performance on the Multi-Luminance Mobility Test (MLMT) at 7 standard light levels as measured by a change in score. Additional endpoints were full-field light sensitivity threshold (FST) testing, visual acuity (VA), and Goldmann kinetic VF (GVF), each averaged over both eyes. Safety outcomes included adverse event reporting, laboratory testing, and changes in physical and ophthalmic examinations.

Results For OI patients at Year 5 (n=18) and DI patients at Year 4 (n=8), the mean (standard deviation) MLMT bilateral light level score change was 1.6 (1.1) and 2.4 (1.5) levels, respectively, compared with baseline. Subsequent to the 1-year outcomes, a change of 1 light level occurred in 6 patients (none were below pre-treatment performance) and no change in the remaining 20 (N=26). Mean change in white light FST in log10 (cd.s/m²) averaged over both eyes was -2.02 (1.45) log10 at Year 5 for OI patients (n=17) and -2.58 (1.04) log10 at Year 4 for DI patients (n=8). Mean change in VA (Holladay Scale) averaged over both eyes (logMAR was -0.00 (0.64) at Year 5 for OI patients (n=18) and -0.06 (0.26) at Year 4 for DI patients (n=8). Mean change in GVF III4e sum total degrees averaged over both eyes was 166.6 (208.7) at Year 5 for OI patients (n=15) and 178.8 (241.9) at Year 4 for DI patients (n=8). Five years after treatment, the safety profile (N=29) was consistent with vitrectomy and subretinal injection procedure with 2 reports of cataract, 1 of ptosis, and 1 new report of retinal detachment since the last update. No deleterious immune responses were reported.

Conclusion Improvements in ambulatory navigation, light sensitivity, and VF are maintained for at least 5 years after VN administration in most OI patients.

Improvements in DI patients were consistent with those observed in OI patients. The safety profile of VN is consistent with the administration procedure.

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THE FIRST CLINICAL CASE OF RARE FORM OF FOCAL EPILEPSY CAUSED BY THE NOVEL MUTATION IN THE NPRL3 GENE IN RUSSIAN FEDERATION AND KAZAKHSTAN

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Objective Mutations in the NPRL3 gene (OMIM 600928) are described predominantly in patients with autosomal dominant focal epilepsy according to the HGMD database.

Methods We want to introduce the clinical case of the female patient, 2 years old, with focal epilepsy from healthy parents. She was born full-term from the 1st pregnancy by caesarian delivery. The cerebellum hypoplasia was suspected during ultrasound and MRI diagnostic at 17th week of gestation.

Weight at birth - 3.780 kg, 7/8 on Apgar scale. Neurosonography at birth has shown left-sided ventriculomegaly. First recurrent afebrile tonic extensor epileptic spasms with head and eyes turns to the left side were noted at the age of 2 months. Eyelid and tongue myoclonias were revealed as well. Later the frequency of seizures has increased to 150 per day. The video electroencephalogram (VEEG) showed sharp, spike waves with partial origin at left temporal region, while clonic seizures in the left arm were recorded. The brain MRI has shown focal cortical dysplasia in the left insular region. Signs

of intellectual impairment and behavioural disturbances were revealed during the neurological examination at the age of

24 months. The patient could not walk without support. We have performed full exome sequencing for our patient to identify the molecular genetic causes of the disease after medical genetic counseling.

Results The nucleotide variant c.481C>T which leads to stop codon p.Q161* in heterozygous state was revealed in exon 5 of the NPRL3 gene. This variant was not described in gnomAD and HGMD databases and was considered as pathogenic according to ACMG criteria. An interesting fact is that the most frequent pathogenic variants in the NPRL3 gene (among the 21 described variants in the HGMD) are nonsense mutations and frameshift deletions.

Conclusion This paper describes the first clinical case of rare form of focal epilepsy caused by the novel mutation in the NPRL3 gene in Russian Federation and Kazakhstan.

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FABRY'S DISEASE WITH MINIMAL MANIFESTATIONS IN GIRLS (CLINICAL CASES)

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Fabry disease (Anderson-Fabry disease) is a rare inherited lysosomal multisystem disease with X-linked inheritance due to the deficiency of lysosomal enzyme α -galactosidase A and leads to accumulation of sphingolipids (globoside, globotriaosylceramide) in the walls of blood vessels in all organs.

Clinical cases of low-symptomatic Fabry's disease in 2 girls (9 and 10 y.o.) with positive family history of the underlying disease are described.

Girl 9 y.o. is granddaughter and girl 10 y.o. is daughter of a male patient with Fabry's disease. Girls had complaints of reduced sweating and febrile acroparasthesia only.

Physical and sexual development according to age, the skin was clean.

Echocardiography, abdominal USE, pulmonary function test, cornea and fundus, ear, nose and throat examination were normal. Urine examination showed 1+ proteinuria both girls have. Glomerular filtration rates were normal. The lyso-Gb3 and galactosidase A levels analyzed in dried blood spots (DBS) by tandem mass spectrometry and molecular genetic analysis was performed. An increase lyso-Gb3 concentration and a change in the nucleotide sequence c.983G>C, leading to the replacement of p.G328A, described in the international database on HGMD mutations (CM 930337) in the hemizygous state has been identified.

Conclusion These cases confirm that it is very important that the pediatricians become aware of the importance of genealogical anamnesis findings and Clinical features of Fabry's disease, so they can participate in the identification of unrecognized patients.

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TYPICAL PROBLEMS OF PARENTS OF CHILDREN WITH CLEFT LIP AND PALATE

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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