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CONGENITAL SIALIDOSIS*

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Congenital sialidosis is a rare disease resulting from the absence of neurominidase and presenting with hydrops fetalis, hepatosplenomegaly, dysmorphic features, vacuolated lymphocytes and extensive vacuolation of the connective tissue. Elevated levels of sialooligosaccharides in the urine is characteristic. We describe a newborn baby with congenital sialidosis and discuss the difficulties in reaching the diagnosis.
Key words: sialidosis, neurominidase, hydrops fetalis.

Sialidosis in hereditary lysosomal storage disease which results from the absence of neurominidase. The absence of the enzyme leads to the accumulation of sialic acid in tissues and in urine. However, more than one clinical subtype is associated with abnormalities of neurominidase deficiency. The inheritance pattern is autosomal recessive.

The congenital form of this disease is extremely rare and presents with hydrops fetalis during pregnancy. We herewith present a case of congenital sialidosis who died in the early neonatal period.

Case Report

The baby boy was the first product of non-consanguineous parents delivered vaginally at 36 weeks of gestational age after an uncomplicated pregnancy. During prenatal follow-up, hydrops fetalis was diagnosed at 26 weeks of gestational age and an amniocentesis was performed. There was no blood group incompatibility and syphilis, toxoplasmosis, rubella, cytomegalovirus, herpesvirus and parvovirus serology were negative. The chromosomal analysis revealed 46XY genotype without any numeric or major structural abnormality. The fetus was evaluated as non-immune hydrops fetalis of unknown etiology.

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A first cousin of the mother had delivered a similar baby two months previously. That baby was also hydropic, had coarse facies and hepatosplenomegaly. A clinical diagnosis of congenital nephrotic syndrome was made and the baby was hospitalized for a month at the Pediatric Nephrology Department. The kidney biopsy suggested a storage disease but further investigations could not be made because the baby died suddenly due to septic shock.

This baby's appearance was hydropic with coarse facies with depressed nasal bridge and frontal bossing (Fig. 1). His weight was 3160 g (75^{th} percentile), length 47 cm (50^{th} centile) and head circumference 33 cm (50^{th} percentile). The abdomen was distended with massive ascites, hepatomegaly of four cm and splenomegaly of five cm. He had tachypnea and respiratory distress due to abdominal distention. There were a few crackles over both lung fields. The heart rate was 140/min with no murmurs. The peripheral pulses were palpable. He had bilateral inguinal herniae with communicating hydrocele. The corneal and funduscopic examinations of the eyes were unremarkable.

Fig. 1: Hydropic baby. Note the protuberant abdomen and swollen testes.

Complete blood count revealed a hematocrit of 41 percent, hemoglobin: 13.1 g/dl, mean corpuscular volume: 106 fl, red cell distribution width: 33 percent, platelets: 121,000/ml, and white blood cells: 10,400/ml. In the peripheal blood smear, most of the lymphocytes contained cytoplasmic vacuoles (Fig. 2). Routine blood chemistry was unremarkable. Slight proteinuria was observed in the urine examination. At the thin layer chromatography of the urine, a sialooligosaccharide band was observed. The amount of sialic acid in the 24-hour urine was 12.3 nmol/mg creatinine, about 12 times the normal amount. Abdominal ultrasonography revealed hepatosplenomegaly, ascites, nephromegaly and an increase in the kidney echogenity (Grade III). Echocardiographic examination was within normal limits. The roentgenographic examination of the bones was normal.

There were multiple foamy cells and lymphocytes with cytoplasmic vacuoles at the bone marrow aspiration. The electronmicroscopic examination of the tissue obtained at the skin biopsy showed extensive "empty" vacuolation at the capillary endothelium and pericytes among the collagen fibers of the subcutaneous connective tissue (Fig. 3). The baby thrived for 27 days during which his condition changed very little. His cardiorespiratory condition then suddenly deteriorated and he died on the 27th day of life.

