Presented review of literature data (medline, eLIBRARY.RU, PabMed) identifies typical problems of parents whose children were born with cleft lip and palate (RGN), as well as research directions in improving the organization of medical care for parents and patients with UAH in solving these problems. Analysis of domestic and foreign authors on MEDLINE databases, eLIBRARY.RU, PabMed Still lacks research on the experiences of parents with RSN, what typical problems they encountered in the maternity hospital and, especially, at home. It is now necessary to carry out research that has traditionally been rely not only on psychological approaches, but also on broader prospects for research in the field sociology, social policy, nursing and health care using both qualitative and quantitative methods. In addition, there is a lack of research in the field of cleft lip and palate to study the experience and needs of parents at different stages of their children's lives.

93 WILLIAMS-BEUREN SYNDROME: A CASE REPORTS

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Introduction Williams-Beuren syndrome (WBS) is developmental disorder caused by microdeletion of genes from chromosome 7. It is estimated in 1 of 10 000 people. WBS could be autosomal-dominant inherited, but usually, it is caused by de novo microdeletion of 26-28 genes on chromosome 7. Usually genes such as CLIP2, NCF1, ELN, GTF2I, GTF2IRD1 and LIMK1 are deleted. ELN gene is detected as a cause of supra-valvular aortic stenosis, while absence of NCF1 gene is related to hypertension. Patients with WBS are characterized by cardiovascular diseases, facial dysmorphic features, intellectual disability, unique personality character and endocrine abnormalities.

Case Report We present the case of three patients, two girls at the ages of one and three years and a boy at the age of two years. All three patients have healthy parents and brothers and sisters without known chronic or genetic diseases. All three were presented with facial dysmorphic features which include broad nasal bridge, microretrognathia, large mouth, upper lip is thin while lower lip is thicker. All three patients are cognitively deficient and they have speech problems. The female patient at the age of three years also has hypertension, small teeth, larger neurocranium, atrial and ventricular (muscular) septal defect, gastroesophageal reflux disease (GERD), hypothyroidism and endocrine disorders; hypercalcemia, hypercalciuria, hypothyroidism and early puberty. The male patient also has prominent ears, palmar crease on left palm, pulmonary stenosis with mitral regurgitation and bilateral inguinal hernia. All three patients were suggestive for WBS.

Karyograms of all patients were normal, but FISH analysis performed with ELN primer for detection of WBS proved microdeletion on chromosome 7 in region 11 (7q11).

Conclusion WBS is rare disorder characterised by wide range of symptoms and signs.

Clinical diagnostic criteria are available for WBS, but confirmation of diagnosis requires detection of microdeletion on chromosome 7q11.2. Early recognition of specific patterns of the disorder, such as facial dysmorphic features together with

heart abnormalities, cognitive deficiency and vision problems, is crucial because those patients need to take speech therapist and psychologist therapy as soon as possible because it improves their integration in social environment. Management is focused on treatment of symptoms (eg. hypertension, hypercalcemia), psychological and psychiatric evaluation and speech therapy.

94 CLINICAL AND GENETIC SPECTRUM OF DYSTROGLYCANOPATHY DUE TO POMGNT1 MUTATIONS IN RUSSIAN PATIENTS

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Dystroglycanopathies are the heterogeneous group of hereditary disorders, caused by the abnormal glycosylation of α -dystroglycan. The most common dystroglycanopathy is muscle-eye-brain disease (MEB) associated with mutations in the POMGNT1 gene. MEB is autosomal recessive disease characterized by congenital muscular dystrophy, ocular abnormalities and brain malformation. The goal of the study is an analysis of clinical findings, laboratory features and results of instrumental researches.

Molecular genetic diagnostics was performed using full exome sequencing. All patients and all parents were confirmed by Sanger sequencing.

We observed 3 boys with MEB disease aged from 25 to 118 months, averaging about 7 years (83 months). The one patient had exceed average values of height and weight at birth, two the other children had normal ranges. All children had severe motor development delay, only one patient could walked without support. Two older patients had mental retardation and lack of speech development. Language skills represented as vocalizations. Physical growth of our patients fluctuated from 3 to 75 percentiles for height and weight. The other clinical features include hypotonia and strabismus (all patients), autistic behavior (2 patients), ataxia, seizures, hepatomegaly (one in each patient). Dysmorphic features were non-specific.

Ophthalmological examination revealed congenital high myopia (2 patients), partial atrophy of an optic nerve (2 patient), nystagmus (1 patient), astigmatism (1 patient), retinal atrophy (1 patient).

Biochemical analysis showed elevated creatine kinase from 1874 to 6266 (averaging 3754 U/L), ALT from 42 to 93(68 U/L), AST from 53 to 106 (80 U/L), LDH from 370 to 503 (437 U/L).

Electromyographic examination has showed that all children had signs of primary muscle lesion. Muscle MRI has displayed a severe atrophy muscles and fatty infiltration in one patient. MRI findings have reported pachygyria and ventriculomegaly (all patients), hypoplasia cerebellum, corpus callosum, pons (2 patients), hypoplasia of temporal lobes (1 patients), cerebellum cysts (2 patients). EEG did not reveal epileptic form activity.

