

Osteogenesis Imperfecta with Chondrodysplasia Punctata: A New Syndrome

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Abstract

A 32 years old G6p5 presented with full-term pregnancy and polyhydramnios. Sonography diagnosed skeletal dysplasia, AFI 38 cm and extremely calcified grade 3 placenta. Postmortem radiograph confirmed osteogenesis imperfecta type 2 and chondrodysplasia punctata. The baby died of respiratory distress. This lethal association should be kept in mind whenever skeletal dysplasia is detected.

Keywords: Osteogenesis imperfecta, chondrodysplasia punctata, polyhydramnios.

We report a case with manifestations of osteogenesis imperfecta type II and chondrodysplasia punctata. The prenatal sonography revealed features of severe skeletal dysplasia and severe polyhydramnios. When delivered, the baby had craniofacial dysmorphism, thick skin folds, short narrow thorax, grey sclera, and died of severe respiratory distress. Postmortem X-ray showed multiple long bone and rib fractures, a small narrow thorax, and punctuate calcification of epiphysis.

Though very rarely reported, this lethal association of these skeletal disorders should be borne in mind whenever coming across a skeletal dysplasia.

INTRODUCTION

Osteogenesis Imperfecta (OI) is a group of heterogenous skeletal dysplasias due to defective collagen synthesis, which mainly constitutes of 4 types, type II being the most severe.¹ The incidence of OI type II is 1 per 55,000.¹ The characteristic features of the disease include widespread fractures, global hypomineralization and shortening of bones.

Chondrodysplasia punctata is a group of rare multisystem developmental disorders leading to abnormal intrauterine bone mineralization. The main types include rhizomelic, X-linked dominant (Conradi Hunermann Syndrome), X-linked recessive, and tibia-metacarpal.²

We report a case of osteogenesis imperfecta type II with sonographic features of X-linked dominant chondrodysplasia punctata.

CASE

The patient was an unbooked 32-year old woman, G6P5L4 presenting to the hospital at term because a sonogram at a private center showed polyhydramnios and fetal skeletal abnormalities. Previous obstetric history was normal except for the last gestation in which a term male baby delivered at home expired soon after birth due to respiratory distress and had a very narrow thorax. In this pregnancy there was no history of intake of any drug or any complication thus far. There was no history suggestive of diabetes, hypertension or any other medical disorder. The parents were not consanguineous. All routine antenatal laboratory tests were within normal ranges. General and systematic examinations of the patient did not reveal any abnormality. Obstetric examination revealed a uterine size of 36 weeks gestation. Abdomen was tense, fetal parts were not easily palpable, and fetal presentation could not be made out due to clinically excessive liquor. Fetal heart-rate was regular, 132 bpm, though faintly audible. Patient was advised a scan. Sonography was performed with linear array real time sonographic system (Siemens-Sonoline Adara, General Electric Model RT-3200). Scan (Figs 1 and 2) reported a live fetus of around 37 weeks gestation with multiple epiphyses of long bones, hypomineralized skull and widespread bone fractures. The bones of extremities were shortened, bowed with angular deformities and multiple fractures. Thoracic cavity was narrow and ribs were seen to have multiple fractures. The findings were consistent with severe skeletal dysplasia. Amniotic fluid index (AFI) was 38 cm and placenta was extensively calcified, of grade III maturity.

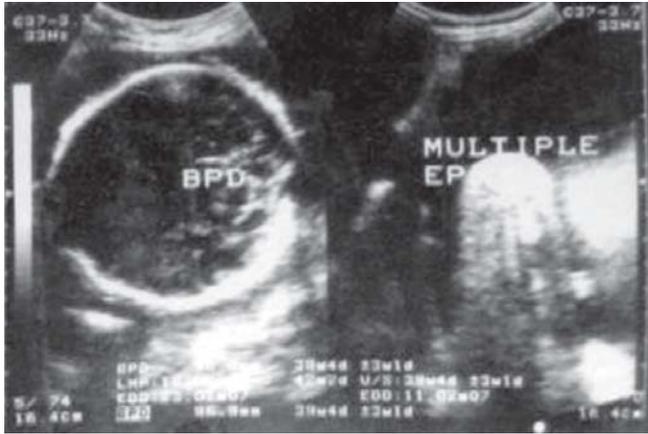


Fig. 1: The USG scan showing hypomineralized skull and multiple epiphyses of long bones

