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CLINICAL CASE OF METHYLMALONE ACIDEMIA IN GIRLS WITH KETOACIDOTIC SYNDROME

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Methylmalonic acidemia / aciduria (MMA) is an inherited autosomal recessive disease, from the group of disorders of organic acid metabolism. Due to the blocking of the metabolism of propionates at the level of the transition of methylmalonyl-CoA to succinyl-CoA. It is characterized by mental and physical retardation, the presence of methylmalonic acid (MMC) in plasma and urine, metabolic ketoacidosis. The incidence in European countries is 1: 48000-61000 newborns [1-3].

The pathogenesis includes methylmalonin-CoA mutase deficiency, mevalonate kinase, methylmalonin-CoA racemase and cobalamin metabolism defects. There are B12-resistant (manifests at the age of 2 weeks-4 months) and B12-dependent (manifests after the neonatal period) forms of MMA. According to the timing of the first signs of the disease, there are neonatal, infant and late forms. In most cases, hereditary MMA is characterized by an early acute onset and crisis. The clinic is dominated by vomiting, dehydration, refusal to eat, weight loss, generalized muscular hypotension, hyperreflexia, weakness, drowsiness, coma, possible convulsions. Mortality at an early age reaches 40%. In older children there is a delay in psycholinguistic and motor development, extrapyramidal disorders, stroke-like episodes, epileptic seizures. Of the extraneural complications, the most severe are liver and kidney lesions such as tubulointerstitial nephritis with hypertension and renal failure, erythematous dermatitis, cardiomyopathy, cardiac arrhythmias, acute pancreatitis, optic nerve atrophy [1-3].

Diagnosis of MMA presents certain difficulties due to the clinical heterogeneity of signs, symptoms and nonspecific manifestation of the disease. The final diagnosis is based on the analysis of pedigree, evaluation of anamnesis data, clinical manifestations, results of laboratory tests. For the diagnosis of MMA, the most informative data are the profile of blood acylcarnitines (propionylcarnitine and free carnitine), blood amino acids (isoleucine, valine, methionine, threonine, glycine) and the presence of MMK in urine. Therefore, first of all, modern biochemical laboratory

diagnostic methods are used to establish the diagnosis: tandem mass spectrometry (TMS) and gas chromatography (GC) with mass spectrometric detection. Based on the analysis of organic acids in the urine, it is possible to make a differential diagnosis with other forms of organic aciduria and defects in the cycle of urea synthesis, as well as with hypoxic lesions of the nervous system, intrauterine infections, diabetes. To confirm the diagnosis, it is recommended to conduct a molecular genetic study: 1) study of MUT and MMAV genes in vitamin B12-insensitive forms and MMAA and MMAV genes in vitamin-B12-sensitive forms; 2) study of the MCEE gene if mutations in the MUT, MMAB, MMAA genes are not detected [3].

It is recommended to perform computed tomography and magnetic resonance imaging to detect cortical atrophy, ventricular dilatation, thickening of the grooves, delayed myelination, foci of necrosis in the basal ganglia, increased signal intensity in the basal ganglia in the T2-image. A patient with suspected MMA is prescribed a consultation of related specialists: psychoneurologist, nutritionist, orthopedist, ophthalmologist, cardiologist, hematologist, allergist, psychologist and speech therapist [1,2].

The strategy of treatment of patients is to reduce the formation of propionates, prevent the development of ketoacidosis, hyperammonemia, toxic lesions of brain tissues and internal organs while ensuring the processes of anabolism, normal growth and nutritional status of children. For the treatment of MMA in patients with mutations in the genes of methylmalonyl-CoA mutase (MUT) and defects in the synthesis of adenosylcobalamin AdoCb1 successfully used specialized medical nutrition and vitamin B12 (hydroxycobalamin) in high doses. Other forms of MMA are virtually untreatable, but they differ in the type of inheritance and the prognosis of the disease. The main components of complex treatment of patients are low-protein diet, levocarnitine and vitamin B12 in B12-dependent form. Therapy is supplemented with the appointment of glycine, antibacterial drugs and other B vitamins (thiamine, pyridoxine). According to the indications, anticonvulsants and symptomatic therapy are prescribed [2,3].

