

Prenatal diagnosis of brachytelephalangic chondrodysplasia punctata: case report

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ABSTRACT

Brachytelephalangic chondrodysplasia punctata is a rare congenital skeletal dysplasia. Within the heterogeneous group of chondrodysplasia punctata, the brachytelephalangic type is noteworthy because it has a better prognosis than do the other types. We report a case of brachytelephalangic chondrodysplasia punctata diagnosed by ultrasound imaging at 30 weeks' gestation; it was associated with polyhydramnios and a normal cervical spinal canal. Imaging features are described and differential diagnosis with other forms of chondrodysplasia punctata is discussed. Copyright © 2009 ISUOG. Published by John Wiley & Sons, Ltd.

CASE REPORT

A 24-year-old woman, gravida 4 para 2, with a history of unexplained spontaneous abortion at 16 weeks' gestation was referred at 30 weeks' gestation following ultrasound detection of a marked flattening of the nose associated with polyhydramnios. The parents were African, unrelated and there was no family history of skeletal, genetic or congenital anomalies. There was no history of exposure to alcohol, drugs or teratogens including warfarin and hydantoin. Infectious disease antibody test showed positive immunoglobulin titers for rubella, and negative titers for cytomegalovirus (CMV), human immunodeficiency virus, and hepatitis B and C viruses. The first ultrasound examination performed at 12 weeks' gestation was normal. Triple test screening for trisomy 21 was performed at 15 weeks' gestation and was normal (risk of 1/3913). At 22 weeks' gestation, ultrasound examination revealed a single male fetus with

a flat nasal bridge and polyhydramnios. Amniocentesis was performed at 27 weeks' gestation. The karyotype was normal (46,XY), and neither CMV nor parvovirus infection was found.

The patient was referred to our institution at 30 weeks' gestation and ultrasound examination confirmed polyhydramnios and facial anomaly with Binder's facial dysmorphism. Moreover, ultrasonography showed skeletal anomalies including stippling of the vertebrae, coccyx, proximal femora, tarsal and carpal bones with triangular hypoplastic tufts (Figure 1). Femoral length was within the normal range. On the basis of these sonographic findings, the diagnosis of brachytelephalangic chondrodysplasia punctata (CDP) was suggested.

However, as the polyhydramnios remained unexplained, fetal magnetic resonance imaging (MRI) of the spinal cord was performed in order to rule out cervical spinal cord compression that could account for swallowing disorders. The cervical spinal cord was normal.

At 40 weeks' gestation, the woman delivered a boy whose birth weight, height and head circumference were within the normal range. No swallowing disorders were observed after birth. Postnatal radiographs of the spine and limbs confirmed the presence of epiphyseal punctuate calcifications in the humeri, femora, tarsal bones and vertebrae, and characteristic triangular hypoplastic distal phalanges in the hands and feet (Figure 2). The fourth metacarpal bone was irregular and shortened. Long bones were of normal length except for mild bilateral humeral shortening. At the time of writing, the infant was 4 months old and showed normal development.

