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HYPOPHOSPHATASIA IN A NEWBORN INFANT*

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Infantile type hypophosphatasia, an autosomal recessive disease with severe clinical manifestations, is characterized biochemically by subnormal activities of circulating alkaline phosphatase. In this report, we presented a five-day-old male with this rare disorder. His parents were first cousins, and he was first seen for jaundice. He had soft calvaria, large fontanel, extremely wide cranial sutures, low-set ears, a depressed nasal bridge, funnel chest, and short and bowed distal limbs. Roentgenographic studies showed widened sutures and poor ossification of the skull, bowing of the femora and slight modeling defects in the long bones. A low serum alkaline phosphatase activity led us to measure excretion of phosphoethanolamine and found it to be increased.

To our knowledge this is the first case of this rare disease reported in the neonatal period from our country. *Key words: hypophosphatasia, newborn.*

Hypophosphatasia is a heritable form of rickets-osteomalasia that is characterized by decreased activity of the tissue-nonspecific (liver, bone, kidney) isoenzyme of alkaline phosphatase (TNS-ALP), and endogenous accumulation of pyridoxal 5-phosphate, phosphoethanolamine (PEA) and inorganic phosphate[1]. Based on the age of clinical presentation, hypophosphatasia can be classified into four forms: perinatal, infantile, childhood and adult. Most of the patients with perinatal or infantile-type hypophosphatasia die shortly after birth or within the next few months due to severe bony deformities[1,2].

This paper presents an infant with the infantile form of hypophosphatasia. To our knowledge, this is the first case of this rare disease reported in the neonatal period from our country.

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Case Report

A five-day-old male infant was first seen at the emergency department for jaundice. He was born at 39 weeks gestation to a 23-year-old, primigravid woman after an uncomplicated pregnancy and delivery. The mother had not been exposed to any drug during her pregnancy. The parents were first cousins. The patient's birth weight was 2700 g, length 46 cm, head circumference 32.5 cm, body temperature 36.5 °C (axillary), pulse rate 136/min (rhythmic) and respiration rate 48/min. The patient was active and in good general condition. On physical examination he had soft calvaria, large fontanel (metopic fontanel), extremely wide cranial sutures, low-set ears, a depressed nasal bridge, funnel chest, and short and bowed distal limbs.

Laboratory studies including a complete blood count, blood sugar, serum electrolytes, blood and urine aminoacids were all within normal limits. Serum total and direct billirubin were 17.5 and 0.5 mg/dl, respectively. Direct Coombs was negative. Glucose-6-phosphate dehydrogenase and thyroid stimulating hormone levels were within normal limits. One remarkable laboratory finding was a low (41 U/L) alkaline phosphatase activity (normal range is 62-348 U/L in term neonates). Serum calcium and phosphorus levels were normal.

Radiological findings revealed widening of sutures and poor ossification of the calvarium, marked in the frontal and parietal bones. Both femurs were bowed in their middle thirds, and there were some slight modeling defects in the humerus, radius and thin ribs (Figs. 1-2). The metaphyses were normally

