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Case Report

Gurler Syndrome: Clinical Case

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Abstract

The article presents a clinical case with the results of examination, treatment and dynamic observation of a child with type I mucopolysaccharidosis. Hurler's Syndrome. The diagnosis was established at the age of: 1 year 9 months on the basis of a combination of clinical and medical history data and the results of laboratory and instrumental examinations. Against the background of therapy, there is a positive dynamics of clinical symptoms, confirmed by the results of laboratory and functional studies. The lack of alertness of doctors regarding this disease is one of the reasons for the late diagnosis, and as a consequence, the formation of complications.

Keywords: Mucopolysaccharidosis; Hurler's syndrome; Gurler syndrome

Introduction

Mucopolysaccharidoses (MPS) - a group of hereditary metabolic diseases associated with impaired metabolism of Glycosaminoglycans (GAG), leading to multi-organ damage. These diseases are caused by mutations of genes that control the process of intralysosomal hydrolysis of macromolecules [1]. The first description of the disease was given by Charles Hunter in 1917, describing a "rare disease of two brothers" of 8 and 10 years with symptoms: hearing loss, dwarfism, macrocephaly, cardiomegaly, umbilical hernia, joint contracture, skeletal dysplasia. The brothers died at the age of 11 and 16, respectively [2]. MPS is a rare disease and occurs with a population frequency of 1:4000-1:100000 live babies [1]. In Russia, according to public organizations dealing with the problem of MPS, about 200 patients with MPS live. In the Republic of Tatars tan there are 6 patients - 4 children and 2 adults. Since 2012, in Russia, MPS has been included in the list of life-threatening orphan diseases and is subject to treatment under the 7 Nosologies program. Since 2018, financing for the purchase of drugs for treatment has been made from the federal budget [2]. The disease is classified according to a genetic defect, leading to a decrease in the activity of lysosomal enzymes. There are 7 types of MPS. The most common type 1 MPS is characterized by a mutation of the IDUA gene, which encodes an alpha-L-iduronidase localized in the 4p16.3 chromosomal region. Type of inheritance of MPS I: autosomal recessive [1]. Alpha-L-iduronidase is involved in the catabolism of dermatan sulfate and heparan sulfate. These glycosaminoglycans as part of proteoglycans are part of the intercellular substance of the connective tissue, are found in the bones, synovial fluid, vitreous body and cornea of the eye. Together with collagen fibers of elastane, proteoglycans form a connective tissue matrix. Thus, GAGs are a "universal" substance for the body, but its excessive accumulation is poorly reflected in the vital activity of the cell and, as a result, leads to multiple organ damage.

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Case Presentation

According to the severity of clinical manifestations, three forms of MPS type I are distinguished: Gurler syndrome (MPS IH - severe form); Gurler-Sheier syndrome (MPS IH/S-intermediate); Cheye syndrome (MPS IS-mild). The severity of Hurler's syndrome is due to an early manifestation of the disease, a rapidly progressing course, the most severe clinic and a reduction in life expectancy. MPS IH is more common in the population compared to other forms of MPS I.

At birth, a child with MPS is often no different from healthy children. Symptoms most often develop on 1 year of life in the form of stunted growth, umbilical or inguinal-scrotal hernias, and liver enlargement. In the future, stiffness of small and large joints, kyphosis, lumbar spine, chronic otitis media and frequent recurrent infectious diseases of the upper respiratory tract join. Already by the year parents can complain of frequent SARS, especially facial features (gargolism: a large head, protruding frontal tubercles, wide cheekbones, sunken nose, short nasal passages with outward-turned nostrils, half-open mouth, large tongue, thick lips), regression of previously acquired skills. It is worth noting that the first manifestations of MPS are hidden under nonspecific symptoms, which leads to a late formulation of the main diagnosis, since these children can be observed for a long time by doctors of various specialties with isolated diagnoses [2]. The early detection of this rare disease is extremely important, since the developed treatment methods can prevent irreversible damage to organs and systems only in the initial stages of the disease.

Diagnosis of IH MPS is based on the clinical picture, laboratory research methods, which include the study of urinary dermatan sulfate and heparan sulfate excretion, the determination of alpha-L-iduronidase activity in a culture of fibroblasts, isolated white blood cells, or in blood stains dried on filter paper. A molecular genetic study is also possible: the identification of mutations in the IDUA gene. Great importance is attached to DNA diagnostics of type I MPS (determination of the proband genotype) [1-5].

The leading treatment method, both in Russia and abroad, is lifelong enzyme replacement therapy with the recombinant form of human alpha-L-iduronidase. It is administered weekly at a dose of 100

pieces/kg as an intravenous infusion [1]. Another treatment option is Hematopoietic Stem Cell Transplantation (HSCT). For patients with MPS 1H, HSCT is performed before the age of two years at normal or subnormal development rates. A retrospective analysis showed that the survival rate of patients after HSCT is 85% [5]. The effectiveness of HSCT depends on the age of the child at the time of surgery, the severity of the clinical manifestations, especially the state of the cardiovascular (in view of the subsequent cardiotoxic chemotherapy) and nervous systems, as well as the type of donor [5].

