

Perinatal lethal hypophosphatasia: Fetopathological findings in three cases

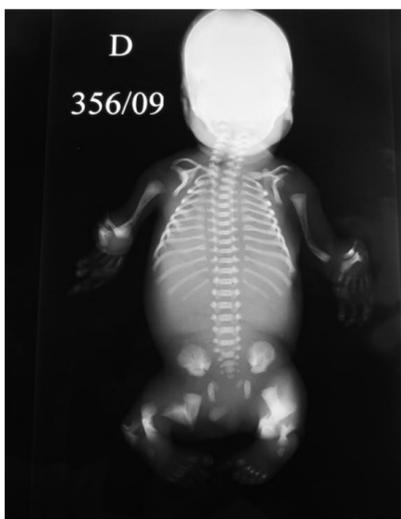
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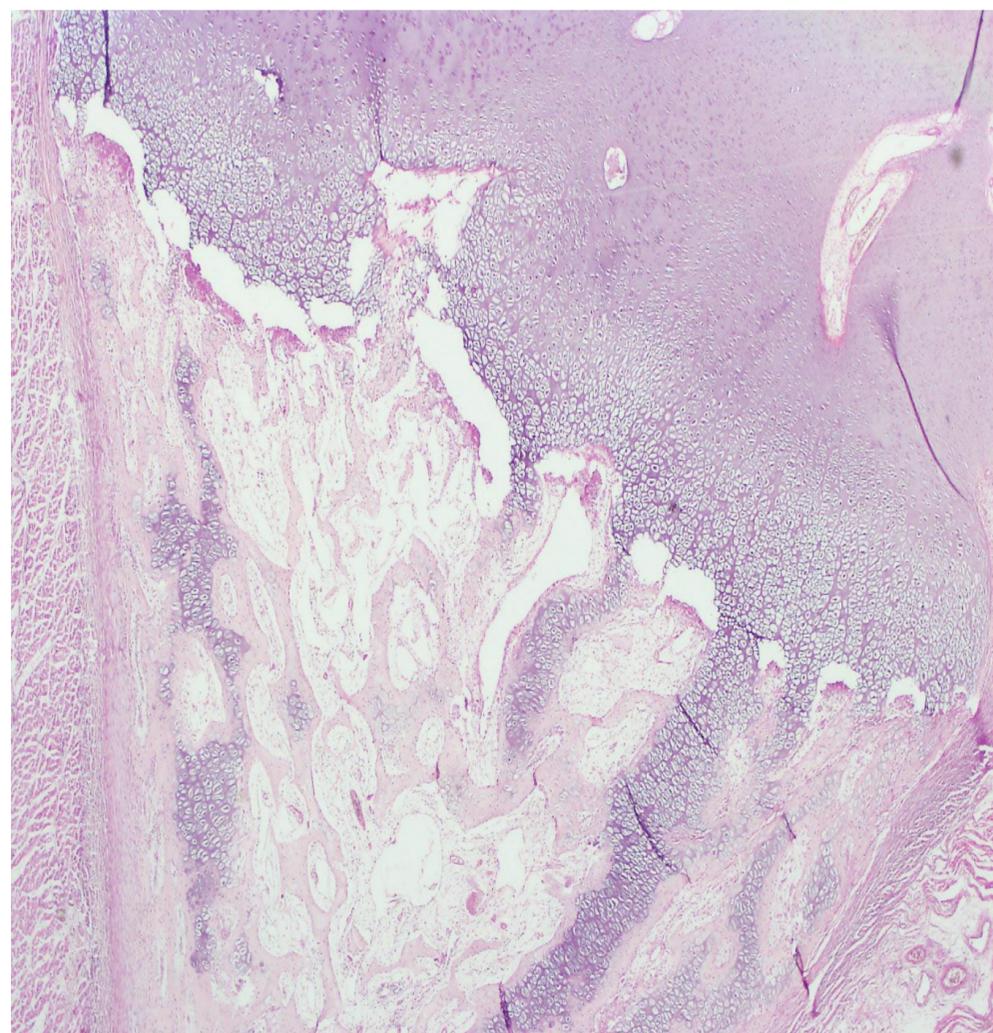
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Introduction: Hypophosphatasia is a rare skeletal dysplasia, related to inactivating mutations in the TNSALP gene encoding the tissue-nonspecific alkaline phosphatase. This enzyme deficiency mainly results in disorders of bone and teeth mineralization. The phenotypic spectrum ranges from perinatal lethal to mild form diagnosed in adulthood. We describe the lethal form in three affected fetuses, one female and two males.

Case report: Antenatal ultrasound detected micromelia and generalized demineralization. Termination of pregnancy was performed at 18, 22 and 25 weeks of amenorrhea. Skeletal radiographs showed irregular ossification in all cases, that was very poor with only few mineralized bones in two cases, and associated with bowing of the long bones and large, irregular metaphyses in one case. Macroscopic examination showed micromelia, bowing of the limbs and a characteristic craniofacial dysmorphism including relative macrocrania, hypertelorism, small nose with anteverted nostrils, long philtrum, thin lips, microretrognathia and low-set ears. Bilateral tibial or tibio-peroneal spurs were observed in two cases :



Note the phenotypic variability of affected fetuses



Histology discloses the presence of columns of hypertrophic chondrocytes invading the diaphysis (H&E, ×20).

Conclusion

Perinatal hypophosphatasia is characterized by severe micromelia and major deficit or complete absence of the bone mineralization. It is often confused with osteogenesis imperfecta on prenatal ultrasound. However, the 3D ultrasound can detect the characteristic bone spurs in the early second trimester and strongly orient the diagnosis towards lethal hypophosphatasia. The diagnosis is confirmed by detailed fetopathological examination including skeletal radiography, macroscopic examination and histological study of long bones. Genetic counseling can be offered with genetic testing to parents.