

BRIEF PAPERS

# Campomelic dysplasia: evidence of autosomal dominant inheritance

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**Abstract**

**We present a mother and daughter with clinical and radiological findings consistent with the diagnosis of campomelic dysplasia. Milder tibial bowing and significant shortening of the phalangeal bones of both hands and feet may distinguish this from the classical autosomal recessive form of the disease.**

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**Case reports**

**CASE 1**

Case 1 was born by brow presentation after a prolonged labour at 37 weeks' gestation. She weighed 2600 g and was admitted to the special care baby unit with mild respiratory distress. She was noted to have short stature and genu valgum. She attended the orthopaedic surgeons regularly as a child and had a right fibular osteotomy to correct a 4 cm asymmetry of her lower limbs at the age of 11. X rays at this time showed bow stringing of the fibula over the tibia.

Epilepsy was diagnosed at the age of 13 years after a number of generalised seizures. An EEG showed frequent discharge activity, spike/wave 3½-4 Hz. She was started on sodium valproate and remained on it throughout pregnancy at the age of 18 years.

Frequent attendances at ENT clinics as a child confirmed a conductive hearing loss in the left ear. Spectacles were prescribed for myopia. She is of normal intelligence.

Physical examination showed a height of 1.5 m (<3rd centile) at the age of 19 years. Minor dysmorphic features included a long philtrum, a small mouth, a flat nasal bridge, and midfacial hypoplasia. Her thumb and little fingers were short bilaterally. There was evidence of skin dimpling on her left shin and a previous osteotomy scar on her right shin. Her big toes were short and medially deviated. Her toenails were hypoplastic.

Campomelia dysplasia is characterised by limb deformities with shortening of both upper and lower limbs. Major diagnostic criteria include congenital bowing of the long bones with pre-tibial skin dimpling, hypoplasia of the scapulae, the presence of 11 pairs of ribs, poor or absent ossification of the pelvis, and talipes equinovarus.<sup>1,2</sup> There is often respiratory distress owing to maldevelopment of the trachea and pulmonary hypoplasia. Dysmorphic features include dolichocephaly, micrognathia, and flattened supraorbital ridges and nasal bridge. A cleft palate is frequently present and sex reversal is sometimes a feature. Generalised hypotonia and oesophageal and ureteric reflux are often present. Death usually occurs in the neonatal period as a result of respiratory distress.<sup>3,4</sup>

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Figure 1 Case 2 showing disproportionately large head, hypertelorism, long philtrum, small mouth, and bilateral tibial bowing.



Figure 2 X ray of pelvis of case 1 showing a hypoplastic left iliac bone and non-ossification of the inferior pubic rami.

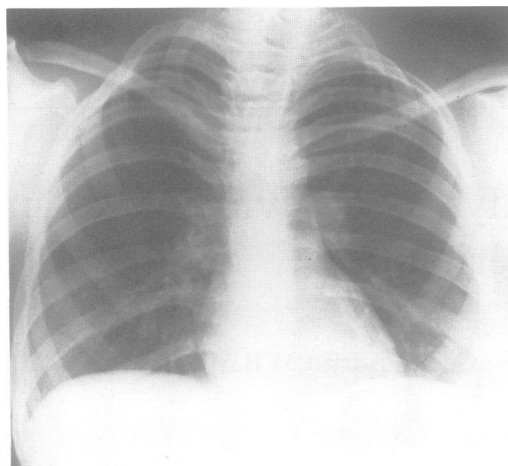


Figure 3 Chest x ray of case 1 showing 11 pairs of ribs, hypoplastic scapulae, long thin clavicles, and a thoracic scoliosis.

#### CASE 2

Case 2 is the daughter of case 1. There was no parental consanguinity. She was born by elective caesarean section because of the maternally contracted pelvis. Routine antenatal scans had shown short femur lengths and polyhydramnios. Repeated antenatal scans throughout pregnancy confirmed this finding and suggested a short limbed dwarfism. The delivery was difficult because of a transverse lie. Resuscitation was required at birth, Apgar scores being 2 at one minute and 5 at five minutes.

The baby became tachypnoeic and required increasing concentrations of oxygen. She subsequently died from respiratory failure on day 5. Necropsy was not performed.

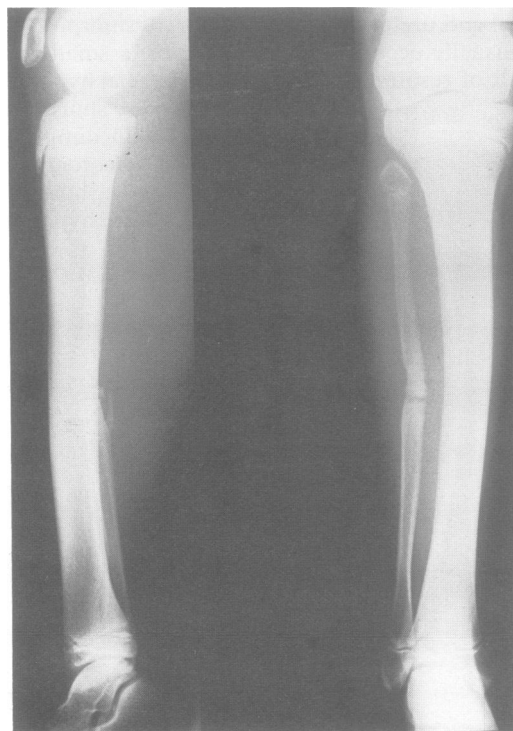


Figure 4 AP and lateral x rays of the right tibia and fibula of case 1 showing previous fibula osteotomy plus tibial bowing.



