The first clinical case of rare form of focal epilepsy caused by the novel mutation in the *NPRL3* gene in Russian federation and Kazakhstan

Kirill Savostyanov, Alisa Nauryzbayeva, Oksana Globa, Alexander Pushkov, Lyudmila Kuzenkova, Olga Kondakova, Alexander Pakhomov, Lyubov Muraveva, Andrey Fisenko, Altynshash Jaxybayeva

National Medical Research Center for Children's Health Federal state autonomous institution of the Russian Federation Ministry of Health, Moscow, Russian Federation

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 myoclonus 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 behavioral 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.