HYPOPHOSPHATASIA: A FAMILIAL CASE OF A RARE DISEASE.

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Annotation: *Hypophosphatasia (HPP) is a rare hereditary disease characterized by a very diverse clinical manifestations, which hinders a timely diagnosis. The article presents a description of a family HPP — two brothers of the same family had the disease manifested in childhood. The first clinical symptoms began to appear in the first year of life. Clinical manifestations were typical for HPP: rickets-like lower limb deformities, muscle weakness, poor exercise tolerance, early tooth loss. The symptoms of the disease were observed from various organs and systems, which significantly affected the physical health and patient's quality of life.*

Keywords: *rickets-like lower limb deformities, muscle weakness.*

Despite the typical clinical manifestations, the diagnosis of HPP was established in the older brother at the age of 6 years. Difficulties in the diagnosis led to a delayed prescription of therapy. It is possible to suspect HPP on the basis of a combination of disease clinical signs and chara cteristic changes according to X-ray examination. For differential diagnosis, it is necessary to determine the activity of alkaline phosphatase. The diagnosis is confirmed by the detection of a mutation in the ALPL gene based on the results of a molecular genetics. Early diagnosis of HPP is essential for the timely prescription of enzyme replacement therapy with asphotase alpha.

For the clinical picture of HPF, the most characteristic manifestations are defects in the formation and development of the musculoskeletal system - shortening and deformation of the limbs, chest, and skull. Children with age may experience low body weight and growth retardation. With age, the risk of pathological, poorly consolidating fractures, often requiring surgical treatment, increases. Pain in muscles and bones leads to gait disturbance and progressive limitation of mobility. Chest deformities contribute to respiratory failure, secondary lung hypoplasia, which can cause severe respiratory disorders. Developing hypercalcemia due to impaired calcium-phosphorus metabolism is often the cause of nephrocalcinosis with the development of progressive kidney damage.

The consequence of impaired metabolism of vitamin B6 are neurological symptoms of the disease: vitamin B6-dependent convulsions, intracranial hemorrhage, muscle hypotension, psychomotor retardation. Craniosynostosis with an increase in intracranial pressure may develop due to a violation of the formation of the skull bones [4, 6]. Premature loss of milk or permanent teeth, most often with an unchanged root, is one of the characteristic features of HPF.

The diagnosis of HPP is based on characteristic clinical symptoms, low ALP activity (taking into account the age and sex of patients), hypercalcemia/hyperphosphatemia, and a characteristic radiological picture. X-rays of long tubular bones reveal deformities, osteoporosis, areas of hypomineralization, as well as expansion, "corrodedness" of growth zones; typical areas of enlightenment in the metaphyses - the so-called "tongues of flame". The diagnosis is confirmed by detection of a mutation in the ALPL gene during a molecular genetic study.

Until recently, doctors did not have sufficient knowledge about HPP, did not know about the importance of reducing ALP. Consequently, patients with HFF passed under any other diagnoses clinically similar to HFF. For this reason, the treatment of HFF was exclusively symptomatic: a low-calcium diet, anticonvulsants, surgical care in the event of fractures or the development of craniosynostosis, physiotherapy and therapeutic exercises to strengthen the musculoskeletal system.

Both patients were recommended to undergo enzyme replacement therapy. From May 2020 to the present, children have been receiving replacement therapy with asfotase alfa at a dose of 2 mg/kg of body weight by subcutaneous injection 3 times a week. Dose adjustment is carried out taking into account the anthropometric parameters of patients. Against the background of therapy, children began to develop hypocalcicis 5mia, which required replacement therapy with calcium preparations. Prior to starting enzyme replacement therapy, patient R. was asked to perform a 6-minute walk test to assess exercise tolerance. During the test, the child walked 320 m, which corresponds to 59% of the normal figure for healthy peers. On the background of therapy, there is a good positive trend. With the start of therapy, the boys stopped losing their teeth. In the older brother, permanent teeth grow in place of the fallen milk teeth. Patient 2 A. (younger brother) attends kindergarten, grows and develops according to age.. The epiglottis is horseshoe-shaped, the cartilages of the larynx are formed correctly. The arytenoid cartilages are enlarged, their mucosa is hypertrophied, the epiglottis does not protrude into the larynx during forced inspiration. The vocal cords are pale and close completely. There is no secret in the pear-shaped sinuses. The conclusion is given: Congenital stridor. Hypertrophy of the arytenoid cartilages. Laryngomalacia. Based on the results of the examination, dynamic observation by an otorhinolaryngologist was recommended and, if stridor breathing persisted, the issue of operative treatment, arytenoidoplasty, was decided in the future.

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