ABSTRACTS COLLECTION

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e-Posters

EP01 Reproductive Genetics

EP01.001 Correlations between cytogenetic findings and spermatogenic failure in Bulgarian infertile men

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Background/Objectives: Chromosomal aberrations have a great impact on spermatogenesis, semen quality, and successful conception. The objective of our study was to determine the type and frequency of chromosomal aberrations and polymorphisms in men with different degrees of spermatogenic failure in comparison to men with normozoospermia, in order to find some correlations between cytogenetic findings and the abnormal results of semen analysis.

Methods: In our study, we have performed cytogenetic analysis in 901 infertile men, divided into 5 groups according to semen analysis—normozoospermia, asthenozoospermia, oligoasthenozoospermia, severe male factor and azoospermia.

Results: The frequency of polymorphisms was similar in all groups (11–16%, without significant differences). The frequency of numerical and structural aberrations increases with the degree of the spermatogenic failure (3.5% in normozoospermia, 5.6% in asthenozoospermia, 9.8% in oligoasthenozoospermia, 9% in severe male factor and 13.5% in azoospermia). We have found significantly higher incidence of numerical chromosome aberrations in severe male factor (7%) and azoospermia (9.3%). Oligoasthenozoospermia was associated with chromosomal translocations, as it occurs in 45% of cases with translocation, compared to 20% in the group with normal karyotype.

Conclusion: We revealed that chromosomal translocations are significantly associated with oligoasthenozoospermia, whereas numerical chromosomal aberrations—with severe male factor and azoospermia. These are important aspects of genetic counseling for those cytogenetic findings. Chromosome polymorphisms don't seem to disturb significantly spermatogenesis and their impact should be studied in regard to unsuccessful pregnancy achievement, even in patients with normozoospermia.

References:

Grants:

Conflict of Interest: None declared.

EP01.002 Comparison of carrier status among patients with or without family history of disease using targeted and expanded panels

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EP12.072 Targeted next-generation sequencing in Bulgarian patients with RASopathies

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Background/Objectives: RASopathies are a clinically defined group of medical genetic syndromes with overlapping phenotypic features caused by germline mutations in genes that encode components or regulators of the Ras/mitogen-activated protein kinase pathway. These disorders include neurofibromatosis type 1 (NF1), Noonan, Leopard, capillary malformation-arteriovenous malformation, Costello, cardio-facio-cutaneous, and Legius syndromes. Therefore, molecular diagnosis is important for genetic counseling and treatment. The aim of the present study was to identify the genetic diagnosis in a group of Bulgarian patients affected by different types of RASopathies.

Methods: In a selected group of 18 patients diagnosed with different forms of RASopathies, we performed targeted sequencing of clinical exome (including 4813 OMIM genes) on MiSeq platform of Illumina. A detailed analysis, followed by Sanger sequencing and segregation analysis when possible, was used to identify pathogenic variants.

Results: Disease-causing mutations were identified in 10 out of 18 patients (55.55%). We found one pathogenic and two variants of unknown significance (VUS) in *NF1* in 3 out of 7 patients with differential diagnosis NF1. Pathogenic variants in the genes *BRAF*, *RAF1* (in two patients), *SOS1* and *PTPN11*, were found in 5/6 patients with suspected Noonan syndrome. In the remaining 4 patients with malformation syndrome but not clinically diagnosed we found pathogenic variants affecting the genes *NF1*, *BRAF* and *PTPN11* and VUS in *KRAS*.

Conclusion: Targeted sequencing of clinical exome allowed detection of disease-causing mutations in over 55% of our cases, a percentage which exceeds previously reported diagnostic yield of 19-36%.

References: none.

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Conflict of Interest: None declared.

EP12.075 Detection rate of 22q11.2 microdeletion using strict diagnostic criteria

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Background/Objectives: 22q11.2 microdeletion, detected in patients with 22q11.2 Deletion Syndrome (22q11.2DS), is the most common microdeletion syndrome in humans. 22q11.2DS has high risk for neurodevelopmental disorders and is associated with more than 180 malformations. Many investigations of the 22q11.2 microdeletion applying different recruitment criteria, revealed detection rate ranging from zero to 34.7%. Here we analyzed the frequency of 22q11.2 microdeletion among children having at least two out of five major characteristics of 22q11.2DS: congenital heart malformations (CHM), facial dysmorphism, immunological problems, palatal clefts and hypocalcemia.

Methods: Children with clinical characteristics of 22q11.2DS were analyzed. Fluorescence in situ hybridization and multiplex ligation-dependent probe amplification analysis were applied for detection of 22q11.2 microdeletion.

Results: 22q11.2 microdeletion was detected in approximately 40% of children. CHM was found in all patients with 22q11.2 microdeletion. Dysmorphic facial features were present in about 45%, immunological problems in 30%, overt cleft palate in about 4% and hypocalcemia in approximately 60% of patients with 22q11.2 microdeletion.

Conclusion: When at least two major features of 22q11.2DS are taking into consideration higher detection rate is obtained compared to one-feature criterion. These criteria could be considered by centers in low-income countries.

References: /.

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Conflict of Interest: None declared.

EP12.076 Early-onset atypical rare disorders: Precision genetic diagnosis aided phenotypic expansion to the rescue!

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Background/Objectives: Rare diseases frequently present with overlapping clinical features and ambiguous genetic findings can affect accurate diagnosis and thereby the clinical management. Here we report two paediatric cases who presented with failure to thrive in addition to other discernible indications. The first child is a two-year-old girl with a hypopigmented skin patch, chronic napkin rash, grey hair, hepatomegaly, liver failure, and coagulopathy. The second child is a six-month-old girl with hypotonia, recurrent fever, seizures, normal brain MRI, and developmental delay.

Methods: Whole-exome sequencing (WES) analysis was done for the index patients using Illumina platform at Igenomix laboratory, Dubai.

Results: WES revealed a homozygous pathogenic variant in the *CFTR* gene [NM_000492.4:c.580-1G>T; p.(?)] in the 2-year-old child; and a novel homozygous pathogenic variant in the *NTRK1* gene [NM_001012331.2:c.1624delG; p.(Glu542fs)] in the infant. Bi-allelic pathogenic *CFTR* and *NTRK1* gene variations cause cystic fibrosis and congenital insensitivity to pain with anhidrosis (CIPA), respectively.

Conclusion: Hair depigmentation and dermatitis are very rare presentations of cystic fibrosis in early childhood and a retrospective chloride sweat test confirmed that the initial clinical features observed in the first patient fits the atypical presentation of cystic fibrosis.

In the infant, a retrospective phenotypic evaluation revealed loss of pain sensation which confirmed the diagnosis of NTRK1-