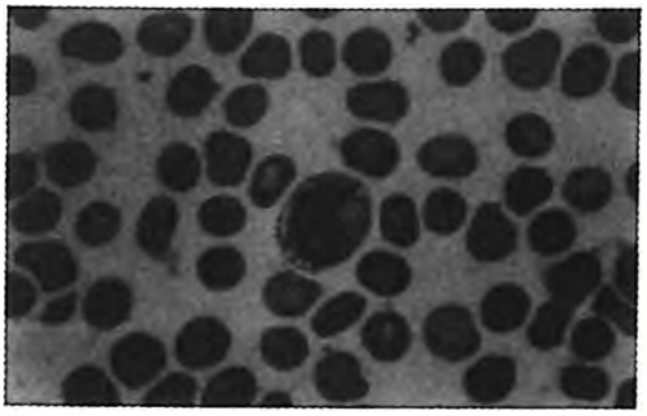

Fig. 2: Peripheral lymphocytes with multiple vacuoles.

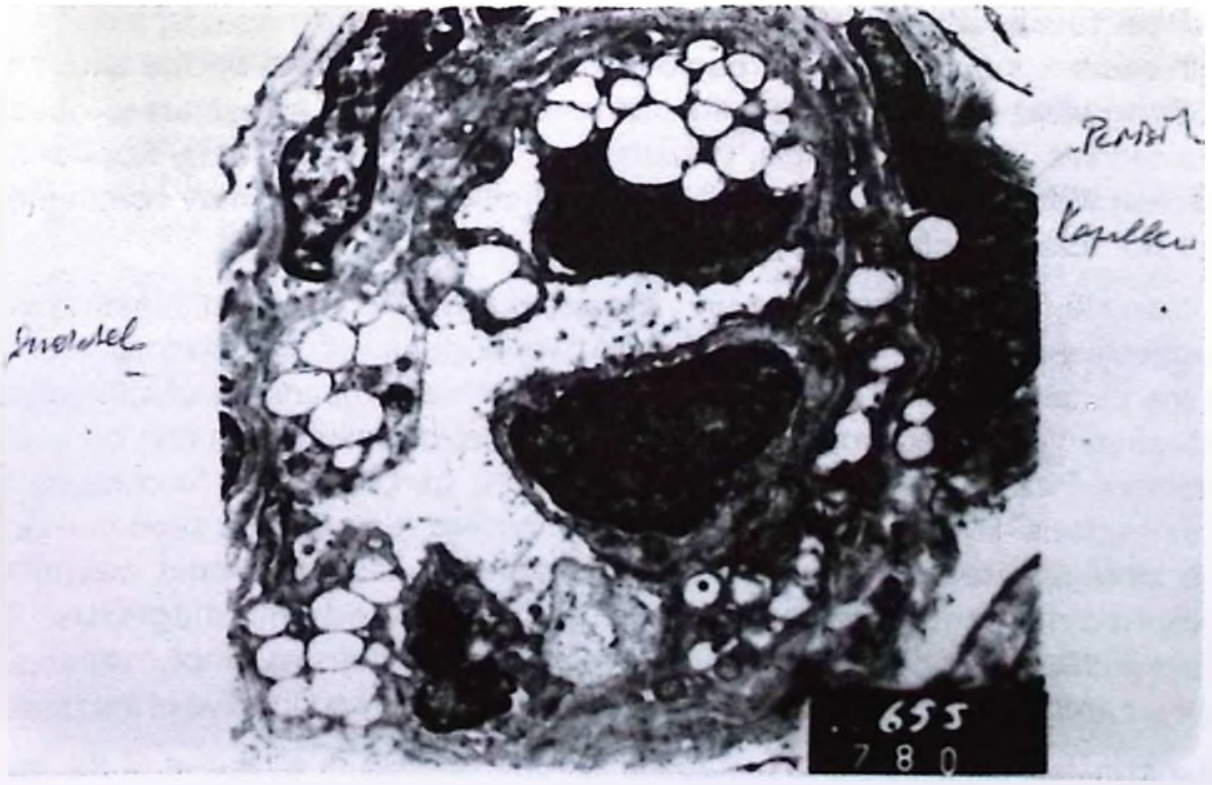

Fig. 3: Electron microscopic appearance of the skin. The "empty" vacuoles in the capillary wall are caharacteristic.

