

A lethal skeletal dysplasia with features of chondrodysplasia punctata and osteogenesis imperfecta: an example of Astley-Kendall dysplasia. Further delineation of a rare genetic disorder

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Abstract

An unusual osteochondrodysplasia presenting with lethal neonatal short limbed dwarfism, defective ossification, and punctate calcification within cartilage is presented. The features resemble four cases previously described with Astley-Kendall dysplasia.

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A review of 3500 cases on the Skeletal Dysplasia Registry of the Department of Radiology, Great Ormond Street Hospital for Children NHS Trust identified a fetus with striking radiological features resembling both chondrodysplasia punctata and osteogenesis imperfecta.

Astley-Kendall dysplasia is characterised radiologically by absent ossification of the cranial vault and multifocal ossification giving a stippled appearance involving the axial skeleton and carpus and tarsus. In addition, the ribs are short and deformed, the vertebral bodies flat, and the long bones short and deformed, with diaphyseal fractures and flared metaphyses.¹

Greenberg dysplasia (hydrops-ectopic calcification-motheaten skeletal dysplasia, HEM) has a poorly ossified skull vault, a fragmented, "mottled" appearance of the long bones, most pronounced at their ends, but extending to involve the diaphyses.²

Dappled diaphyseal dysplasia (DDD) has more severe features than HEM. The skull

vault is unossified. The long bones are extremely short, deformed, and appear fragmented because of multiple ossification centres. The tubular bones of the hands and feet are unossified. Multicentric ossification is also present in the scapulae, pelvis, and facial bones. The vertebrae are less severely affected.³ Both HEM and DDD are severely hydropic.^{2, 3}

Case report

This stillborn female was delivered at 34 weeks' gestation. The Pakistani parents were young and healthy. No malformations or bone diseases were known to be present in the family. Neither necropsy nor histochemical examination of the cartilage was performed and no photographs of the patient were obtained.

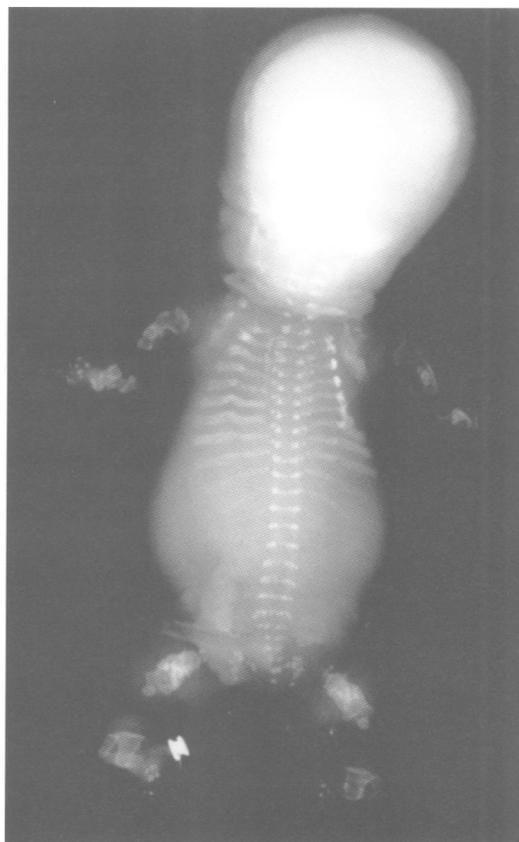


Figure 2 Babygram showing short, deformed limbs, short ribs with transverse defects, and multiple centres of increased bone density in the spine. Wormian bones are visible in the skull.

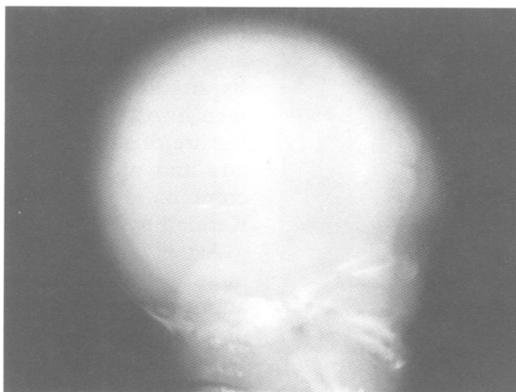


Figure 1 Lateral skull: absent ossification of the vault.

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Table 1 Comparison of the radiological findings of the present case with the reported Astley-Kendall cases and related conditions

