FATAL ACIDOSIS IN A NEONATE WITH PEARSON SYNDROME*

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SUMMARY: Gürakan B, Özbek N, Varan B, Demirhan B. (Departments of Pediatrics and Pathology, Başkent University Faculty of Medicine, Ankara, Turkey). Fatal acidosis in a neonate with Pearson syndrome. Turk J Pediatr 1999; 41: 361-364.

We report a neonate who presented with hypotonia, hypoglycemia, and severe lactic acidosis. The patient's acidosis did not respond to bicarbonate replacement and dialysis. Postmortem liver samples revealed portal dilatation, fibrosis, canalicular proliferation, cholestasis, and hepatocellular hemosiderosis. Vacuolization of bone marrow precursors suggested a diagnosis of Pearson syndrome. A common mitochondrial DNA deletion of 4,978 bp was found. We emphasize that Pearson syndrome should be considered in neonates with lactic acidosis despite absence of anemia. *Key words: lactic acidosis, neonate, Pearson syndrome.*

Pearson syndrome is a fatal disorder involving the hematopoietic system, exocrine pancreas, liver, and kidneys[1]. In most previously reported patients, diagnosis of this syndrome has been based on the presence of anemia and vacuolization of marrow precursors[1-4]. However, diagnosis by demonstrating mutations in mitochondrial DNA (mtDNA) is possible today.

Metabolic acidosis in neonates has been reported in only a few cases[3,5-7]. Here we report a neonate with Pearson syndrome who presented in the first days of her life with severe acidosis and hypoglycemia.

Case Report

A 2,100 g girl was born after a normal pregnancy and delivery. She was the third child of consanguineous parents. The other siblings were alive and healthy. Physical findings at birth were reported to be normal, apart from a wasting of the buttocks and thighs, compatible with intrauterine growth retardation. She was referred to our hospital due to vomiting, poor sucking ability and grunting on the first postnatal day.

On admission the baby was hypoactive, hypotonic and was experiencing mild respiratory difficulty. Her length and head circumference were 48 cm and 33 cm, respectively. The liver was 3 cm palpable under the right costal margin on the midclavicular line.

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Laboratory studies were as follows: hemoglobin 16.4 g/dl, white blood cell count 27.9 x 10^9/L, blood glucose 9 mg/dl, blood urea nitrogen 12 mg/dl, aspartate aminotransferase 310 U/L, alanine aminotransferase 200 U/L, total bilirubin 3 mg/dl, direct bilirubin 0.5 mg/dl, arterial pH 7.02, HCO_3 4 mEq/L, base excess-24, lactic acid (LA) 39 mg/dl (normal 10-14), and pyruvic acid (PA) 0.85 mg/dl (lactic acid/pyruvic acid = 45). Urinalysis and chest x-ray findings were normal. The infant was suspected to have sepsis, and antibiotic treatment, glucose infusion, and bicarbonate replacement were initiated. Since severe acidosis persisted, peritoneal dialysis was performed. Despite intensive treatment the patient's condition deteriorated and she died on the eighth postnatal day. Histopathological examination of the liver necropsy revealed portal dilatation, fibrosis, canalicular proliferation, cholestasis and hepatocellular hemosiderosis (Fig. 1). A bone marrow smear was normocellular with vacuolization of precursor cells of the erythroid and myeloid series (Fig. 2). The mtDNA analysis of a liver necropsy sample revealed the deletion of 4,978 bp (nt8469-13447) between the ATPase 8 gene and the ND5 gene.