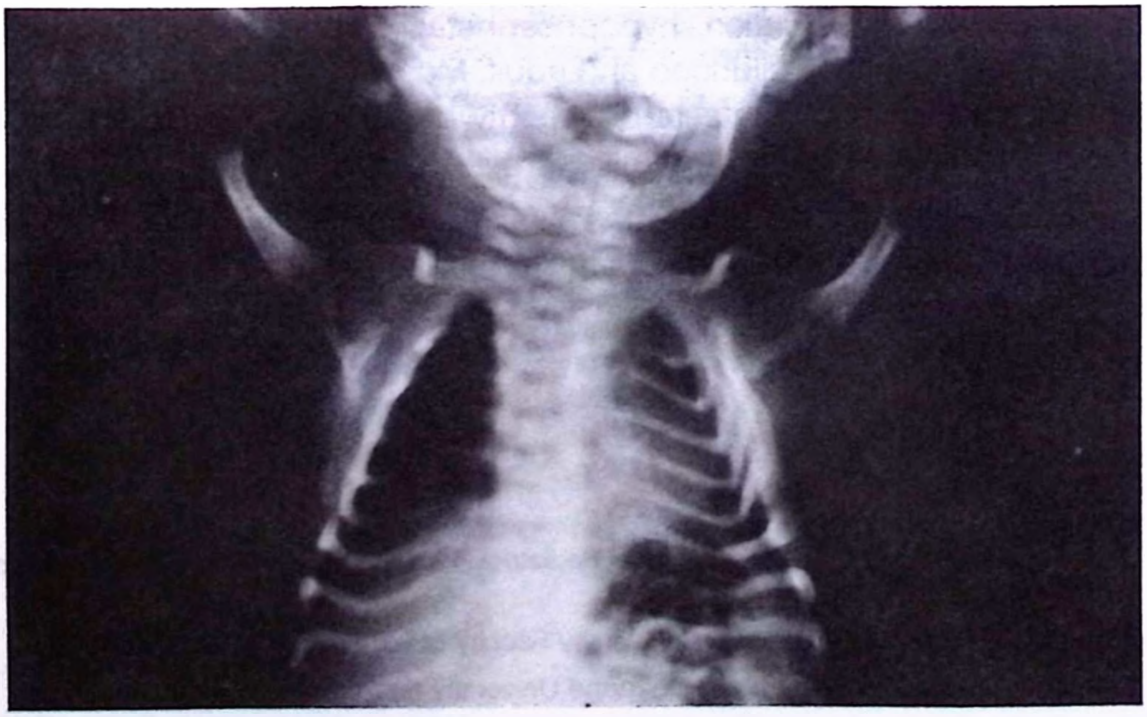

Fig. 1: Posterior-anterior chest x-ray showing generalized osteopenia, slight modeling defects in humerus and radius with deformed, thin ribs.

