IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

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Case Report

A Rare Case of Neonatal Hypophosphatasia: A Case Report

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ABSTRACT

Hypophosphatasia is a rare hereditary disorder of bone metabolism. In this article, we presented the case of a male infant with a soft skull and short, deformed limbs at birth, followed by seizures and respiratory distress during admission in the neonatal intensive care unit (NICU). Prenatal ultrasound showed limb hypoplasia, skull hypomineralization, and polyhydramnios. Seizures occurred on day nine of admission. The neonate was intubated after pneumonia on day 12 of birth and died due to the same cause and respiratory failure on day 14. Clinical presentation and low alkaline phosphatase (ALP) confirmed the diagnosis of hypophosphatasia. The disorder covers a spectrum of severe neonatal type with severe hypomineralization to various adult types with osteomalacia and dental problems. Prenatal hypophosphatasia is diagnosed based on the clinical signs, including soft skull, short limbs, breathing difficulty, seizures, respiratory distress, laboratory results (low ALP and high pyridoxal 5-phosphate), and radiographic findings (hypomineralization and metaphyseal dysplasia.

Keywords: Hypomineralization, Hypophosphatasia, Rickets

Introduction

In 1948, Dr. Campbell characterized hypophosphatasia by the low level of alkaline phosphatase (ALP) and rickets in an infant who died of rickets and seizures (1). Hypophosphatasia is a rare disorder of the bone metabolism. The disease covers a spectrum of severe neonatal types with severe hypomineralization to adult types with osteomalacia.

Hypophosphatasia is associated with a molecular defect in the gene encoding tissues-nonspecific ALP (TNSALP). Deficiency of TNSALP in the osteoclasts and chondrocytes leads to bone mineralization disorders (2-4).

The present study aimed to report a rare case of prenatal hypophosphatasia.

Case report

A male neonate was referred to Ghaem Hospital in Mashhad, Iran in May 2016. He was born in week 39 of gestation to a 40-year-old mother through vaginal delivery. Birth weight of the infant was 2,820 grams with the height of 47 centimeters and head circumference of 34 centimeters. He was admitted to the neonatal intensive care unit (NICU) at birth due to respiratory distress and tachypnea.

On day nine of birth, the neonate had a seizure. The cognation was normal between the parents and three other siblings, and there was no family history of bone disease. In the prenatal ultrasound, the femur length of the infant was shorter than normal, and the absence of skull bones was observed as well. In the neurological examination, the patient was conscious and had eye contact with no abnormal facial expressions (Figure 1).

Tachypnea with subcostal retraction was detected. The limbs of the neonate were short and deformed (Figure 2). In addition, his skull was soft and without bones. Auscultation of the heart and lung sounds was normal, and there was no organomegaly. The genitalia of the infant were normal as well.

Laboratory test results showed the calcium level of 9.6 mg/dl, phosphorus of 3.8 mg/dl, ALP of 6 u/l, parathyroid hormone level of

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Please cite this paper as:
Pouralizadeh N, Boskabadi H, Mamouri Gh. A Rare Case of Neonatal Hypophosphatasia: A Case Report. Iranian Journal of Neonatology. 2018 Mar: 9(1). DOI: 10.22038/ijn.2018.21593.1248

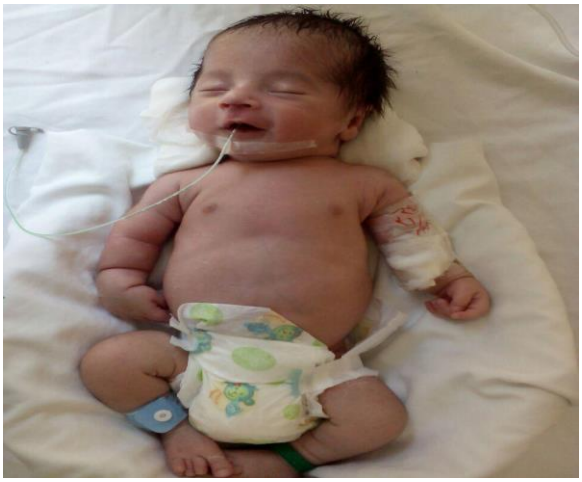

Figure 1. Photograph of the whole body of neonate showing short and deformated limbs

