A CASE WITH LETHAL PERINATAL HYPOPHOSPHATASIA

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Introduction: Hypophosphatasia (HPP) is a rare metabolic bone disease caused by loss-of-function mutations in the gene ALPL encoding the tissue nonspecific alkaline phosphatase (TNSALP). HPP is associated with significant morbidity and mortality in paediatric patients, with high rates as high as %100 in perinatal-onset HPP and 50% in infantile-onset HPP. Serum alkaline phosphatase (ALP) activity is markedly reduced, which leads to increased serum/urine phosphoethanolamine (PEA), inorganic pyrophosphate and pyridoxal-5′phosphate (PLP). Asfotase alfa is the first-in-class, bone-targeted, enzyme-replacement therapy designed to reverse the skeletal mineralization defects in HPP. We present here a male infant with perinatal lethal HPP.

Case: He was a full-term infant of a G6P1 mother who delivered by Cesarean section. After birth, he was promptly intubated and ventilated because of respiratuary distress. Prenatally, bone deformities had been noticed. On physical examination his weight was 3020 g, length was 45 cm and head circumference was 33 cm. His skull bones were not formed. Radiographs demonstrated thin ribs, thoracic cage deformities, poor ossification of the skull, and epiphysis of the long bones. Laboratory examinations revealed serum ALP was 0 U/l , serum phosphate was 7.3 mg/dl (range 2.5–4.5), serum calcium was 9.8 mg/dl (range 9-11) and parathyroid hormone level was 40 pg/ml (range 12–72). Serum total 25-hydroxy vitamin D levels were normal. Perinatal lethal HPP diagnosis was based on physical findings, laboratory investigations, and radiographic skeletal features. Urine PEA and plasma PLP levels were markedly elevated (1081 µmol/L (normal range 15-341), 3942 µg/L (0-50) respectively).

Asfotase alfa (Strensiq) therapy (2 mg/kg/d s.c three times per week) was started at 30 d of age. Serum calcium and phosphate levels were normal but ALP levels increased as high as 12700 U/L during treatment (Figure1).He died at the age of 65 days because of ventilator associated pneumonia and sepsis.

Conclusion: Perinatal lethal hypophosphatasia is the most severe form of hypophosphatasia. These severely affected babies often die at or soon after birth from respiratory insufficiency due to pulmonary hypoplasia, a consequence of poorly mineralized bones of the chest.Therefore early treatment is crucial for prognosis.

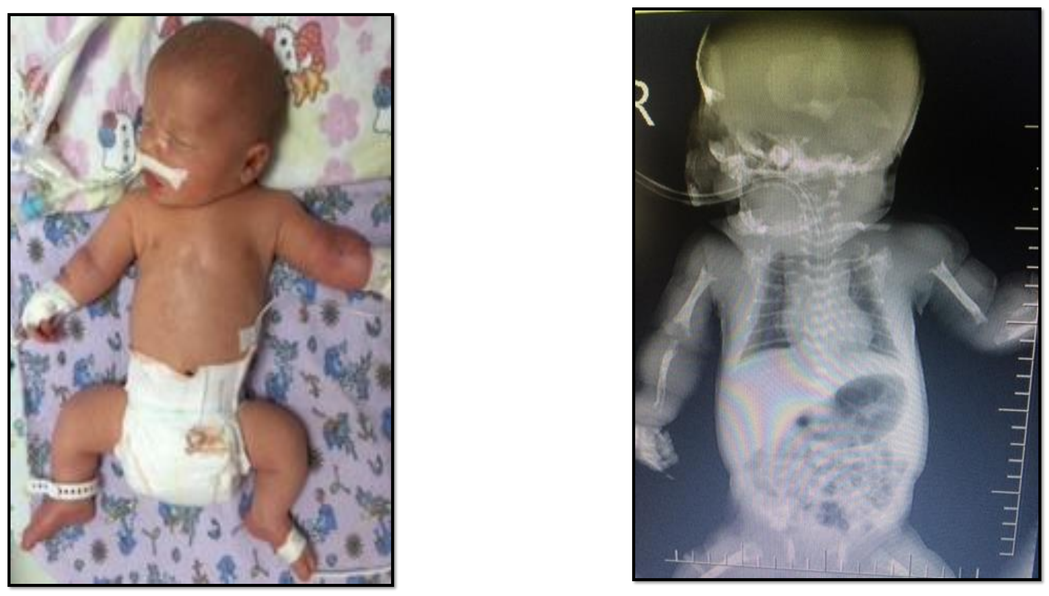
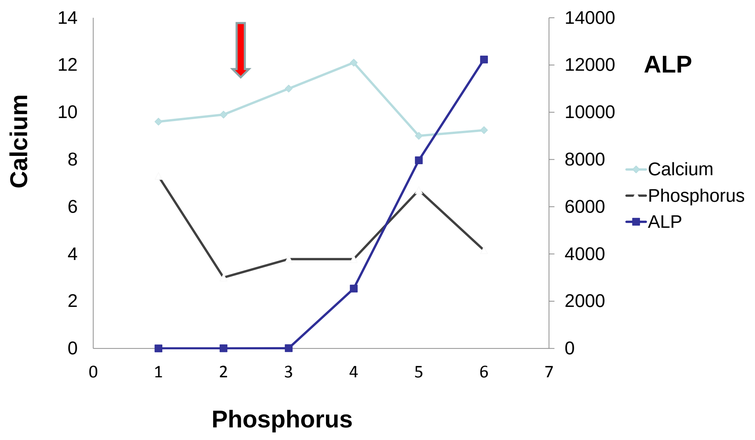


Figure 1. The patient's Serum Ca, Phosphorus and ALP levels



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