milestones. She had microcephaly, hypoplastic labia minora, mild facial dysmorphism comprising bitemporal narrowing, strabismus, prognathism(mild), prominent nasal root(mild), smooth philtrum and low-set ears. The family had undergone genetic counseling but deferred molecular testing at that moment. At 22 months, she presented immunodeficiency, complicated with recurrent infections/intractable diarrhea and anemia. Physical examination showed oral leukoplakia, thin/sparse hair, lacy reticular hyperpigmentation on left axillary region and right hemithorax; cranial MRI showed cerebellar hypoplasia. WES revealed a homozygous missense variant in the reverse transcriptase domain of the *TERT* gene. Short relative telomere length(TL), measured by flow-FISH, was compatible with infancy-onset short telomere syndrome. Detailed pedigree analysis showed no clinical evidence of DC except premature hair graying, anemia and cancer in blood relatives across three generations. Identification of heterozygous *TERT* mutation and short TL in extended family members, segregating with the phenotype, highlighted disease anticipation and further confirmed the diagnosis of DC. Our findings expand the genotype-phenotype correlation of DC; thus underline the importance of integrating clinical information, molecular data and TL to facilitate the recognition of the etiopathogenesis of telomere syndromes.

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P11.046.D Detection of 3p25 microdeletion syndrome in the Macedonian patient with significant psychomotor retardation

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Introduction: The array Comparative Genomic Hybridization (aCGH) is a first tier diagnostic tool for detection of submicroscopic genomic changes and pathogenic copy number variants (CNVs) in the patients with pathological conditions and wideranging phenotypes.

Materials and Methods: aCGH was performed in a 7.5-year-old female Macedonian patient with clinical signs of dysmorphia and significant developmental delay using the Affymetrix® CytoScan™ 750K Array (Applied Biosystems), that comprises 550 k non-polymorphic and 200 k SNP markers. The data was analysed using Chromosome Analysis Suite (ChAS) Software (v4.0).

Results: The child was referred for further evaluation on 8th postnatal day because of dysmorphic features. She was born small for gestational age, after 39 weeks of gestation with a birth weight of 2340g and birth length of 45cm. Hypertelorism and antimongoloid eye slant, micrognathism, webbed neck, pyelonidal cyst and preaxial polydactily both on the left foot and right hand were noticed. During the follow up the child had several hospitalizations because of failure to thrive requiring a tube feeding, anemia and significant psychomotor retardation. The karyotype was normal (46,XX). aCGH analysis showed deletion of 3,243 segment on 3p25.3 chromosome (30 OMIM genes) classified as pathogenic according to aDGV, ClinVar and OMIM databases. The genes, SETD5, SLC6A1 and SLC6A11, have been proposed as the main candidates that when deleted contribute to the key features associated with 3p25 deletion syndrome.

Conclusions: The aCGH analysis as a widely accepted tool that supplements conventional karyotyping allowed genetic diagnosis of our patient with significant psychomotor retardation.

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P11.047.A Evaluation of the diagnostic rate in children with dysmorphic features - one genetic center experience

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Introduction: Dysmorphic features/multiple congenital anomalies in children are common indication for genetic counseling. In some patients the cause is a recognizable syndrome, but in most cases the initial diagnosis is unclear, the process is time-consuming and difficult. Moreover, the condition often cannot be confirmed etiologically. The aim of the study is to summarize our experience in establishing the diagnoses in dysmorphic children.

Materials and methods: The study includes 706 pediatric patients (0-18 years), referred to the Genetics Unit of the University Hospital Saint Marina, Varna for a period of five years (2015-2019). Clinical phenotyping, imaging examinations, appropriate genetic and metabolic investigations were offered to children with dysmorphic features/ multiple congenital anomalies. Specialized computer programs/dysmorphology databases were applied.

Results: 336 out of 706 (47.5%) consulted children (mean age 3.9 years) with multiple congenital anomalies with or without developmental delay were suspected of malformative/dysmorphic syndrome. Karyotyping, molecular genetic or metabolic tests were performed in 306 (92%) children (≥ 2 genetic tests were appropriately applied to 104 patients). Based on these analyses, 121(36%) children were genetically diagnosed: 70 patients (25%) with chromosomal pathology, 32 (9.5%) with single-gene pathology and 19 (5.6%) with microdeletion/microduplication disorder. Other 41(12%) children were clinically diagnosed based on specific phenotype.

Conclusion: The role of the medical geneticist in achieving an accurate diagnosis among children with dysmorphic features is essential. Once confirmed, it could affect the disease management, as well as provide more personalized approach and contribute families with proper evaluation of the recurrence risk.

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P11.048.B A new heterozygous c.730T>A, p.(Cys244Ser) variant in *TP63* associated with severe hydronephrosis and volar nails

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Introduction: *TP63*-related pathologies are a group of autosomal dominant phenotypes with variable features of ectodermal dysplasia, distal limb malformations/dysplasia and lip/palate clefts. These can occur as distinct syndromes (AEC, ADULT, EEC3, LMS) or has isolated malformations (split-hand/foot malformation and

CERTIFICATE OF ATTENDANCE

This is to certify that

Violeta Anastasovska

ESHG

has participated in the

European Human Genetics Virtual Conference 2021

taking place on August 28-31, 2021

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