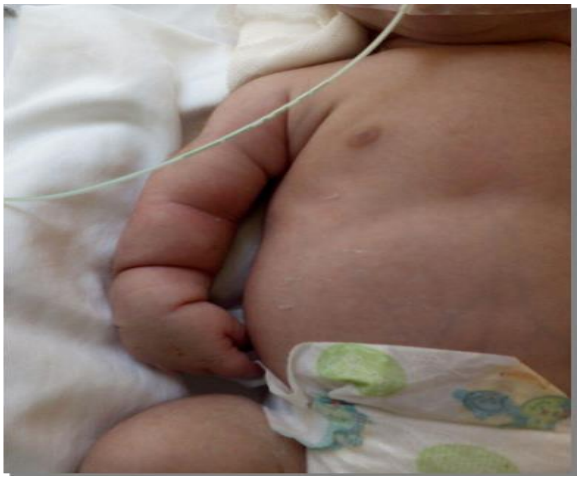

Figure 2. Right upper limb with deformation

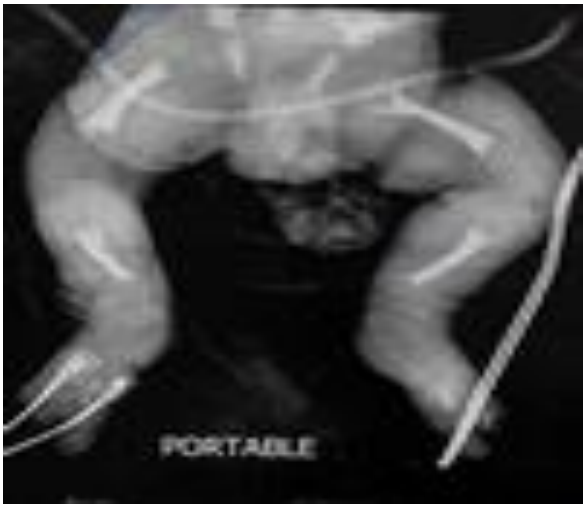

Figure 3. Distal limbs radiogram showing shortening of long bons

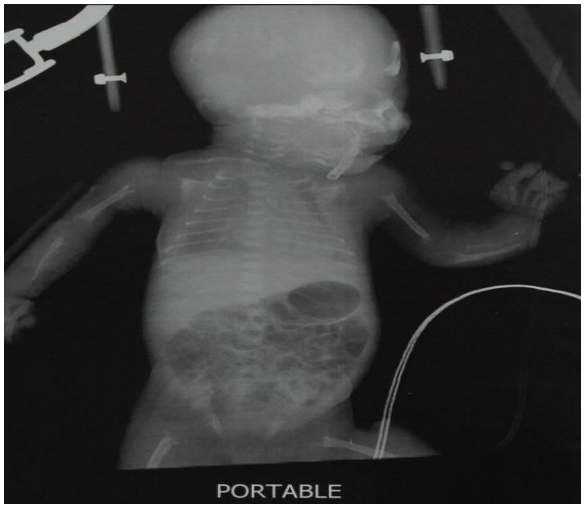

Figure 4. Whole body radiogram showing generalized hypomineralization and absence of mineralization of skull

5.4 mg/dl, hemoglobin level of 9.14 g/dl, and urinary calcium of 10.7 mg/dl. Moreover, C-reactive protein and blood culture were negative, with the ammonia level of 164 µmol/l, and lactic acid of 44 ml/dl. Radiologic assessment showed hypomineralization, metaphyseal dysplasia, narrow ribs, and no ossification in the skull bone (figures 3 & 4).

The patient was administered with phenobarbital and vitamin B6 in order to control the seizures. Additionally, he received mechanical ventilation due to respiratory failure. Despite the clinical measures, the infant died after 14 days due to severe pneumonia and respiratory distress.

Discussion

Hypophosphatasis is a rare disease with the incidence of one per 100,000 live births. Clinically, there are four types of hypophosphatasis (1, 2). Prenatal hypophosphatasis presents at birth and is an autosomal, recessive hereditary disorder. Infants born with this disease often have short extremities, a soft skull, and bone defects. Respiratory failure is also a common manifestation due to pulmonary hypoplasia and osteomalacia in these patients. Furthermore, seizures simultaneously occur due to the vitamin

B6 deficiency in the brain. Anemia is another complication, which is due to osteoid growth and reduced bone marrow (5).

Radiologic findings regarding prenatal hypophosphatasis indicate mineralization disorders and severe osteomalacia, while ossification of the skull is only detected in the center of the bone. These neonates usually have hypercalcemia, hypercalciuria, and low ALP as well.

In prenatal hypophosphatasis, the symptoms present within the first six months of birth, including eating disorders, poor weight gain, and rickets. In addition to the hypomineralization of the skull bones, the ribs and vertebral ossification defects are possible. It is notable that radiologic findings are often milder in the prenatal type of the disorder. Neonatal and adult types of hypophosphatasis are characterized by rickets and dental disorders (6, 7).

Mutations in the gene encoding TNSALP could lead to the deficiency of this enzyme. TNSALP hydrolyzes compounds such as inorganic pyrophosphate (PPi) and pyridoxal 5-phosphate (PLP). PPi accumulation results in the inhibition of hydrate pyruvate formation, eventually causing osteomalacia and rickets. PLP is an active form of vitamin B6, which should be dephosphorylated by TNSALP. TNSALP deficiency leads to the deficiency of vitamin B6 in the brain, as well as neurotransmitter synthesis disorder (8).

Laboratory diagnosis of hypophosphatasis is associated with the reduction of ALP and increased PLP. Radiologic assessment shows hypomineralization, rickets, and incomplete spinal mineralization. Definitive diagnosis of the disease is based on detecting the gene mutation coding of TNSALP (1, 2). Hypophosphatasis has supportive treatment, in which vitamin B6 is used to control neonatal seizures. In 2015, the Food and Drug Administration (FDA) approved enzyme replacement therapy (phosphatase alpha) to be an effective measure in this regard (9, 10).

Conclusion

Neonatal hypophosphtasia is a rare severe bone disorder that may have other manifestations such az siezure and respiratory distress so control of siezure and respiratory support are very important in this patients.

Acknowledgments

None.

Conflicts of interests

None.

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