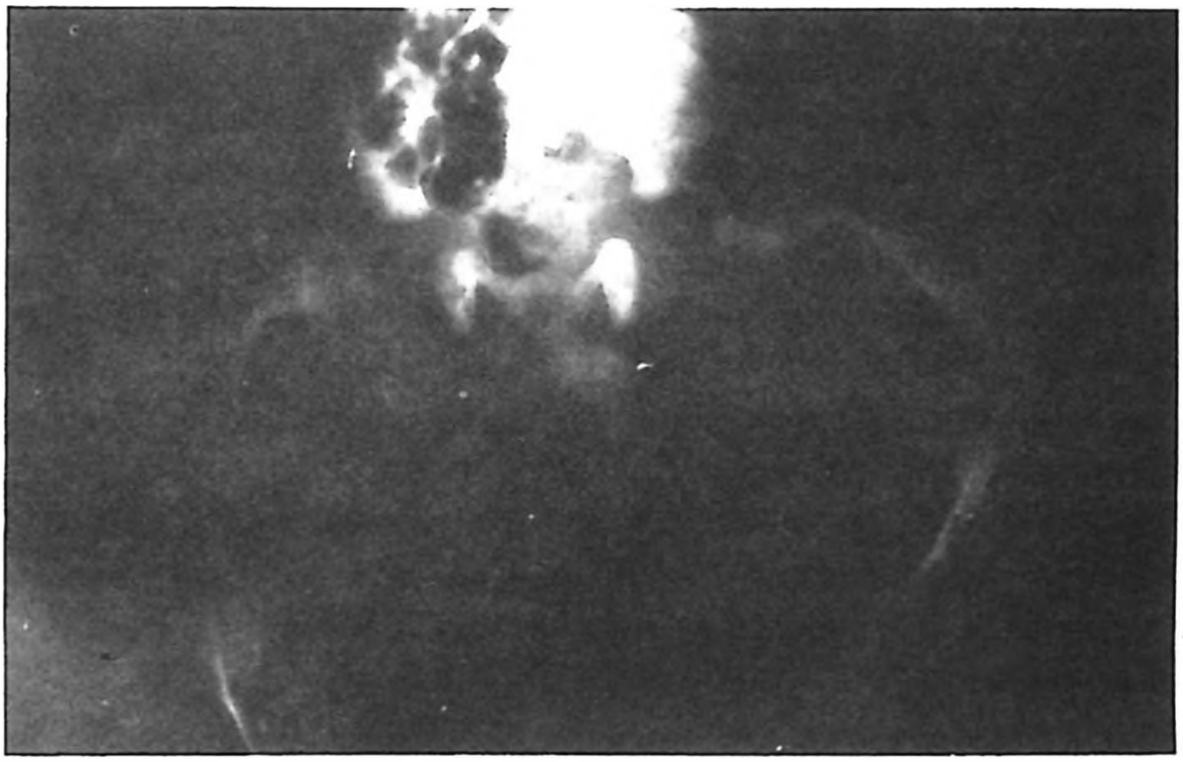

Fig. 2: Defective ossification of the long bones, and bowing of the femora.

mineralized. Because of the low alkaline phosphatase activity as well as phenotypic and radiologic findings resembling hypophosphatasia, we measured the urinary phosphoethanolamine level and found it to be increased (1.4 mmol/g creatinine; normal < 0.3 mmol/g creatinine). The patient was managed for indirect hyperbilirubinemia with phototherapy and exchange transfusion. On the seventh day he was discharged with no clinical problem. Genetic counseling was given to the parents.

Discussion

Hypophosphatasia, which is characterized by a reduced or abesnt alkaline phosphatase activity in the liver, kidney and bone, is transmitted by different modes of inheritance. Perinatal (lethal) and infantile types of hypophosphatasia are autosomal recessive diseases, whereas childhood and adult types have been described as autosomal dominant forms[1,2]. The severity of hypophosphatasia correlates directly with the degree of deficiency of TNS-ALP activity in serum and tissues[3]. Perinatal hypophosphatasia, which manifests at birth, is lethal. Infantile hypophosphatasia presents during the first six months of life, and the disease is also lethal in over half of affected subjects[1,4].

Our patient might be classified as having infantile hypophosphatasia. Moor et al.[2] also described a case of infantile-type hypophosphatasia who was diagnosed on the first day of life and whose brother died of the same disorder. On follow-up, most cases with infantile hypophosphatasia have failure-to-thrive and rachitic like skeletal deformities that result in recurrent respiratory difficulties and hypercalcemia[1,2].

The characteristic radiographic findings are irregularity of the metaphyses of various bones, generalized osteopenia, delayed ossification of the cranial vault, defective ossification of the ribs and long tubular bones, and bowed or deformed long bones. In childhood, metaphyseal lesions may simulate rickets. Bowing deformities and increased bone fragility are characteristically present in both the most severe form (seen in infants) and the mildest form (seen in adults) of hypophosphatasia. Thanatophoric dwarfism has also been taken into consideration in the differential diagnosis[5,6].

In our case, bowing of the femora and the appearance of the metaphyses were different from that seen in rickets. Thanatophoric dwarfism is differentiated by well-ossified calvaria, flat vertebral bodies and short-bowed long bones.

The laboratory findings of pseudohypophosphatasia are quite different from hypophosphatasia, with elevated urinary phosphoethanolamine but normal serum alkaline phosphatase[7].

The methods employed so far in the prenatal diagnosis of infantile hypophosphatasia include ultrasonographic examination of the fetus, measurement of alkaline phosphatase activities in amniotic fluid, and cultured cells from amniotic fluid or chorionic villi[4,8]. Recently, prenatal diagnosis of the disease was successfully carried out using the cDNA for the human-liver-type alkaline phosphatase as a probe with chorionic villi samples[9]. As in our case, the diagnosis of the index case is important, because genetic counseling can be given to the parents.

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