A case of atelosteogenesis

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Abstract

Atelosteogenesis is a rare chondrodysplasia characterised by rhizomelic short limbed dwarfism, thoracic hypoplasia, multiple joint dislocations, talipes equinovarus, and early death. The diagnosis is confirmed radiologically: short, distally tapering humeri, absent or hypoplastic fibulae, deficient vertebral ossification with coronal clefting, and anarchic ossification of phalanges are characteristic findings. We report a male child with this condition born to first cousin Bengali parents.

Atelosteogenesis is a rare lethal chondrodysplasia that can be differentiated from other lethal skeletal dysplasias by characteristic radiological findings.¹

Pregnancy is often complicated by polyhydramnios and premature delivery.^{2,3} Patients may be stillborn and all have died within 24 hours of birth.¹⁻⁴ Clinical features include rhizomelic dwarfism, thoracic hypoplasia, multiple joint dislocations, and talipes equinovarus. The nasal bridge can be depressed and cleft palate has been reported in one patient.¹

The diagnosis is confirmed radiologically. The most characteristic sign is short, symmetrical humeri that taper distally. The femora may be similarly affected. Fibulae are hypoplastic or absent. Another constant finding is deficient vertebral ossification often with coronal clefting. Scoliosis can result from these anomalies. The thoracic cage is short and associated with 11 pairs of ribs in several patients. Irregular, deficient ossification of the phalanges of the hands and feet is an important feature. Histological examination of growth plates has shown giant cell chondrocytes in three^{2,3} of five^{1,4} patients

studied, but this is not pathognomonic of the condition.

Atelosteogenesis has been described in both sexes and all 10 cases have been sporadic. We report a further patient with this rare chondrodysplasia born to first cousin Bengali parents and review the published reports.

Case report

The proband, a male, was the second child of healthy, first cousin Bengali parents aged 25 years (father) and 22 years (mother). Their first child, a girl, was healthy and there was no relevant family history.

Figure 1 Upper limb with distally tapering humerus; dislocated elbow; short distal ulna and irregular ossification of distal radius and ulna; absent or poorly ossified metacarpals and proximal rows of phalanges but relatively normal terminal phalanges.

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Pregnancy was complicated by polyhydramnios and at 28 weeks an ultrasound scan showed marked shortening of all four limbs in the fetus. The pregnancy continued and the proband was born by normal delivery at term weighing 2000 g. Immediate resuscitation was necessary and continued ventilatory support was required. Proximal limb shortening was noted at birth with left talipes equinovagum and a small thoracic cage. Ventilation proved increasingly difficult and he died within 24 hours. No necropsy was performed.

RADIOLOGICAL FINDINGS

In the upper limbs the humeri were short and tapering. Proximally, the metaphyses were broad but distally they tapered to a point, appearing club shaped. Both elbows were dislocated and there was significant shortening of the ulnae distally, with unusual defects of the ulnar borders of the distal metaphyses. The terminal phalanges in the hands were well ossified but there was no ossification of the proximal phalanges, and the metacarpals and middle phalanges were short, with many bizarre shapes (fig 1). The pubic rami were short with unusual, separate, rounded, lateral ossification centres and the ischia were relatively large. The iliac wings appeared widely spaced and flared laterally, but were hypoplastic inferiorly with poorly formed acetabular roofs. In the lower limbs the left hip was dislocated. Both femora were short with loss of normal modelling and unusual irregular cortical thickening. There was mild mid-diaphyseal bowing. Both knees appeared dislocated

Figure 2 Lower limbs showing flared iliac wings, dislocated left hip and both knees, and short bowed femora and fibulae. Defective tarsal and phalangeal ossification.

Figure 3 Lateral spine showing lumbar platyspondyly with anterior tongues of the vertebral bodies. Pronounced angulation of the sacrum.

Figure 4 Lateral skull with wide occipital synchondrosis. Poorly ossified cervical vertebral bodies with a reversal of the cervical lordosis.

Comparison of features of our patient with previously reported cases.

