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## A NEW PATHOGENIC VARIANT OF THE NUCLEOTIDE SEQUENCE AS A RISK FACTOR FOR THE DEVELOPMENT OF EPILEPSY AND MENTAL RETARDATION

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## НОВЫЙ ПАТОГЕННЫЙ ВАРИАНТ НУКЛЕОТИДНОЙ ПОСЛЕДОВАТЕЛЬНОСТИ КАК ФАКТОР РИСКА РАЗВИТИЯ ЭПИЛЕПСИИ И УМСТВЕННОЙ ОТСТАЛОСТИ

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Mental retardation is a state of retarded or impaired cognitive development that is characterized by impaired abilities that appear during maturation and provide an overall level of intelligence. Mental retardation is often combined with symptomatic epilepsy. The etiology of these pathological conditions is often unclear. The case of mental retardation and convulsive syndrome in a 7-year-old girl with a previously unspecified pathogenic variant of the nucleotide sequence that was the cause of these pathologies is described.

*Keywords: mental retardation, epilepsy, nucleotide sequence, molecular genetic study*

Умственная отсталость представляет собой состояние задержанного или неполного развития психики, которое характеризуется нарушением способностей, проявляющихся в период созревания и обеспечивающих общий уровень интеллектуальности. Умственная отсталость часто сочетается с симптоматической эпилепсией. Этиология данных патологических состояний зачастую остается невыясненной. Приводится описание случая умственной отсталости и судорожного синдрома у девочки 7 лет, с не описанным ранее патогенным вариантом нуклеотидной последовательности, который явился причиной данных патологий.

*Ключевые слова: умственная отсталость, эпилепсия, нуклеотидная последовательность, молекулярно-генетическое исследование*

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**M**ental retardation and unspecified epilepsy are conditions whose causes often remain unclear, their treatment is not always effective, and the result is a disability. According to the World Health Organization, the prevalence of mental retardation ranges from 1 to 3 % [1]. Among men, mental retardation is about 1.5 times more common than among women. This ratio is most pronounced with moderate mental retardation. With a high degree of mental disability, there is no difference between boys and girls. In the Russian Federation, the proportion of mentally retarded among the population is 0.6 % [2]. Despite advances in neuroimaging using computed tomography and magnetic resonance imaging, biochemical and genetic testing, a large number of epilepsy forms fall under the rubric «undetermined cause» (in the

old terminology of «cryptogenic epilepsy»). The percentage of unidentified etiology ranges from 20 % to 64 % of all cases. According to a clinical and epidemiological study in the Russian Federation, localized epilepsy of unknown etiology in adults and children was observed in about 34 % of cases [3]. We present a clinical example that demonstrates the difficulties of diagnosing the causes of mental retardation and convulsive syndrome, as well as the results of molecular genetic research explaining the genesis of the disease.

The purpose of the study was to clarify the genesis of early mental disability and convulsive syndrome in a child.

**Clinical case.** In February 2021, a 7-year-old girl was hospitalized at the Republican Children's Clinical Hospital with complaints of generalized tonic-clonic seizures

with loss of consciousness, foaming at the mouth, jaw clenching, turning her head to the side, and fixing her gaze upward, lasting about 3–4 minutes. Convulsions were stopped independently. At the end of the attack, sometimes vomiting, involuntary urination, followed by sleep lasting about half an hour. According to the mother, seizures are noted 3–4 times a month. In addition, complaints about attention instability, low level of perception, and primitive vocabulary. The girl is irritable, whiny, and hyperdynamic.

It is known from the anamnesis of life that the child is from the third pregnancy, the second birth. The first pregnancy was a miscarriage in the 8th week. The second pregnancy ended with a physiological birth in 2011. The girl is healthy. Pregnancy with this child was physiological. The baby was born at the 38th week of gestation on 06.02.2014. The girl was born without asphyxia, weighing 2750 g, height – 48 cm. She was breastfeeding for the first time on the second day of life. The family history of neurological diseases is negative.

**Anamnesis of the disease.** Seizures were first noted at six months of age. Anticonvulsant therapy was prescribed, which did not stop (valproic acid, levetiracetam, topiramate, lamotrigine, and oxcarbazepine).

**Psychomotor development:** keeps the head upright from 4 months, turns over from the stomach to the back from 6 months, sits from 8 months, walks from one and a half years, the first words – at one and a half years. Simple phrases and sentences from the age of 4. Attends a preschool correctional group. Statistical data: height – 110 cm, weight – 19 kg. ANTROplus Developmental Scale: height inappropriate for age (WAZ – 1.12; HAZ – 2.01; BAZ – 0.17).