We revealed compound heterozygous mutations in all three patients. These were five different mutations: missense c.385C>T (p.R129W) and c.1325G>A (p.R442H), nonsense

c.643C>T (p.R215X), splicing c.1539+1G>A and frameshift duplication c.453_456dup (p.S153Vfs*5). The last one was not previously described in the HGMD database.

Clinical and genetic features were described in Russian patients with dystroglycanopathy due to POMGNT1 mutations.

95 CDHR1 AND RGR MUTATIONS IN TWO PATIENTS WITH RETINITIS PIGMENTOSA

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Retinitis pigmentosa (RP) is a group of inherited retinal disorders characterized by progressive photoreceptors and pigment epithelial cells dysfunction. Patients initially present with nyctalopia from rod photoreceptor loss, progress to tunnel vision and ultimately experience central vision loss. In majority of cases (70-80%) RP is nonsyndromic and may be inherited in an autosomal dominant, autosomal recessive and X-linked recessive manner. The most frequent forms of syndromic RP are Usher and Bardet-Biedl syndrome. It is estimated that RP affects 1 in 3,000 to 1 in 5,000 people worldwide and so far mutations in more than 300 genes have been associated with development of this disorder.

We present two patients with referral diagnosis of RP in whom we performed molecular analysis of clinically relevant genes using NGS. In both patients we detected mutations in CDHR1 and RGR genes. First patient is a 36-year old female homozygous for the p.Ile841Serfs119 mutation in CDHR1. Variations in this gene can cause autosomal recessive retinopathy with clinical manifestations ranging from RP to cone-rod dystrophies. This patient is also homozygous for p.Ser66Arg mutation in RGR gene that can cause autosomal recessive/dominant RP type 14. Second patient is a 39-year old male with two heterozygous mutations: p.Ile841Serfs119 and p.His206Thrfs61 in CDHR1 gene.

This patient is also heterozygous for p.Ser66Arg mutation in RGR gene. Arno et al. have previously described 6 unrelated families in whom homozygous mutations p.Ile841Serfs119 in CDHR1 and p.Ser66Arg in RGR genes were detected. Four of these families were of Albanian origin as is our female patient.

Our findings confirm the hypothesis of Arno et al. that homozygous and compound heterozygous mutations in the CDHR1 gene may co-segregate with mutations in the RGR gene that are likely to have a modifying effect on the phenotype. This constellation is common in the Albanian population indicating a founder effect.

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96 HOMOZYGOUS ABCG8 MUTATION IN A 14-YEAR-OLD BOY WITH SITOSTEROLEMIA

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Introduction Sitosterolemia is a rare, inherited, autosomal recessive lipid disorder characterized by the accumulation of plant sterols and cholesterol in plasma and tissues as a consequence of hyperabsorption and impaired biliary secretion of sitosterol. It is caused by mutations in ABCG5 and/or ABCG8 genes that encode a pair of ABC half transporters and form a heterodimer (ABCG5/G8), which then traffics to the surface of hepatocytes and enterocytes and promotes the secretion of sitosterol into the bile and the intestinal lumen. Here we report on a 14-year-old boy with hypercholesterolemia, failure to thrive and short stature.

Methods Patient was referred to use due to suspicion of familial hypercholesterolemia (FH). His father has hypercholesterolemia and arterial hypertension, grandfather on father's side also has arterial hypertension and his mother and grandmother on mother's side have thrombocytopenia. One of his two younger brothers has unilateral perceptual hearing loss, hypercholesterolemia, thrombocytopenia and short stature. NGS analysis of clinical exome (CES, Clinical Exome Sequencing) was performed using peripheral blood DNA obtained from patient and his parents. CES analysis in affected brother is ongoing.

Results CES revealed homozygous missense mutation ABCG8: c.584T>A, p.(Leu195Gln) in patient. His parents are heterozygous carriers of the same mutation. According to ACMG/AMP classification and publications data this variant is classified as likely pathogenic.

Discussion and Conclusion Leucine at codon 195 is highly conserved among all five human ABCG transporters. This mutation is localized within the nucleotide-binding domain (NBD) that powers the transport of substrates by binding and hydrolyzing ATP molecules. Phenotypically, sitosterolemia is very heterogeneous. It includes hypercholesterolemia, accelerated atherosclerosis, premature coronary artery disease, xanthomas, hemolytic anemia, stomatocytes, macrothrombocytopenia, arthralgia, splenomegaly and elevated liver function test. Because of this it is considered extremely underdiagnosed with over 100 cases reported so far. According to rough estimations the frequency could be at least 1 in 200,000 individuals. It is also considered a recessive disorder, but recent studies have revealed that heterozygous carriers also exhibit milder manifestations as seen in this patient's parents. Sitosterolemia is also often misdiagnosed as FH and mistreated with statins that are partially or completely ineffective. In conclusion, sitosterolemia should be considered in children with hyperlipidemia, especially with a significant hypercholesterolemia and increased low-density lipoprotein levels.

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