Hypophosphatasia: Misleading In Utero Presentation for Childhood and Odonto Forms

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Abstract

Hypophosphatasia (HPP) is a rare hereditary disease that presents with perinatal or infantile bone fractures, rickets/osteomalacia featuring deficient activity of the "tissue nonspecific"isoenzyme of alkaline phosphatase (TNSALP) from deactivating mutation of the TNSALP gene. In many cases, the clinical course is characterized by severe bone deformities, micrognathia, hypogonadism, and thoracic deformities. The birth weight of most patients is normal, but skeletal hypomineralization in utero may precede birth by 1 to 2 months. When skeletal radiographs are obtained in utero, findings similar to those in some patients with perinatal HPP may be observed. However, these findings may not imply a severe course. We present the clinical findings of 11 patients with perinatal HPP. Eight of the 11 patients presented in the perinatal or infantile period. The only patient with onset of clinical manifestations before birth was a stillborn infant, who presented with hypomineralization found at autopsy. In this particular child, there was also oligohydramnios and his physical examination showed dimples overlying his lateral forearms and thighs, slight gray sclera; rib flaring, knock-knees, 5º bowing in HPP.

Introduction

Hypophosphatasia (HPP) is a rare hereditary disease that presents with perinatal or infantile bone fractures, rickets/osteomalacia featuring deficient activity of the "tissue nonspecific"isoenzyme of alkaline phosphatase (TNSALP) from deactivating mutation of the TNSALP gene. In many cases, the clinical course is characterized by severe bone deformities, micrognathia, hypogonadism, and thoracic deformities. The birth weight of most patients is normal, but skeletal hypomineralization in utero may precede birth by 1 to 2 months. When skeletal radiographs are obtained in utero, findings similar to those in some patients with perinatal HPP may be observed. However, these findings may not imply a severe course. We present the clinical findings of 11 patients with perinatal HPP. Eight of the 11 patients presented in the perinatal or infantile period. The only patient with onset of clinical manifestations before birth was a stillborn infant, who presented with hypomineralization found at autopsy. In this particular child, there was also oligohydramnios and his physical examination showed dimples overlying his lateral forearms and thighs, slight gray sclera; rib flaring, knock-knees, 5º bowing in HPP.

Discussion

The first patient: A 3-9/12 year old Caucasian boy (II-5) was 3 lbs 14 oz at birth. His family was counseled concerning possible termination of the pregnancy. Premature labor and delivery was complicated by fetal distress. Concerns regarding his skeletal abnormalities led to C-

Conclusions

Over the past 5 years, 50 new HPP patients have been diagnosed in a large national database. HPP patients have been described at birth, and many have presented with bone fractures, characteristic facial features, and bone deformities. Three additional cases, each with distinct clinical features, are described here. The clinical presentations of these cases are not characteristic of the severe course seen in perinatal HPP. As such, these cases may represent a milder form of the disease. We recommend that clinicians consider the diagnosis of HPP in cases of perinatal or infantile onset of bone fractures, hypocalcemia, or rickets/osteomalacia. The diagnosis of HPP should be considered in all cases of skeletal hypomineralization in utero and after birth. The diagnosis of HPP should be considered in all cases of skeletal hypomineralization in utero and after birth.