girl with treatment-resistant tonic-clonic seizures, psychomotor developmental delay, autistic findings, and obesity. As a result of the patient's examination, karyotype analysis and Prader-Willi FISH (15q11-13) tests for chromosome 15 were requested. In the patient whose marker chromosome was detected in the karyotype analysis, four centromere signals belonging to the 15th chromosome were seen in the Prader-Willi FISH (15q11-13) analysis. The patient's family members were evaluated for idic(15). No chromosomal anomaly was detected in his mother, father, sister or brother. It was thought that the marker chromosome in the patient might be related to advanced maternal age (age of birth was forty-four years old). The 15th chromosome duplication was confirmed with the array CGH study. We present the clinical findings of idic(15) through this case, along with a literature review.