Clinical Example

Patient S., girl, 11 years old

Anamnesis vitae. Baby from 4th pregnancy, 2nd urgent birth, Birth weight 3550 g, height 58 cm. On the Apgar scale, 8-9 points. In the maternity hospital on the 2nd day systolic murmur was diagnosed. From 7 days of life, icteric syndrome is expressed. At the age of 5 months, an umbilical hernia was found, adenoids of the I-II degree; from 6 months, malnutrition of the 2nd degree and signs of delayed psychomotor development. At the age of 1 year, a change in the shape of the head in the form of an enlargement of the frontal region (ovoid form) is noted. According to brain NMR (dated 07.12.10): dislocation of the tonsils of the cerebellum by 10 mm, Atrophic changes in the brain, periventricular gliosis changes. By the age of 1.5, the girl develops keeled chest deformity, kyphosis, and contracture of the elbow joints. Also at 1.5 years old, corneal opacity was diagnosed; ultrasound enlargement of the liver: right lobe 82 mm, left lobe 39 mm. The hereditary history is burdened: the first child in the family (boy) died at the age of 9 months. Mother and father are somatically healthy.

Anamnesis morbi. At 1 month, the girl was first hospitalized in the cardiac surgery department of the Children's Republican Clinical Hospital of the Ministry of Health of the Republic of Tajikistan with complaints of shortness of breath at rest, fatigue. On X-ray analysis of OGK: the vascular pattern is not clearly differentiated, the heart is expanded across. On an ECG: sinus rhythm with a heart rate of 176 per minute; the position of the electrical axis of the heart is vertical; episodes of atrial pacemaker migration; increased electrical activity of the myocardium of both ventricles; in lead I: ventricular complex q=r, ST increase by 1 mm. On ECHO-KG, signs of dilatation of the left heart, mitral valve insufficiency of the third degree, aortic valve insufficiency of the first degree, multiple atrial septal defects (total size 8 mm). Neurosonography: moderate tissue hypertension syndrome. In the biochemical analysis of blood: total bilirubin is 148 μmol/L (normal 3.4 μmol/L to 20 μmol/L), direct 10.2 μmol/L (normal 0.8 μmol/L to 3.4 μmol/L). Based on the clinic, laboratory and instrumental methods, the study was diagnosed with congenital insufficiency of the mitral valve of the III stage. With severe dilatation of the left heart. Pulmonary hypertension art. Multiple atrial septal defects. Dilated cardiomyopathy? The disease of accumulation? Circulatory failure IIA. Prolonged conjugation hyperbilirubinemia. In therapy: veroshpiron, digoxin. Recommended consultation in the SC SCX them. Bakuleva AN. At the age of 6 months, she was hospitalized in the SC SCX named after Bakuleva AN. According to the conclusion of the consultation, it was decided to perform mitral valve repair with suturing of the open oval window under conditions of cardiopulmonary bypass and hypothermia. The postoperative period without complications.

At 1 year and 9 months, a preliminary diagnosis of type I mucopolysaccharidosis was first made. Recommended genetic testing and determination of the level of alpha-L-iduronidase. Blood was examined at the Federal State Budgetary Scientific Institution Medical Genetic Research Center in Moscow, hereditary mucopolysaccharidosis of type I was confirmed; the level of alpha-L-iduronidase in leukocytes is 0.01 nm/mg/hour (normal 61-175.5).

In January 2011, the girl was consulted at the Russian Children's Clinical Hospital in Moscow, and enzyme replacement therapy (FCT) with laronidase was recommended for health reasons. Since June 2011, the patient receives 1,500 units of Aldurazim intravenously drip weekly. The tolerance of therapy is good. Due to the increase in weight-bearing indicators, the dose of the drug was doubled from 03.16.15. Until 2000 units, and from 07.20.19. up to 2500 units. During treatment, a positive trend was noted: urine glucosamine glycans decreased, the size of the liver decreased, and the size of the left heart by ECHO-KG decreased. According to the latest ECHO-KG (July 2019), mitral valve insufficiency of the II degree. The overall well-being of the child also improves tolerance to physical activity increases, activity and interest in what is happening increase. Facial features became less rough, the severity of contracture changes in the joints of the upper extremities decreased.

Objective status for September 2019: moderate state, clear consciousness, active position. Physical development is sharply reduced: growth of 100 cm (below 3 percentiles), weight 19 kg. (Below 3 percentile). The skin is swarthy, Mongoloid spots throughout the body. Stigmatization: gargoyleism: low-lying ears, wide nose, large ovoid head; keeled chest, short limbs. Joints changed: brachidactyly, flexion contracture of elbow and distal interphalangeal joints. Varus installation stop. The borders of the heart are extended in both directions. The tones are muffled, rhythmic. The abdomen is enlarged, umbilical hernia. The liver is palpated + 1 cm from under the costal arch, the spleen is not palpable. Against the background of FZT, there is a positive trend in relation to psychophysical development. The girl attends correctional school, her performance is good. At the age of 7, she learned to read and write, knows the multiplication table, and is able to memorize verses. To study in the 2nd grade of a correctional school in Kazan.

Conclusion

Thus, the presented clinical case demonstrates the complexity of early verification of mucopolysaccharidosis. A feature of the example is the relatively favorable course of the disease. Against the background of therapy, there is a positive dynamics of clinical symptoms, confirmed by an improvement in the condition of the child, as well as laboratory results (a significant decrease in the level of GAG in the urine) and functional studies. The lack of alertness of doctors regarding this disease is one of the reasons for the late diagnosis, and, as a result, the formation of serious complications.

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