**Somatic status.** There were no changes from the respiratory, cardiovascular, urinary system and digestive organs.

**Neurological status.** No signs of the brain were found during the examination. Higher cortical functions: Comes into contact with difficulties and calmly responds to research: behavioral disorders – hyperactivity, hyperexcitability, emotional instability. Attention is unstable and diffuse, concentration decreases. Simple sentences represent expressive speech. Sound reproduction is not disturbed. Impressive speech, the understanding of reverse speech is limited; the most straightforward commands are executed. She has a short interest in learning. The skull has a typical configuration. The circumference of the head is 51 cm. The large fontanel is closed. There is a tension of the venous pattern on the forehead and temples.

During the Electroencephalogram in the state of active and passive wakefulness, the frequency characteristics of the cortical rhythms of wakefulness do not correspond to age. Sensorimotor rhythm is not regis-

tered. There are differences between zones. Against the background of morphofunctional immaturity of cortical rhythms, changes of diffuse nature in a moderate degree with signs of diffuse irrigation with the participation of subcortical structures, the synchronization of mechanical dysfunction of diencephalic structures prevails.

After consultation with a geneticist aged two years and ten months, it was established: slow physical and psychomotor development of uncertain etiology, symptomatic epilepsy in the form of generalized convulsive seizures. A mass spectrometry of the tandem over three years was performed. No data were found on hereditary aminoacidopathy, organic acidity, and mitochondrial beta-oxidation defects. The concentration of organic acids in the patient's urine is within normal limits. Results of molecular genetic diagnostics showed a variant of the nucleotide sequence, not previously described as pathogenic, was identified in exon 15 of the GLDC gene (chr9:6587268 C>T) and 19 of the GLDC gene (chr9:6554754>T), leading to the formation of a missense replacement (p.Glu75Lys, NM\_000170), in a heterozygous state. Homozygous and compound-heterozygous variants in these genes are described in glycine encephalopathy, OMIM:605899).

**Discussion.** In this clinical case, we described a combination of two pathological conditions: mental retardation (F79 ICD-10) and unspecified epilepsy (G40.9 ICD-10), noted from the first months of life. Their etiology was not associated with hypoxia, trauma, or infectious brain damage. Anticonvulsant medications poorly controlled seizures. Early mental retardation was noted. Early diagnosis of perinatal encephalopathy did not answer the question about the reason for the formation of neurological symptoms. In this connection, three years later, mass spectrometry in tandem was conducted. Of the gene mutations described earlier in the literature, in which a similar clinical picture was observed, mutations in the SPATA5 gene were noted in the homozygous and compound-heterozygous states [4]. However, in the clinical picture, in addition to mental retardation and epilepsy, deafness was noted, which was not present in our observation. Changes in the MTRNR1 gene with the primary mutation LHON m.3460G in association with m.T961delT+C9(n)ins, which led to mental retardation and convulsive syndrome, but they were combined with optical neuropathy and migraine, were also described [5]. In a homozygous duplication mutation with a shift in the reading frame of 13 nucleotides c.2134\_2146dup13 in the coding region of FRMD4A, mental retardation was combined with congenital microcephaly, maxillofacial dysmorphic disorder [6].

**Conclusion.** Genetic research has revealed a previously unspecified mutation that causes congenital seizures and mental retardation.

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**Disclosures:** The authors declare no conflict of interest.

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## DISSECTING HOFFMAN'S CELLULITIS: CLINICAL CASE WITH SUCCESSFUL THERAPEUTIC RESPONSE

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## ПОДРЫВАЮЩИЙ ФОЛЛИКУЛИТ ГОФФМАНА: КЛИНИЧЕСКИЙ СЛУЧАЙ С УСПЕШНЫМ ТЕРАПЕВТИЧЕСКИМ ИСХОДОМ

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The article presents our clinical observations and results of Hoffman folliculitis detonation treatment in a 25-year-old patient with hair loss lesions on the scalp, in which the area is dense inflammatory, Hyperemic, painful knots with fluctuation and pus content. Timely prescribed adequate therapy led to the regression of dense nodules, which led to the cosmetic recovery of scalp hair in areas of pronounced inflammation.

*Keywords: dissecting cellulitis, scalp, dissecting Hoffman's folliculitis, alopecia, isotretinoin, treatment*

Представлены собственное клиническое наблюдение и результаты лечения подрывающего фолликулита Гоффмана у пациента 25 лет с очагами выпадения волос на коже волосистой части головы, в области которых определялись плотные воспалительные гиперемизированные болезненные узлы с флюктуацией и гнойным содержимым. Вовремя назначенная адекватная терапия привела к регрессу плотных узлов, в результате чего достигнуто косметически приемлемое восстановление волос на коже волосистой части головы в местах выраженного воспалительного процесса.

*Ключевые слова: рассекающий фолликулит, подрывающий фолликулит Гоффмана, алоpecia, изотретиноин, лечение*

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ALT – alanine aminotransferase  
AST – aspartate aminotransferase

GGT – gamma-glutamyltransferase