CLINICAL CASE

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CLINICAL CASE OF GLYCOGENOUS DISEASES TYPE III IN A CHILD

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Glycogenosis type III (Cori disease) is one of the most common glycogen storage diseases in the world. The disease is associated with a disorder of carbohydrate metabolism: glycogen metabolism, leading to disruption of its synthesis or breakdown and is characterized by excessive accumulation of this polysaccharide in the organs and tissues of the body, most often in the liver or muscles. This article presents a clinical case of glycogen storage disease type III.

Keywords: glycogenosis, storage diseases, glycogen accumulation, children, liver, hypoglycemia, diagnosis, treatment.

Introduction. Glycogenous disease (GD, synonym: glycogenosis, glycogen storage disease, ICD10 - E 74.0) is a group of hereditary diseases of carbohydrate metabolism disorder – glycogen metabolism, leading to disruption of its synthesis or breakdown and accompanied by excessive accumulation in the liver or muscles. Currently, 15 types of GB have been described [1,3,4]. Hepatic forms of GB include types I, III, VI and IX.

The frequency of GB type III is 24% of all types of GB. It is characterized by an autosomal recessive type of inheritance, resulting from mutations of the AGL gene and deficiency of the enzymes amylo-1,6-glucosidase and 4a-glucanotransferase. An enzyme defect leads to the accumulation of glycogen of an abnormal structure in the liver or muscles. Clinically manifested by: cardiomyopathy, muscle weakness, muscle atrophy, states of acute hypoglycemia from birth, general intoxication, nosebleeds, growth retardation in combination with excess body weight. The formation of liver adenomas and cases of left ventricular hypertrophy have been described; in rare cases, life-threatening rhythm disturbances can be recorded. Damage to the diaphragm can cause frequent pneumonia with the development of cor pulmonale [2,5,6,7].

The main methods of confirming the diagnosis are biochemical - determining the activity of the enzyme in leukocytes, erythrocytes or fibroblasts. It is also possible to conduct molecular genetic studies [4,5].

No specific treatment has been developed. The main thing in the treatment of GB is strict adherence to the diet and a specialized diet to prevent glucose levels from falling below acceptable values. Great importance is attached to the organization of fractional meals [3].

Purpose of the study: to describe the clinical and laboratory picture of glycogen disease type III in a 9-year-old child.

A retrospective analysis of the medical history of a patient who was hospitalized in the Department of Pediatric Endocrinology and Gastroenterology of the Pediatric Center of the State Autonomous Institution of the Republic of Sakha (Yakutia) "RB No. 1-NCM named after. M.E. Nikolaev". The department conducted a full in-depth examination. Laboratory tests were performed (general blood and urine analysis, biochemical blood test, glycemic profile study, immune status, thyroid hormone analysis) and instrumental studies (ultrasound of the internal organs, ECG, ECHO-CG, FEGDS, chest radiography, computed tomography of internal organs, hepatoscintigraphy, liver biopsy, tandem MAS spectrometry).

Clinical example. Child D., 9 years old, girl, Sakha, was admitted with complaints of nosebleeds, frequent and prolonged acute respiratory viral infection (ARVI), episodes of hypoglycemia, moodiness, tearfulness, difficulties in learning at school.

Anamnesis of life. The child is from the second pregnancy, which proceeded physiologically. First birth, on time, natural. Birth weight: 4080 g, body length 56 cm. Apgar score 8/9 points. Attached to the breast for 1 day, breastfed until 1 year 1 month. Psycho-motor development: walking with a delay from 1 year 8 months, speech development according to age. She received preventive vaccinations on an individual schedule due to frequent acute respiratory viral infections. Mother is 39 years old, father is 48 years old, no chronic diseases. They have a child who is 5 years old and healthy.

Anamnesis of the disease. At the age of 5 months, the mother noticed an increase in the size of the child's abdomen, but due to the remoteness of her place of residence, she did not seek medical help or examination.

In April 2015 a girl with suspected pneumonia was hospitalized at the Central District Hospital, where a biochemical blood test revealed high cytolytic activity and elevated triglyceride levels. With suspicion of viral hepatitis, she was transferred to the Children's Infectious Clinical Hospital in Yakutsk, where this diagnosis was excluded. The child was hospitalized in the gastroenterology department of the Pediatric Center of the State Autonomous Institution of the Republic of Sakha (Yakutia) "RB No. 1-NCM named after. M.E. Nikolaev".

Upon admission, complaints of severe sweating, abdominal enlargement, rashes, anxiety, tearfulness.

