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EXPERIENCE OF USING A SCORE SCALE FOR DIAGNOSTICS OF WILSON-KONOVALOV DISEASE

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The problem of diagnosing orphan diseases is relevant due to the extreme heterogeneity of these diseases both in terms of the organs and systems they affect and in the degree of clinical polymorphism. The patient visits a number of specialists before receiving the correct diagnosis. [6]

Wilson-Konovalov disease (WKD) or hepatolenticular degeneration is one of the few metabolic diseases that can be treated pathogenetically if diagnosed correctly [3].

WKD is an autosomal recessive hereditary disease that occurs as a result of copper metabolism disorder, which leads to liver and neurological dysfunction. The etiology of WKD is associated with a mutation in the gene of copper-transporting P-type ATPase (ATP7B) encoding the protein ATP7B, the main regulator of copper metabolism in the liver. The prevalence of WKD in Russia, according to the rare disease registry, is 1:166600 [2, 4].

For diagnostics and objective assessment of patients with WKD, a quantitative point scale is used (Leipzig quantitative scale, 2001), which is based on the assessment of the main manifestations of the disease (clinical manifestations and genotype characteristics) [7]. A special role in the scale is given to genetic testing - if mutations are present in both copies of the gene, the maximum number of points is assigned, and this result is sufficient to clarify the diagnosis of WKD even in the absence of such clinical signs as the Kayser-Fleischer ring, ceruloplasmin level and copper excretion in urine. [1, 5]

Based on the above, we provide a description of a clinical case of the disease confirmed by a molecular genetic study.

Child N.M., born in 2012. The family sought medical genetic counseling at the age of 6 years. The child is from a consanguineous marriage. The mother's age at the time of birth was 31 years, the father's age was 34 years. The parents are healthy.

The anamnesis showed that psychomotor development up to 1 year was normal.

In 2017, he was operated on for testicular prolapse. During the examination, a sharp increase in ALT and AST was detected. Viral hepatitis was excluded in the hepatology department of the Research Institute of Pediatrics.

Neurological status. Minor disturbances in drawing are noted - he cannot draw a straight line or a clear circle. Hypermobility of joints is determined, tendon reflexes in the upper limbs are brisk, in the lower limbs they are increased with expansion of reflexogenic zones,

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abdominal reflexes are evoked, in the Romberg pose he is stable, the finger-nose test is performed.

Laboratory and instrumental data:

Liver ultrasound: acoustic access is satisfactory, contours are clear, the surface is smooth, angles are sharp. The capsule is clearly differentiated as a hyperechoic line. Right lobe: CKR - 115 mm, PZR - 88 mm. Left lobe: CKR - 81 mm, PZR - 40 mm. The parenchyma is fine-grained, heterogeneous due to small structures of different density. Increased echogenicity. Sound conductivity is preserved. The vascular architecture is not impaired. Gallbladder: pear-shaped. The walls are uneven, compacted. Thickness is 2 mm. The contents are anechoic, there are no stones. Spleen: sickle-shaped. The contours are smooth, clear, the echostructure is homogeneous.

MRI of the brain: no signs of structural changes in the brain were found. Indirect signs of intracranial hypertension.

Consultation with an ophthalmologist: a slight opacity (opaque) is formed on the cornea near the limbus; the Kaiser-Fleischner ring is forming.

Liver fibroscan: stage F0 of liver fibrosis was determined (mean median 3.0).

Biochemical studies: alkaline phosphatase - 950 ↑, LDH - 599 IU ↑, copper level in daily urine 201 μg / l ↑, ceruloplasmin level in the blood 17.51 ↓. Copper level in the blood is 12.0 μg / dl ↓, glucose - 2.8 mmol / l ↓.

The proband underwent molecular genetic testing of the ATP7B gene using the NGS method, as a result of which the patient was found to have a heterozygous mutation ATP7B delC3402 and a heterozygous mutation ATP7BCly1267Arg.

The identified mutations have proven pathogenicity, leading to a defect in copper excretion into bile and its binding to ceruloplasmin.

A comprehensive examination of the patient in combination of clinical symptoms, laboratory, instrumental and molecular genetic testing data using a point assessment, in which the sum of points of 4 and above is considered reliable diagnosis.

Determined:

- decreased ceruloplasmin level in the blood serum - 1 point;

- increased copper level in daily urine - 1 point;

- the presence of Kayser-Fleischner rings - 1 point;

- the presence of neuropsychiatric symptoms (or MRI changes) - 0 points

- homozygous/compound - heterozygous carriage of the ATP7B gene - 2 points

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On the scale, the sum of points was - 5, which confirmed the diagnosis of Wilson-Konovalov disease, liver form.

Thus, the use of the Leipzig quantitative scale, based on the assessment of the main manifestations of the disease and the characteristics of the genotype, made it possible to establish a diagnosis with a high degree of reliability in this patient.

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