Mild Hypophosphatasia In Utero

Bent Bones in a Family With Dental Disease

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When fetal bones appear fractured or severely bent, the differential diagnosis includes such worrisome diagnoses as osteogenesis imperfecta. This case illustrates a relatively benign cause of angulated bones that can be discerned by asking several pertinent questions about the family's dental history.

Case Report

A 35-year-old patient, gravida 2, para 1, had a sonographic examination at 18 weeks' gestation to assess fetal growth. The scan showed acute angulation of the humeri (Figures 1 and 2). The remainder of the fetal long bones appeared straight and of normal length. The ends of the long bones were not flared and were of normal sonographic density. Chest size was normal, and the skull and spine were normally calcified. Serial scans throughout the course of pregnancy showed appropriate interval growth of the angulated humeri and the remainder of the long bones. The differential diagnosis included the various types of skeletal dysplasias that could produce angulated or broken bones such as osteogenesis imperfecta, camptomelic dysplasia, achondrogenesis, and thanatophoric dysplasia. The primary diagnosis would have been a mild form of osteogenesis imperfecta. However, the patient gave the following history on further questioning. The mother-in-law, brother-in-law, and husband had an abnormality of the gums or teeth. The records the patient provided showed that an evaluation was made by a professor of oral genetics at a dental

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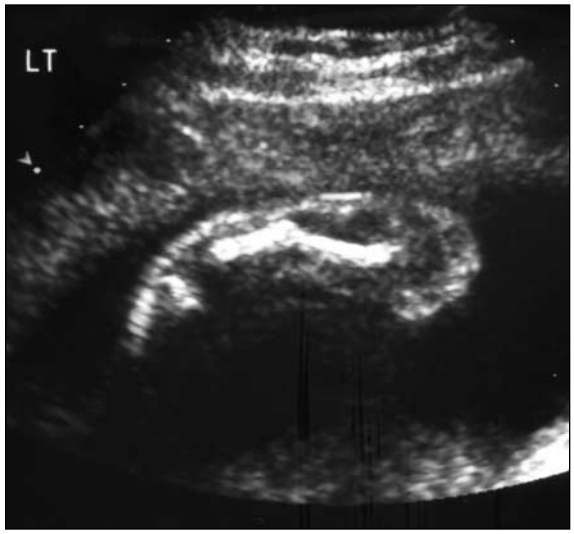
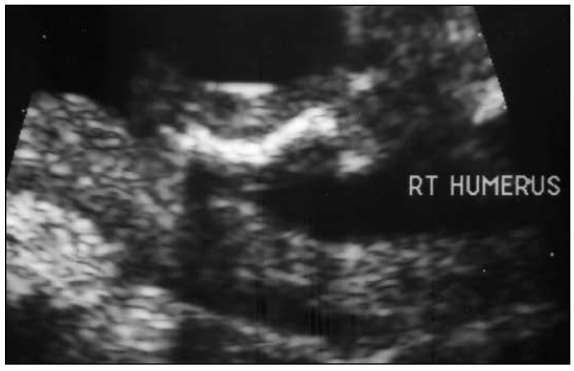


Figure 1. Left humerus, prenatal. There is marked angulation, which gives the appearance of a fracture.

school when the husband was 2 years old. At that time, the observation was made that he had little dental cementum present at the roots of the teeth. He was told that he also had a slightly short right leg at that time. The possibility of hereditary hypophosphatasia was mentioned in the differential diagnosis. Further evaluation was suggested but had never been performed except on his brother, who was found to have a borderline low level of alkaline phosphatase. Later, the husband reported multiple cavities and crowns. Alkaline phosphatase and paternal bone-specific alkaline phosphatase levels in the husband were ordered during this pregnancy, and each was low (26 and 6.4 U/L, respectively). Diagnostic DNA analysis performed on cells obtained by amniocentesis showed a V365I sequence variant that was predicted to be pathologic.

Figure 2. Right humerus with angulation.



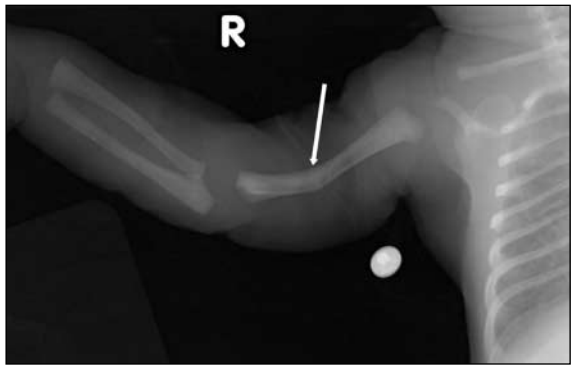
The patient gave birth to a boy weighing 3650 g at 40 weeks' gestation. Neonatal radiographs showed slightly angled humeri (Figure 3), but the remaining long bones were otherwise normal. The bone-specific alkaline phosphatase level was decreased at birth (18 U/L) and then later low normal. A follow-up level obtained later in the neonatal period was within the low normal range.

Discussion

Hypophosphatasia causes defective bone mineralization because of a mutation in the gene encoding tissue-nonspecific alkaline phosphatase, which results in less than adequate activity of alkaline phosphatase. There are at least 128 described mutations of this gene. The more severe forms result in stillbirth or children with markedly abnormal bones, whereas the milder forms may be limited to low alkaline phosphatase levels and poor dentition. The teeth are predisposed to cavities and may be lost prematurely.

Mild autosomal dominant hypophosphatasia has been report in utero.[1,2] In 4 pregnancies in 2 families, severe long bone bowing of the humeri, femurs, and tibiae was reported in utero. The bowing was so angulated that the long bones appeared to be fractured. Improvement in the degree of bowing was noted during the postnatal follow-up. The 4 children in study by Moore et al[2] had low alkaline phosphatase levels at birth. By age 5 years, 1 had dental anomalies that included exposure of the roots of the teeth below the gum line. Family 1 did not have the tissue-nonspecific alkaline phosphatase gene mutation found in family 2.

Figure 3. Radiograph of the neonate's right humerus with angulation (arrow).



The child in the case described here can be predicted to have dental problems in the future but have no other apparent abnormalities. When bent bones are identified during prenatal sonography, a brief dental history of the family can be invaluable in limiting the differential diagnosis because bone angulation in mild odontohypophosphatasia shows improvement and suggests a good prognosis.

References

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