In the department, the child underwent a complete clinical, laboratory and instrumental examination. Viral hepatitis, yersiniosis, and CMV infection were excluded. According to the results of FEGDS, no changes were detected; sigmoidoscopy revealed catarrhal proc-

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titis. Ultrasound of the liver revealed an increase in its size, increased echo density, and splenomegaly. According to CT scan of the abdominal cavity, no signs of biliary or portal hypertension were detected. In order to clarify the diagnosis, a liver biopsy was performed; fibrosis of the portal tracts, with areas of bridging fibrosis, and moderate infiltration of lymphocytes, hysteocytes, and single eosinophils were revealed. Index of histological activity excluding fibrosis according to Knodell: 5. Stage of fibrosis 1. A preliminary diagnosis was made: Congenital fibrosis of the liver. Treatment provided: ursosan, hofitol, infusion therapy with glucose-salt solutions, aminoven.

Repeated hospitalization after 2 months due to the lack of positive dynamics in the child's condition, the abdomen increased, tearfulness and sweating persisted. Upon examination, the liver dimensions were +9+9+8 cm, spleen +3 cm. In the biochemical blood test, ALT/AST 596/1169 U/l, GGT 270 U/l, alkaline phosphatase 417.5 U/l, LDH 1036 U/l l, glucose 2.74 mmol/l, TG 4.71 mmol/l, cholesterol 5.59 mmol/l, cortisol 484.8 nmol/l, insulin 6.0 cd/l, growth hormone 42.28 ng/ml.

The child was additionally examined by geneticists, and tandem MAS spectrometry was performed. No aminoacidopathy was detected, and no defects in mitochondrial beta-oxidation were detected. In therapy she received heptor, viferon, ambroxol. With suspicion of glycogen storage disease, the girl was sent to the Federal State Institution "National Medical Research Center for Children's Health" of the Ministry of Health of the Russian Federation (Moscow) to clarify the diagnosis.

In the Federal State Institution "National Medical Research Center for Children's Health" of the Ministry of Health of the Russian Federation, the department of gastroenterology, the child was from 10/06/15 to 10/20/15, a clinical diagnosis was established: Glycogen disease (type 1b?), moderate to severe course.

Conducted research. Blood test for mutations in the G6PC, SLC37A4 genes, corresponding to glycogen storage disease type 1, results in the work. Three-day monitoring of blood glucose levels did not reveal any episodes of hypoglycemia.

The liver biopsy was reviewed, description: low quality materials. Serial sections of liver puncture biopsy, staining with hematoxylin and eosin according to Van Gizzon, according to Masson, PAS reaction. The biopsy is 1.4 cm long and very thin. In the section, up to 6-7 complete and incomplete portal tracts, 2-3 central veins are identified. The portal tracts are fibrotic, with multiple porto-portal septa. 1 porto-central septum, areas of perihepatocellular fibrosis. In the portal tracts there are scanty infiltrates of lymphocytes, histiocytes with an admixture of a few eosinophils. The border plate is preserved. Hepatocytes are round in shape, of various sizes, some are large, the beam structure is not distinguishable. The cytoplasm of hepatocytes is very light, fine-grained, and vacuoles are visible in some hepatocytes. The nuclei are small, shifted to the periphery, the membrane is clearly contoured. When carrying out the PAS reaction, there is an uneven accumulation of PAS-positive substance. Conclusion: Low quality of materials. Liver preparations contain signs of chronic periportal hepatitis of low histological activity without taking into account sclerosis. Sclerosis index according to Desmet 3 points (severe), perihepatocellular fibrosis. The detected changes do not contradict the diagnosis of glycogen storage disease; a final conclusion can be made after preparing additional materials. Therapy performed: glycogen diet, corn starch, heptral intravenously, Elcar, Reamberin, Polydexa, calcium D3 nycomed, leucostim 5 mcg/kg-75 mcg subcutaneously on 10/13/15 and 10/19/15. The child was discharged with recommendations to follow a diet excluding sugar, lactose, limiting fat, and taking medications.

During the next hospitalization in the gastroenterology department of the Federal State Institution "National Medical Research Center for Children's Health" of the Ministry of Health of the Russian Federation in April 2016, the final clinical diagnosis was confirmed: Glycogen disease type III, mutation c.3980G>A, pW1327* in a homozygous state in the AGL gene.

The girl is regularly observed in the department of pediatric endocrinology and gastroenterology of the Pediatric Center of the State Autonomous Institution of the Republic of Sakha (Yakutia) "RB No. 1-NCM named after. M.E. Nikolaev", follows a diet, receives leukostim subcutaneously, hepatoprotectors. The dynamics are stable. Height 128 cm, weight 34 kg. The condition is of moderate severity due to the underlying disease. The increase in abdominal size due to hepatomegaly persists.

Conclusion: This clinical case confirms the need for further research to develop optimal management tactics for patients with clear recommendations on the frequency and scope of laboratory and instrumental examinations in order to identify complications. The creation of a national registry of patients with GB is required. Conducting of children with glycogenosis requires the vigilance of specialists in many fields: pediatricians, gastroenterologists, endocrinologists, hematologists, geneticists, etc. Timely diagnosis and initiation of adequate therapy will significantly improve the quality of life of patients, the prognosis of the disease and reduce the development of complications.

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