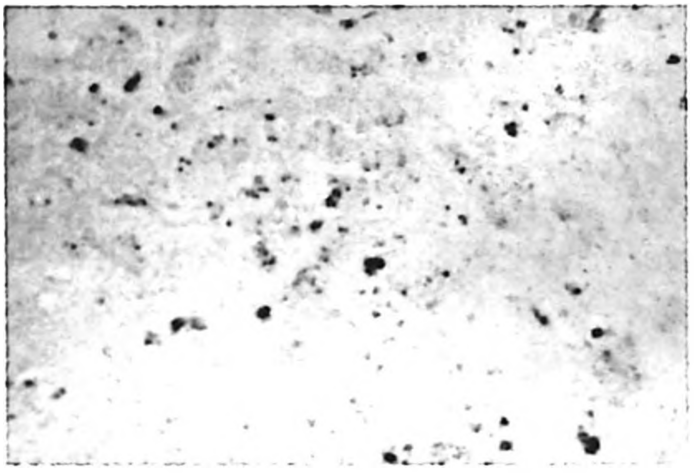

Fig. 1: Iron deposition in the patilent's liver (Perls' stain, x 230).

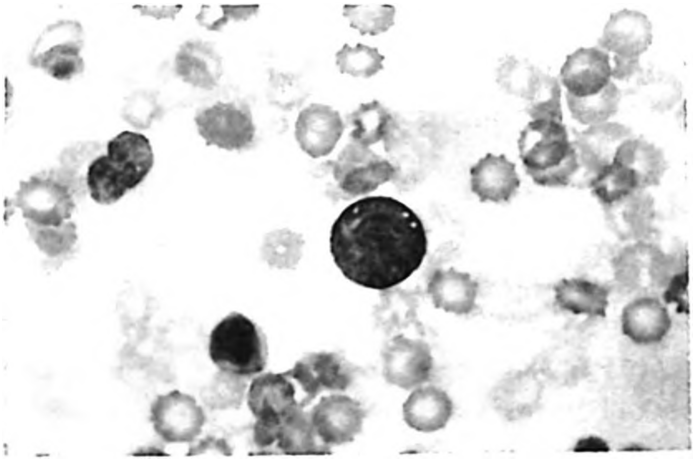

Fig. 2: Vacuolization of bone marrow cells (Wright's stain, x 1000).

Discussion

Pearson et al.[1] described a fatal syndrome in 1979 which involved severe anemia, vacuolization of marrow precursors, and pancreatic dysfunction. In the following years, case reports similar to this syndrome indicated that the disease was not limited to the bone marrow and pancreas the liver, kidneys, and other systems were involved[3-9]. In addition to multisystemic involvement, acidosis was another common finding. Evaluation of acidosis and hyperlactatemia in these patients resulted in the identification of this syndrome as the first mitochondrial disorder without neuromuscular expression[3]. Subsequently, deletions of mtDNA were found between 8 and 13 bp directly repeated sequences[10].

The patient reported here presented with hyhpotonia, hypoglycemia, and acidosis. Her liver was slightly enlarged and transaminases levels were high. An inborn error of metabolism or a mitochondrial disorder was considered after her refractory acidosis was identified as lactic acidosis (LA/PA > 40). Blood samples were obtained for further metabolic investigations. The diagnosis of Pearson syndrome was strongly suggested based on postmortem bone marrow aspiration and liver necropsy, and was confirmed with the demonstration of mtDNA deletion. The identification of this syndrome has important implications for clinical management and genetic counselling. Bone marrow transplantation seems difficult because of the multisystemic nature of the disease. A carbohydrate-rich diet which can precipitate hepatic failure should be avoided. Pearson syndrome results from de novo mutations and, due to random partitioning of mitochondria during embryogenesis, chorionic villi or amniotic fluid samples would give unreliable results. Thus, prenatal diagnosis is not available.

Gürgey et al.[6] reported a newborn patient with similar findings who had a 3.5 kb mitochondrial deletion which mapped to the ND5 region.Furthermore, postmortem examination revealed that their patient had multiple renal cysts. Since we could not obtain consent for an autopsy, we do not know whether our patient had other organ anomalies. Our case is one of few in which patients present with severe acidosis in the newborn period due to Pearson syndrome. Involvement of liver mtDNA may be responsible for the early appearance of the disease. We conclude that Pearson syndrome should be considered in the differential diagnosis of acidotic neonates prior to the development of anemia and pancreatic dysfunction.

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