	Maroteaux et al ¹										Sillence et al ²		Yang et al ³	Kielowski et al ⁴	This patient
	1	2	3	4	5	6	1	2							
Sex	M	M	F	NA	NA	NA	F	F					M	F	M
Polyhydramnios	NA	NA	NA	NA	NA	NA	NA	NA					+	NA	+
Gestation (wk)	42	24	NA	28	NA	NA	30	33					26	40	40
Age at death	SB	2 h	Minutes	SB	Minutes	NA	SB	2 h					46 min	9 h	<24 h
<i>X ray appearances</i>															
Humeri	+	+	+	+	+	+	+	+					+	+	+
Distally tapering															
Femora															
Short	+	+	+	+	+	+	+	+					+	+	+
Distally tapering															
Fibulae															
Hypoplastic/absent	+	+	+	+	NA	+	+	+					+	+	+
Hands/feet															
Irregular ossification of phalanges	+	-	+	NA	+	+	+	+					+	+	+
Spine															
Poorly ossified vertebrae	+	+	+	+	+	+	+	+					+	+	+
Cervical	+	NA	+	NA	NA	NA	+	-					+	-	+
Thoracic	+	NA	+	+	NA	NA	+	-					+	+	+
Lumbar	-	NA	NA	+	NA	NA	+	-					+	+	+
Coronal clefting	NA	NA	NA	+	NA	NA	+	+					NA	+	-
Thoracic cage															
Narrow	+	+	+	+	+	+	+	+					+	NA	+
11 pairs of ribs	+	NA	NA	NA	NA	NA	+	+					+	-	+
Joints															
Dislocations	NA	NA	NA	NA	NA	NA	-	-					-	+	+
<i>Histology</i>															
Giant cells present	-	NA	NA	NA	NA	NA	+	+					+	-	NA
Karyotype	NA	NA	NA	NA	NA	NA	NA	NA					46,XY	NA	NA

NA=Information not available.
SB=stillbirth.

and there were no ossification centres at the knees or tarsus. The tibiae were short with marked shortening of the fibulae, which were bowed. In the feet only a few phalanges were ossified and some of these were triangular (fig 2).

In the spine the vertebral bodies of the cervical region were small or absent and there was a reversal of the normal cervical lordosis. A mid-dorsal scoliosis was present and in the lumbar region there was platyspondyly with anterior tongues of the vertebral bodies. There was pronounced backward angulation of the sacrum (fig 3).

The thoracic cage was rather narrow with 11 pairs of short, slender ribs, reaching only to the mid-axillary line.

The occipital synchondrosis was wide, but the skull appeared otherwise normal (fig 4).

Discussion

There have been very few published reports of atelosteogenesis and 10 previous cases are reviewed in the table. This rare, lethal chondrodysplasia is characterised by deficient ossification of several bones and is diagnosed radiologically. Most striking in our patient was the tapering of the humeri to give an elongated triangular appearance owing to lack of ossification distally. This feature is so unusual that the diagnosis should always be considered in such patients, but a similar shape is sometimes seen in patients with Larsen's syndrome.⁵ The femur is similarly affected in many patients and hypoplastic or absent fibulae are consistent findings.

Irregular incomplete ossification of the spine, a small thoracic cage, and unusual ossification of the phalanges with absent or poor ossification of the proximal and middle phalanges, but relatively normal terminal phalanges, are additional features and help to confirm the diagnosis. The spine in our patient was not as severely affected as in many cases and did not show coronal clefting.

The clinical picture is similar in all patients.

Polyhydramnios is a complication in pregnancy and in our patient led to detailed ultrasound examination at 28 weeks when rhizomelic shortening of the limbs was noted, but the parents chose to continue the pregnancy. Herzberg *et al*⁶ described a fetus with probable atelosteogenesis who was diagnosed at 20 weeks' gestation by ultrasound suggesting prenatal diagnosis is possible in this condition. The condition has been lethal in all patients because of thoracic complications. Other features include a characteristic face with depressed nasal bridge and dislocation of several joints with severe talipes.

While it is unknown whether the condition is inherited, all previous cases have been sporadic and have affected both sexes. We have looked at paternal age and birth order in the other reported cases but information is too scanty to draw conclusions. This is the first report of an affected baby born to consanguineous parents. The family are Bengali among whom consanguineous marriages are common and further case reports are needed before recessive inheritance can be considered.

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