RELEVANCE OF THE PROBLEM OF MISDIAGNOSES OF ORPHAN DISEASES (ON THE EXAMPLE OF GAUCHE'S DISEASE)

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Orphan diseases – rare congenital or acquired diseases that are characterized by severe, chronic, progressive course, accompanied by the formation of degenerative changes in the body, reduced quality and reduced life expectancy of patients and even life-threatening.

The term "orphan disease" or “rare disease” was introduced in 1983 in the United States with the adoption of the legislation "OrphanDrugAct", which defined 1,600 rare diseases of unknown etiology.

Worldwide, more than 300 million people suffer from one or more orphan diseases. 72% of orphan diseases are genetically determined, and the remaining 28% are diseases that have a bacterial, viral allergic nature or are caused by adverse environmental factors. According to the European Alliance of Patients with Orphan (Rare) Diseases (RareDiseasesEurope), 2 out of 3 orphan nosologies are detected in early childhood, in 65% of cases they have a severe disabling course, in 50% - a worse prognosis for life, in 35% - cause of death under the age of 1 year, 10% - at the age of 1-5 years, 12% - at the age of 5-15 years.

Each orphan disease is considered rare, at the same time, according to epidemiological data, from 6 to 8% of the total population of EU member states suffer from rare diseases, and their total number is 27-36 million patients, which allows to attribute orphan disease to an important medical and social problems of the health care system and society as a whole.

As of 01.01.2020, according to the Kharkiv Interregional Specialized Medical and Genetic Center - Center for Rare (Orphan) Diseases in Kharkiv, patients with various rare diseases are registered and registered at the dispensary, the most common of which are: hyperhomocysteinemia (749 cases, including 640 in children), mitochondrial dysfunction (411 people, including 382 in children), amino acid

metabolism disorders (137 cases, including 108 in children), phenylketonuria (107 cases, including 67 in children), Gaucher disease (59 cases), vitamin B deficiency (59 cases, including 38 inchildren), cystic fibrosis (71 people, including 45 children), Shereshevsky-Turner syndrome (40 cases, including 32 in children), homocystinuria (11 cases, including 6 in children), Marfan syndrome (18 cases, including 8 in children).

Gaucher disease is one of the most common genetic lysosomal storage diseases, characterized by a deficiency of the enzyme glucocerebrosidase, which leads to the accumulation in the patient's body of a fatty substance - glucocerebroside in the lysosomes of macrophages and other cells such as osteoblasts. Lipid-filled "Gaucher cells" accumulate in various tissues and organs, especially in the spleen, liver, bone marrow, lungs. Macrophage cells with accumulated substrate are called Gaucher cells.

This disease occurs in all ethnic groups with a frequency of 1 in 40,000 to 1 in 60,000, but the highest incidence of the disease is characteristic of Ashkenazi Jews (1 in 450). Gaucher disease is a very rare disease in Ukraine. According to unofficial data for 2018, there are 59 patients diagnosed with Gaucher disease in Ukraine. In 2/3 of patients the disease is diagnosed before the age of 20 years.

Although Gaucher disease manifests itself within a range of symptoms, it is common clinical classification with a division into three types: type I - non-neuropathic), type II - acute neuropathic, and type III - chronic neuropathic. In Europe, Canada and the United States, the most common form of Gaucher disease (94%) is type I, characterized by a lack of primary involvement in the pathological process of the central nervous system. In other parts of the world, such as Egypt, Japan, Sweden, Poland, neuropathic forms may be more common than Gaucher disease type I. Gaucher disease type II and III has a similar pathogenesis, differing mainly in the degree of neurological degeneration - rapid / acute course is characteristic of type II, chronic - for type III. Acute neuropathic Gaucher disease (thia II) is very rare (1: 500,000) and is pannetic. Sick children can be healthy at birth, but by the age of 2 there are systemic and neurological signs of pathology, which are rapidly increasing. Most children die in early childhood, some in utero, others after a few years.

Specialized literature review has shown the results of analyzing the experience of 362 patients with Gaucher disease - the authors found a stable pattern of previous misdiagnosis, including leukemia, immune thrombocytopenic purpura, autoimmune diseases, liver cirrhosis, idiopathic aseptic necrosis, viral diseases, idiopathic aplenomegia and splenomega. Misdiagnosis has led to complications such as auscular sclerosis, osteopenia, liver disease, bleeding, ineffective medical procedures such as splenectomy, liver biopsy, and empirical short-term steroid therapy.

Usually, the first diagnosis made in patients who actually have Gaucher disease is a malignancy. In the first case of Gaucher disease in 1882, Dr. Philippe Gaucher suspected a latent form of malignancy affecting the spleen. In one study, the most common misdiagnosis was blood cancer (leukemia - 65%, lymphoma - 36%, multiple myeloma - 22%, chronic granulocytic leukemia - 14%). Among the most common possible misdiagnosis are coagulation disorders, osteomyelitis, Legge-Calve-Perthes disease also. It should be noted that patients with Gaucher disease have an increased risk of blood malignancies, especially multiple myeloma. Compared with the general population, such patients have a 25 times higher risk of multiple myeloma

At the time of diagnosis, more than 80% of children have splenomegaly, hepatomegaly and bone pathology. Among children who do not receive treatment, the average volume of the spleen is more than 20 times higher than normal, and the average volume of the liver is twice the normal size of the organ for a given age and weight.

The main and effective method of treating Gaucher disease is enzyme replacement therapy, which is indicated for use as a permanent life therapy in patients with a confirmed diagnosis of Gaucher disease type I and III, which significantly improves the quality and life expectancy of patients with Gaucher disease.

Concluding it should be noted the actuality of early diagnostic that allows to receive better results from the early long-life therapy that is vital forGauche disease’s patients. In Ukraine the problem of correct diagnosis and early therapy is actual considering the quantity of patients and their costs burden for families.