Radiological findings	Astley-Kendall	Nairn-Chapman (all cases)	Present case	Dappled diaphyseal	HEM
<i>Skull</i>					
Lack of ossification of vault	+	+	+	+	+
Normal skull base	+	+	+	-	-
<i>Spine</i>					
Multiple dense centres (stippling)	+	+	+	+	+
Platyspondyly	+	+	+	+	+
<i>Thorax</i>					
Small	+	++/-	+	+	+
Transverse translucent rib defects	+	+	+	+	+
Ribs deformed (wavy)	+	+	+	-	+
Ribs broad	+	++/-	+	-	-
Scapulae subglenoid defect	+	+	+	-	-
<i>Pelvis</i>					
Crescentic ilia	+	+	+	-	-
<i>Limbs</i>					
Short and deformed	+	+	+	+	+
Constriction and fracture near midpoint of long bones	+	+	+	-	-
Angulated tibia/fibula	+	+	+	-	-
Normal sized hands and feet	+	+	+	-	-
Stippled carpus/tarsus	+	+	+	+	+
Punctate epiphyses	+	++/-	+	+	+
Splayed metaphyses	+	+	+	-	+
Multiple ossification centres of diaphyses	-	-	-	+	+
Severe hydrops	-	-	-	+	+
Pattern of inheritance	AR	AR		AR	AR

The postmortem radiographs show short, deformed limbs and a narrow thorax with a moderately protuberant abdomen. In the skull there is very poor ossification of the vault which shows multiple wormian bone formation. The base of the skull and facial bones are well developed (fig 1).

In the spine, multiple areas of stippling are seen in the vertebral bodies in the lower thoracic and lumbar regions and the pedicles and transverse processes throughout. There is marked platyspondyly and absent ossification of vertebral bodies in most of the thoracic region with only a trace of ossification at the levels of D1 and D2. The thorax is narrow with short, broad, spatulate ribs widened at the anterior ends. The ribs are deformed (wavy)

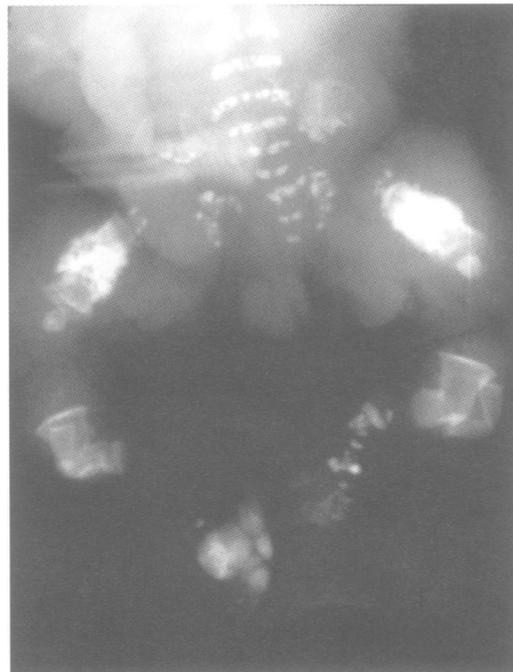


Figure 3 Lower limbs and pelvis showing crescentic ilia, stippled ischia, short, deformed femora with wide diaphyses, and angulated tibiae/fibulae.

with a few transverse defects suggesting intra-uterine fracturing. Punctate calcification is present at the posterior ends of the ribs. The scapulae have an unusual configuration with some deficiency laterally in the infraglenoid position. In the upper limbs, the long bones are short and bowed or angulated. The metaphyses of the proximal humeri are flared. There are radiolucent defects across the mid diaphyses of the humeri with marginal sclerosis and callus indicating healing fractures. Stippling is present in the carpus (fig 2).

In the pelvis, the iliac wings are wide, short, and concave inferiorly (crescentic). There is extensive stippling affecting the pubic bones and ischia. Stippling is also present in the upper femoral regions and extensively throughout the tarsus. There is expansion owing to callus with some sclerosis of the diaphyses of both femora and transverse lytic areas representing fracturing. The distal metaphyses and epiphyses are well maintained. The tibiae and fibulae are extremely short and angulated. In the feet, the short tubular bones are well developed with no evidence of deformity (fig 3).

Discussion

This stillborn infant shows a number of features reminiscent of several conditions. In particular, the poor ossification in the cranial vault, transverse defects in the diaphyses of long bones with surrounding callus and sclerosis, angulated tibiae, and broad ribs are features seen in osteogenesis imperfecta. Stippling is a feature of all forms of chondrodysplasia punctata and of other disorders.⁴ In this case the combination of findings is diagnostic of Astley-Kendall dysplasia.

Astley and Kendall¹ described a stillborn infant and Nairn and Chapman⁵ reported another three female sibs from a consanguineous marriage with this condition. However, there have been suggestions published^{6,7} that these sibs had features of DDD and not Astley-Kendall dysplasia. It has also been suggested

that HEM represents a milder form of DDD.^{6 7} We feel that Astley-Kendall dysplasia is distinct from both DDD and HEM on radiological grounds (table 1).

The chondro-osseous morphology of Astley-Kendall dysplasia has been well described.⁷ There is dystrophic globular calcification within epiphyses, vacuolated chondrocytes, widened lacunae, and disorganised growth plate with irregular columns, maturational arrest, and thin cortex. Fractures of the diaphyses were present with fibrous tissue proliferation and callus formation. The chondro-osseous morphology of HEM is significantly different.²

Our case represents the fifth published report of Astley-Kendall dysplasia. To date, all

cases of this presumed autosomal recessive disorder, interestingly, have occurred in Asians from the Midlands area of the United Kingdom.

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