Preventive measures include family IGC, prenatal and / or preimplantation diagnostics, which are performed by molecular genetic testing of a chorionic biopsy to detect mutations in relevant genes. Establishing a primary molecular genetic defect allows you to adjust the tactics of pregnancy [1-3].

We present a clinical case of methylmalonic acidemia in a one-year-old girl. A child from the first pregnancy (in vitro fertilization), the first term delivery. She was born by elective caesarean section at 39-40 weeks of gestation. Body weight at birth - 3900 g, length - 53 cm, Apgar score - 8/9 points. She was fed a lactose-free formula. Before 5 months, weight was gained by age, psychomotor development occurred by age. At 6 months, the child's condition worsened: appetite decreased, weight gain, vomiting, vomiting, acetonuria, and anxiety attacks stopped. Weakness increased, there were signs of hypotension with regression of psychomotor functions. She began to refuse food. The girl was treated for functional disorders of the digestive tract and acute bronchitis. The child weighed 9700 g per year. At the age of 1 year and 3

months, she underwent inpatient treatment in the neurological department due to delayed statokinetic development and metabolic acidosis. Discharged with a diagnosis of metabolic disorders of unknown origin, ketoacidotic syndrome, neuroarthritic constitution, first degree anemia. Allergic and hereditary history is not burdened.

At the age of 1.5 years, due to a severe recurrent ketoacidotic crisis, it was assumed that there was a violation of the metabolism of organic acids. The girl underwent a comprehensive examination: determination of the blood acylcarnitine profile by TMS, blood amino acids by high-performance rare chromatography (HPLC), determination of renal excretion of organic acids using GB; determination of the level of lactate, blood ammonia, glycemic profile; EFGD, ultrasound of the abdominal organs, Echo-CG; molecular genetic research; consultation with an ophthalmologist, neurologist, orthopedist.

According to the results of blood TMS (increased concentration of propionylcarnitine (C3), C3 / C2, C3 / C16, C3 / Met); gas chromatography of organic acids in urine (presence of methylmalonic acid); high performance rare chromatography (elevated levels of glycine, cystine and proline); DNA analysis (pathogenic mutation c.655A> T (p.Asn219Tyr) of the MUT gene), confirmed metabolic disorders from the group of organic aciduria - methylmalonic acidemia.

Treatment included: dietary correction (low protein diet); specific drug therapy (L-carnitine, hydroxycobalamin, biotin, glutargin). Hydroxycobalamin sensitivity was tested, no efficacy was found. The child was discharged under the supervision of a neurologist, orthopedist and geneticist at the place of residence, recommendations for diet therapy and dynamic monitoring were provided.

Thus, MMA is a progressive disease that leads to severe developmental delay and requires early diagnosis and treatment.

References:

1. Kurkina M.V., Baydakova G.V., Zakharova E.Yu. Molecular genetic and biochemical characteristics of isolated methylmalonic aciduria in Russian patients. Medical genetics, 2016. No. 9. S.17-28.

2. Baranov A.A., Namazova-Baranova L.S., Borovik T.E., Bushueva T.V. et al. Methylmalonic aciduria in children. Pediatric Pharmacology, 2017. Vol. 14, No. 4. S.258-271.

3. Matthias R Baumgartner, Friederike Hörster, Carlo Dionisi-Vici, Goknur Haliloglu et al. Proposed guidelines for the diagnosis and management of methylmalonic and propionic acidemia. Orphanet Journal of Rare Diseases, 2014. https://ojrd.biomedcentral.com/track/pdf/10.1186/s13023-014-0130-8