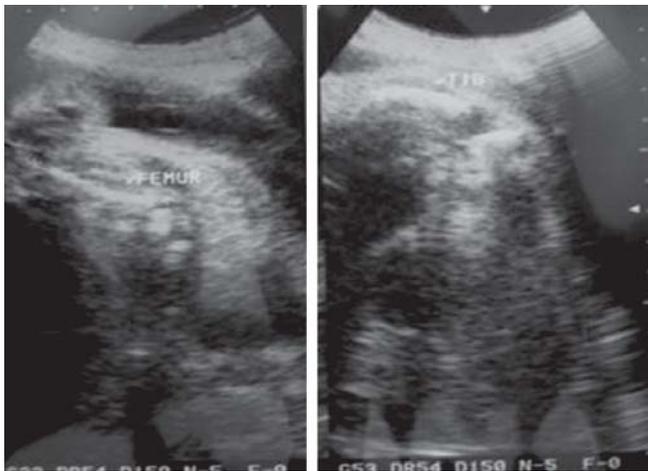


Fig. 2: The USG scan showing femur with multiple fractures and bowing of the tibia

Prognosis of the baby was discussed with the parents. Amniotic fluid decompression was started, followed by induction of labor. A live male baby of 2.8 kg was delivered. The Apgar Score at 5 minutes was 2/10, baby was in severe respiratory distress, and could not be resuscitated. Head and chest circumferences were 40 and 20 cm, respectively. Noteworthy external features included a narrow thorax, concave chest contour, thick cracked skin folds, proptotic eyes, grey sclerae, facial dysmorphism with low-set ears, and a depressed nasal bridge (Fig. 3).

Gross examination of the placenta showed no appreciable cotyledons and microscopy revealed marked fibrosis, extensive calcification and thrombosis of blood vessels. Parents did not consent for autopsy.

Postmortem fetal radiograph (Fig. 4) showed stippling or punctuate calcification of long bone epiphyses and vertebral transverse processes. Multiple fractures were seen in different stages of healing involving almost all the long bones, ribs, bilateral scapulae, mandible and facial bones. Cranial vault was



Fig. 3: Postmortem photograph of the baby (with permission) showing a narrow thorax, concave chest contour, thick cracked skin folds, proptotic eyes, grey sclerae, facial dysmorphism with low-set ears, and a depressed nasal bridge



Fig. 4: The postmortem X-ray of the patient (with permission) showing stippling or punctuate calcification of long bone epiphyses and vertebral transverse processes. Multiple fractures are seen in different stages of healing in long bones, ribs, mandible, and facial bones. Orbits are looking prominent due to hypomineralized skull. Long bones are shortened and angulated due to multiple fractures

hypomineralized with prominent orbits. Long bones were shortened and angulated due to multiple fractures. These radiographic findings were again consistent with Osteogenesis Imperfecta type II and chondrodysplasia punctata and could have been confirmed by peroxisome and cholestanol test results and fibroblast studies.

COMMENTS

Fetuses with osteogenesis imperfecta type II are divided into 3 groups: A, B, and C. Subtype A exhibits typical triad of bone shortening, diffuse hypomineralization and multiple fractures of long bones including beaded ribs. Chest cavity is small. This subtype is lethal either prenatally or in early infancy. Babies are born with severe respiratory distress. Subtype B shows shortening of only femurs, normal bone echodensity and isolated fractures of long bones. Subtype C is the most severe form with extensive demineralization and widespread fractures. Other findings, occasionally found, may include amniotic fluid abnormalities, hydrops fetalis and small for gestational age.³ Sonographic features like bone shortening, hypomineralization and multiple fractures can help in making a confident diagnosis of OI type II.

X-linked CDP, also known as Conradi-Hunermann Syndrome is a rare, multisystem, developmental disorder, characterized by the presence of stippled foci of calcification, dwarfing, joint contractures, congenital cataract, ichthyosis, and severe mental retardation. Punctate calcifications are also seen in multiple forms of the Zellweger syndrome, maternal ingestion of anticoagulants like dicoumarol or warfarin in early pregnancy, and even trisomies.⁴ The cataracts are present in about 72% of cases, and cutaneous manifestations in about 27%.⁵ Biochemically, these patients have subnormal levels of red cell plasmalogens and progressive accumulation of phytanic acid starting from normal at birth and increasing to levels more than 10 times normal by age 1 year.^{6,7} The combination of punctate calcifications, rhizomelia, and the biochemical abnormalities (deficient red cell plasmalogens and accumulation of phytanic acid) is pathognomic of X-linked CDP.

In this case, the long bones were shortened, irregular, and fractured. Skull bones were hypomineralized, ribs were fractured and beaded and the thoracic diameter was very narrow. Baby was born with severe respiratory distress and mother had polyhydramnios. These features favor OI type II.

However, in addition to these features, long bones had multiple epiphyses, there were thick cracked skin folds and facial dysmorphism was evident. Popcorn calcifications were seen at the epiphyseal ends of humeri and femori. A definitive diagnosis of CDP could have been made with the help of fetal autopsy and biochemistry, which, unfortunately, could not be done in this case.

Family history of this case was relevant as the previous male child had died of severe respiratory distress at birth and had features similar to this baby. No records were available as that was a home delivery.

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