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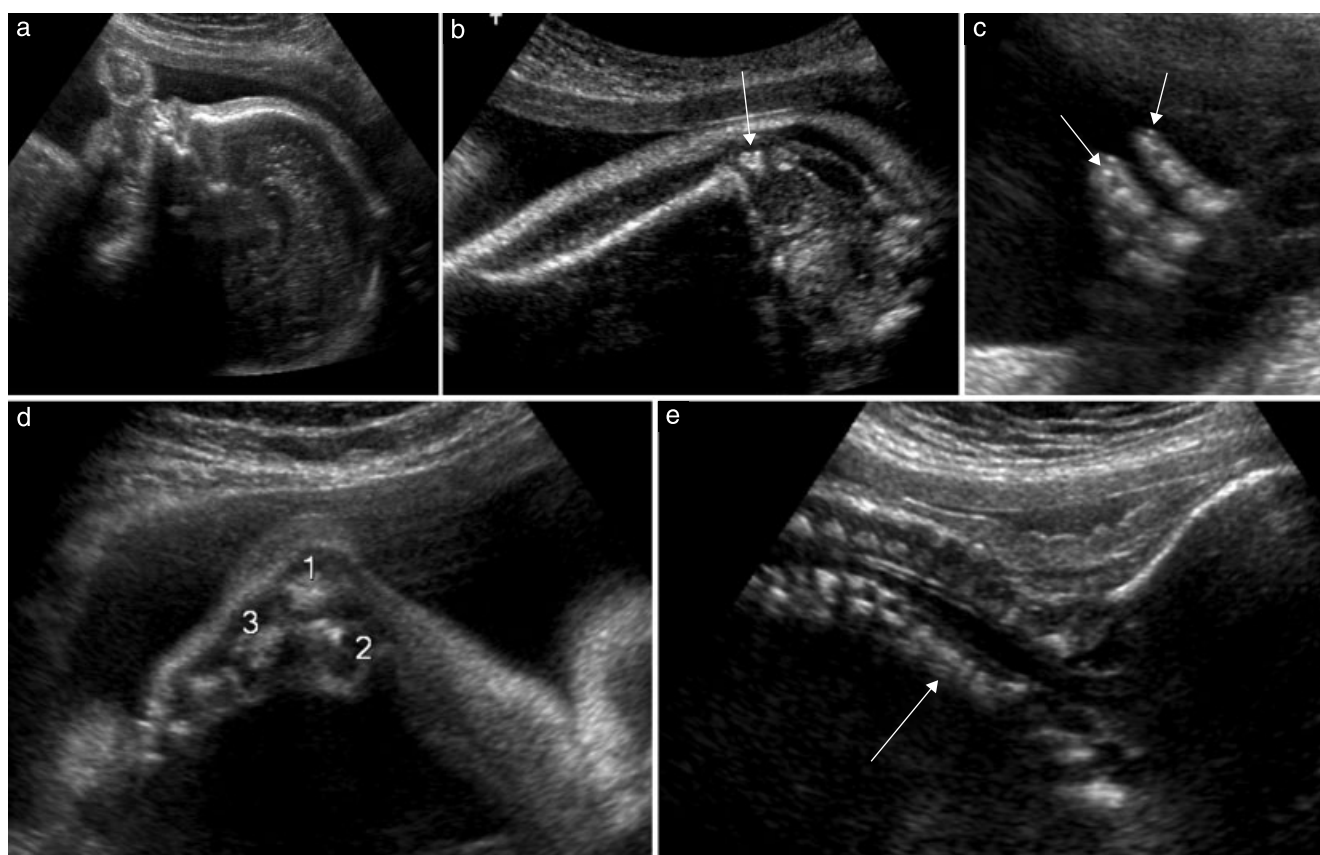


Figure 1 Prenatal ultrasound examination performed at 30 weeks' gestation. (a) Binder's dysostosis with depressed nasal bridge. (b) Proximal end of the femur with stippling close to the femoral head (arrow). (c) Second, third and fourth fingers with hypoplastic distal phalanges (arrows). (d) Lateral view of the foot. The ossification centers of the calcaneus (1) and the talus (2) are enlarged owing to stippled calcification. The ossification center of the cuboid bone (3) is visible prematurely. (e) Lateral view of the cervical spine. Diffuse stippling of the vertebral bodies (arrow) is responsible for their blurred appearance.

DISCUSSION

CDP represents a heterogeneous group of skeletal disorders characterized by premature and disordered stippling of cartilage. The differential diagnosis includes chromosomal abnormalities and abnormal fetal morphology caused by maternal diseases such as lupus erythematosus, and maternal exposure to viruses including CMV or to drugs such as warfarin or alcohol¹. Different types of CDP have been described, with different modes of inheritance. Most of them carry a poor prognosis being associated with dwarfism, cutaneous and ocular abnormalities, and psychomotor retardation².

Brachytelephalangic CDP is an X-linked inherited form and is caused by mutations in the arylsulfatase E gene. It is noteworthy because of its better prognosis, without dwarfism and cutaneous or ocular abnormalities. Patients present with short hands and feet with hypoplastic nails. As in other types of CDP, the patients present with characteristic facial dysmorphism (Binder's maxillo-facial dysostosis), but their psychomotor development is normal². A few severe cases of brachytelephalangic CDP have been described. They were characterized by severe respiratory distress, secondary to spinal cord compression related to marked cervical spinal canal stenosis^{3,4}. In our case, fetal MRI of the spinal cord was performed in order

to rule out this complication, as polyhydramnios might be the consequence of cervical spinal cord compression. In the literature, polyhydramnios has been reported in association with such a compression³ or with foramen magnum stenosis⁵, but it has also been reported in other cases of CDP and remained unexplained^{6–8}.

Specific radiological findings of the brachytelephalangic form include punctate calcifications of the vertebrae and tarsal bones, proximal phalangeal and metacarpal hypoplasia, and triangular hypoplastic distal phalanges. Punctate calcifications disappear in infancy and childhood with reversion to normal bones². Metacarpal shortening has been reported in the tibia–metacarpal type of CDP^{6,7}, which can be considered a subtype of brachytelephalangic CDP.

Both skeletal and facial anomalies of CDP are detectable with prenatal ultrasound imaging, and a few cases of prenatal Binder's dysostosis with a flattened nasal bridge and vertebral and limb stippling have been reported^{5,6,8–14}. However, so far, the specific findings of the brachytelephalangic type have not been diagnosed by prenatal ultrasound examination. In our case, careful analysis of the hands showed shortened and triangular distal phalanges.