Discussion

Neurominidase is a lysosomal enzyme the absence of which leads to an accumulatilon of sialic acid in the tissues. According to Lowden and O'Brien[1] there are two types. Type I sialidosis is also called the normosomatic type or cherry-red spot myoclonus syndrome. Typical symptoms begin at eight to 25 years of age and the red degeneration of the macula with subsequent vision loss is characteristic. Lenticular opacities may be seen in some cases. Myoclonus is generalized and responds poorly to medical therapy. Most patients die at young ages[2].

Type II sialidosis is also called the dysmorphic type and there are three forms of this type. Coarse facies and dysostosis multiplex are common to all of them. The juvenile form is seen predominantly in Japan, at two to 20 years of age. Hepatosplenomegaly and renal involvement are not common. Most patients live until the fourth or fifth decade. The infantile form is symptomatic within the first 12 months of age and hepatosplenomegaly and renal involvement are common. Most patients die in the first or second decade. The congenital form is the rarest form and presents with hydrops fetalis in the perinatal period. Widespread edema, ascites, hepatosplenomegaly, inguinal hernia, renal involvement, epiphyseal stippling and corneal clouding are common features of the disease. Survival is limited in these infants[2-4].

In our patient, hydrops fetalis was diagnosed antenatally but the amniocentesis did not reveal any positive finding. Hydrops fetalis and hepatosplenomegaly with ascites, inguinal hernia, coarse facies, depressed nasal bridge and frontal bossing were all compatible with sialidosis[5]. The cause of ascites is obscure in sialidosis. Hypoproteinemia, sinusoidal obstruction in the liver by Kupffer cells swollen with storage material and diaphragmatic dysfunction may contribute to, but not totally explain, ascites.

Proteinuria, nephromegaly and an increase in the echogenity of the kidney were suggestive of renal involvement. Multiple lymphocytes with cytoplasmic vacuoles in the peripheral blood smear and bone marrow were important clues for storage diseases. Vacuolated lymphocytes and bone marrow foamy cells can be seen in Niemann-Pick disease, Wolman's disease, GM_1 gangliosidosis, fucosidosis and nannosidosis. Hydrops fetalis and neonatal ascites may also be seen in most of the storage diseases[2]. However, high levels of urinary sialic acid, vacuolated lymphocytes and dysmorphic features supported the diagnosis. The electronmicroscopic findings of the skin biopsy with extensive "empty" vacuolation of the capillary endothelium and pericytes were also highly suggestive of the disease.

The previous diagnosis of a metabolic storage disease in a relative of the family stimulated us to search for storage diseases in this patient also. The diagnosis of sialidosis was highly suspected after the observance of the sialooligosaccharide

band in the urinary thin layer chromatography and was confirmed by the more than 12-fold increase in the levels of sialic acid in the 24-hour urine. A definite diagnosis of sialidosis requires showing the deficiency of neurominidase activity in the fibroblast culture[2,5,6]. This investigation could not be performed due to technical difficulties. However, since the elevated levels of sialic acid in the urine is also definitive for diagnosis, the patient was evaluated as having congenital sialidosis[2].

Since a relative of the mother had died with similar findings, a prenatal diagnosis of this patient might have been made[7,8]. However, it was only after the baby was born that a detailed history was taken from the family which revealed this connection. Sialidosis and other storage diseases are rare causes of nonimmune hydrops fetalis; however, they should be kept in mind when evaluating a baby with hydrops fetalis. Detailed health histories are of paramount importance in this regard.

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