Figure 5 X ray of the left hand of case 1 showing short first and fifth metacarpals plus shortening of the middle and distal phalanges in the second to fifth fingers.

Physical examination at birth showed multiple congenital abnormalities, which included shortening of all four limbs, tibial bowing and skin dimpling over the apex of each tibia, and bilateral talipes equinovarus (fig 1). Her head circumference was just above the 50th centile but appeared disproportionately large. The anterior fontanelle was small. Micrognathia was present. The baby was in obvious respiratory distress with a respiratory rate of 60 to 70/min and indrawing of the costal margins and nasal flaring.

#### INVESTIGATIONS

A skeletal survey on case 1 at 18 years showed a number of abnormalities (figs 2 to 6). These included a small left iliac bone with non-ossification of the pubic rami on both sides. Eleven pairs of ribs were present, the scapulae were hypoplastic, and the clavicles were long and straight. A thoracic scoliosis was also present. Significant shortening of the tibiae and fibulae were noted. The first metacarpals were



Figure 6 X ray of the right foot of case 1 showing short first metatarsal plus shortening of several phalanges.



Figure 7 Pelvic x ray of case 2 showing splayed pubic symphysis and small iliac bones.

very short as were the middle phalanges of the index and little fingers. Previous radiographs showed abnormalities of the metatarsals and phalanges of the feet, shortening of the left tibia in comparison to the right, and evidence of previous surgery to the right leg.

A skeletal survey on case 2 at birth showed similar findings (figs 7 to 10). The pubic symphysis was widely spaced. There were 11 pairs of ribs with a bell shaped thorax and hypoplastic scapulae. There was shortening of all four limbs with bowing. The tibia was less severely bowed and shortened than the femur. There was evidence of shortening of the first metacarpal, with shortening of the phalanges in both hands and feet.

Chromosome analysis on case 2 showed a normal female karyotype, 46,XX. A cranial ultrasound was performed on case 2 which showed a large third ventricle with widely spaced lateral ventricles suggestive of agenesis of the corpus callosum.

### Discussion

Autosomal recessive inheritance has been suggested for campomelic dysplasia because of recurrence in sib pairs and also the presence of consanguinity in some of these families.<sup>4-7</sup>

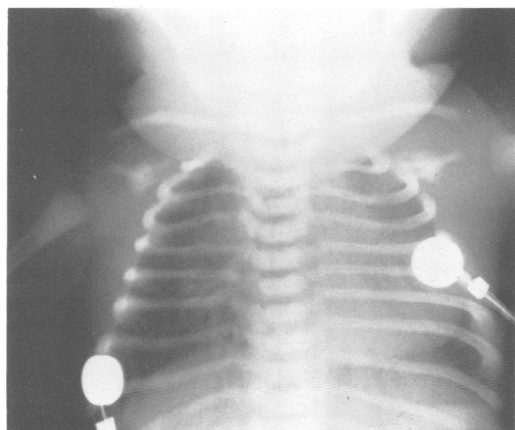


Figure 8 Chest x ray of case 2 showing a bell shaped thorax, 11 pairs of ribs, hypoplastic scapulae, and long thin clavicles.

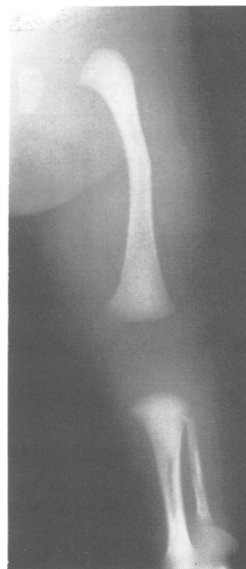


Figure 9 AP x ray of left lower limb of case 2 showing marked bowing of the femur.

However, Thurmon *et al*<sup>8</sup> noted recurrence in half sibs, the mother of whom had mild tibial bowing. We suggest that this could be because of autosomal dominant inheritance with reduced penetrance or maternal gonadal mosaicism. Gonadal mosaicism may explain recurrence in families where neither parent is affected.

Campomelic dysplasia is usually fatal within days to months although several survivors have been reported.<sup>3</sup> The majority of survivors, however, have been developmentally delayed. Our patients have many features consistent with this diagnosis (table).

Autosomal dominant inheritance may therefore be the mode of inheritance in some of these families. We conclude that these cases may represent an autosomal dominant variant of campomelic dysplasia. In our family, the tibiae were not as severely bowed as one would expect, and the first and fifth phalanges of the hands were significantly shortened. Although first metacarpal and phalangeal shortening has previously been reported,<sup>3</sup> our cases seem more severe. If there are autosomal recessive and dominant campomelic dysplasias, these may be distinguishing features.



Figure 10 Lateral x ray of the right lower limb of case 2 showing tibial bowing.

Comparison of clinical and radiological features between cases 1 and 2 and 43 published cases of campomelic dysplasia.<sup>2</sup>

Abnormalities	Case 1	Case 2	43 published cases <sup>2</sup> (%)
Tibial bowing	+	+	100
Poor pelvic ossification	+	+	100
Bell shaped chest	-	+	100
Eleven ribs	+	+	87
Hypoplastic scapulae	+	+	100
Brachydactyly	+	+	100
Absent talus	-	-	75
Birth head circumference	NK	36 cm	36.1 cm (90%)
Large fontanelle	NK	-	55
Hypertelorism	+	+	59
Flat nasal bridge	+	+	96
Long philtrum	+	+	94
Small mouth	+	+	100
Cleft palate	-	-	80
Micrognathia	+	+	100
Pretibial skin dimples	+	+	90
Talipes equinovarus	-	+	100
Hallux deviation	+	+	87.5
Hypotonia	-	+	100
Absent corpus callosum	?	+	?

NK = not known.

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