Characterization of the type of CDP is very important as the brachytelephalangic type carries a much better prognosis than the other types.

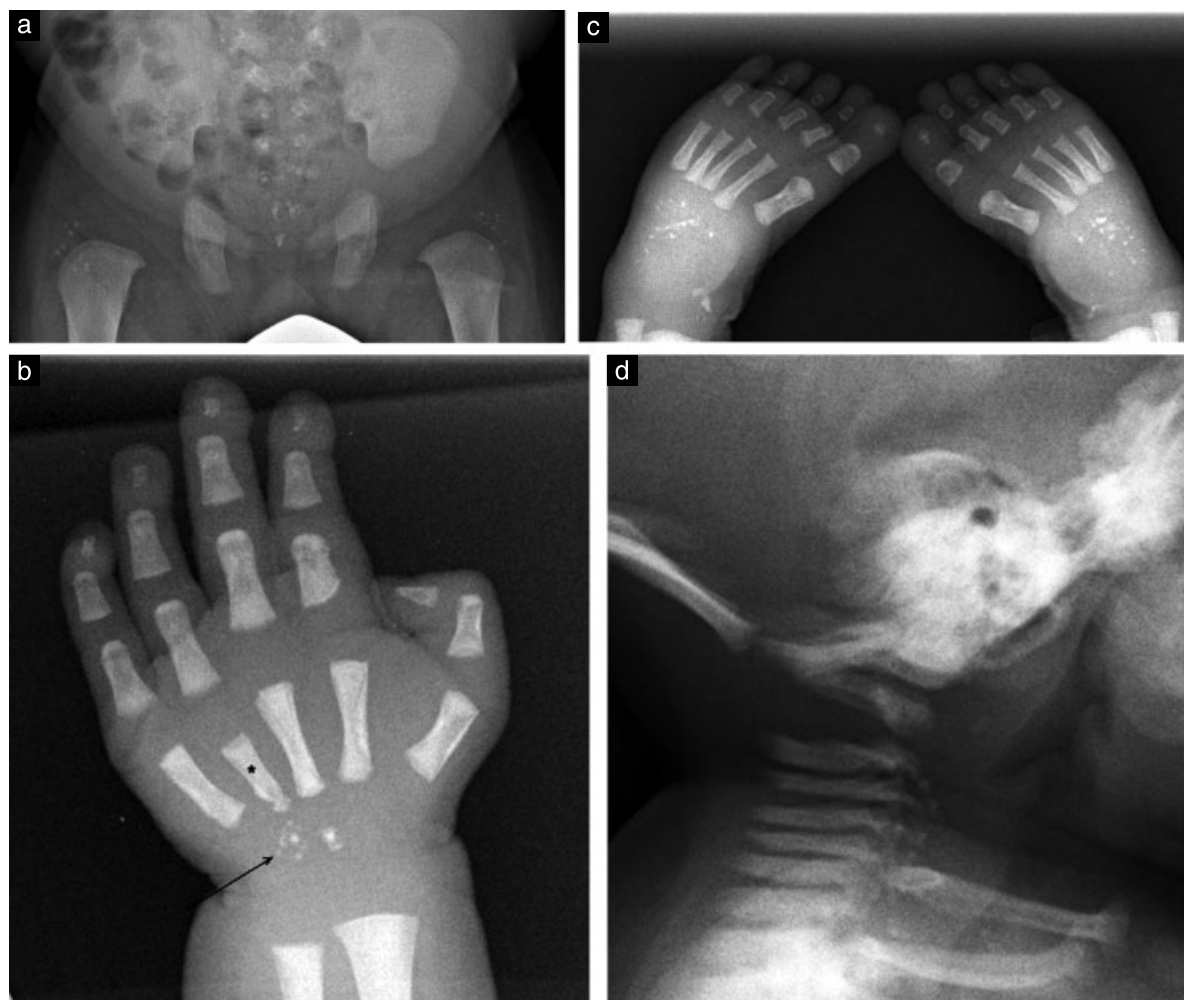


Figure 2 Radiographs at birth. (a) Anteroposterior view of the pelvis showing stippling in the proximal femora and the coccyx. (b) Anteroposterior view of the left hand. The distal phalanges are markedly hypoplastic. Note irregularity and shortening of the fourth metacarpal bone (*) as well as stippling of the carpal bones (arrow). (c) Anteroposterior view of the feet. The last phalanges of the toes are hypoplastic and there is stippling of the tarsal bones. (d) Lateral view of the cervical spine, showing stippling and absence of visibility of the vertebral bodies.

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