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Kyphomelic dysplasia

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SUMMARY A case of kyphomelic dysplasia is reported in a boy followed up over three years. The most striking feature of this recessively inherited generalised bone dysplasia is marked angulation of the femora, associated with short stature, bowing and shortening of other long bones, metaphyseal changes in infancy, flared ribs, small thoracic cage, and platyspondyly. The good prognosis regarding motor and intellectual development in this condition is stressed and the association with cleft lip and palate is described for the first time.

Kyphomelic dysplasia was first described by Khajavi *et al*¹ in 1976 as a 'variant' of campomelic dysplasia. Since then, eight cases of this rare, generalised skeletal dysplasia have been reported including two pairs of sibs.²⁻⁵ It is thought to be autosomal recessively inherited. We report a further case to help delineate the features and natural history of the syndrome over three years.

Case report

The proband was the first child of unrelated Caucasian parents aged 32 years (father) and 22 years (mother). He was born by normal delivery at term, with a birth weight of 3070 g, after a pregnancy complicated by maternal hypertension. He was conceived while his mother was taking indocid which was stopped once pregnancy was confirmed. Glycosuria was not present on routine prenatal testing. At birth, breathing was initially poor and he was nursed in an incubator with supplementary oxygen for two days; however, he

improved quickly and was home by 10 days. Multiple congenital anomalies were noted at birth and confirmed when he was seen at our unit.

Examination at three months of age showed weight 5.25 kg (10th to 25th centile) and height 54 cm (<3rd centile). The most striking feature was the grossly abnormal, short, curved femora. Rhizomelic shortening of the upper limbs was also present, but was not so marked. In addition, a unilateral cleft lip and palate was noted, and mild dysmorphic features including micrognathia, a flat nasal bridge, and a flat malar region were present. Clinically, the chest appeared broad and short with widely spaced nipples and some subcostal and sternal recession. He was also noted to have bilateral talipes equinovarus. The hands, genitalia, and skin were normal.

TABLE Clinical and radiographical features of present case and previously reported cases.

Manifestation	Previous reports (n=8)	Present report (n=1)
Clinical		
Sex	5M:1F	M
Normal intelligence	4/4	+
Normal OFC	7/7	+
Short limbs	8/8	+
Small chest	6/6	+
Limited joint movements	3/3	+
Normal hands and feet	4/4	+
Skin dimples	2/2	+
Cleft lip and palate	0/8	+
Micrognathia	3/4	+
Midfacial hypoplasia	3/4	+
Radiographical		
Bowed femora	8/8	+
Bowed humeri	6/8	-
Bowed tibiae	5/7	-
Bowed radii	7/8	-
Short, flared ribs	6/6	+
Eleven pairs of ribs	2/6	-
Platyspondyly	3/5	+
Metaphyseal flaring	7/7	+

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He was obviously thriving and responding normally and had good tone in all limbs.

X rays showed marked, symmetrical angulation of the femora and mild bowing of the ulnae. The long bones were generally short with some metaphyseal flaring. The pelvis was small and triangular with a shallow acetabular roof. There was mild platy-

spondyly with some end plate irregularity of the vertebrae but no obvious subluxation in the cervical spine. The ribs were short, reaching only the mid-axillary line, and were broad anteriorly. The chest shape gave the impression of small volumed lungs. The clavicles were normal (fig 1).

Other initial investigations, including a brain

FIG 1a Chest x ray at three months to show short ribs which are broad anteriorly.

FIG 1b X ray of pelvis at three months showing shallow, sloping acetabular roofs with marked flaring of the iliac wings. Marked femoral angulation is visible on the left.

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scan, renal ultrasound, TORCH screen, and karyotype (46,XY), were all normal.

At four months of age the cleft lip was repaired uneventfully. A few days after discharge he had a 'near miss cot death' requiring mouth to mouth resuscitation. A succession of apnoeic attacks occurred up until the age of six months. The family used an apnoea alarm and genuine episodes occurred

about once a week. No explanation was found for these episodes. The palate was closed successfully at eight months.

On review at 14 months his progress was encouraging. The femoral angulation was less marked and function was good (fig 2). He was up on his feet cruising around furniture at eight months. He did not sit unsupported until 14 months but walked at 16

FIG 2 X ray of femora aged 14 months showing slight improvement in femoral bowing. The lesser trochanters are unusually prominent.

FIG 3 The proband aged three years three months. Note his short legs and pterygia, absence of natal cleft, and mild pectus excavatum.

FIG 4 *X ray of pelvis at three years three months showing flattening and fragmentation of the right capital femoral epiphysis. The acetabular roofs now appear well developed.*

months. Pterygia were noted in the intercrural and popliteal regions.

A repeat chest x ray at 20 months showed some improvement. The anterior widening of the ribs had largely disappeared and the ribs were a normal length.

He was last reviewed aged three years three months. His development, including motor milestones, was normal and he was in good general health. Examination showed head circumference 52 cm (75th centile), length 87.9 cm (3rd centile), sitting height 58.3 cm (+1 SD), subischial leg length 29.6 cm (>-4 SD), and upper to lower segment ratio 1.97 (mean 1.45). His short stature was therefore the result of marked leg shortening. His weight was 14.7 kg (25th to 50th centile). He remained mildly dysmorphic with a slightly flat nasal bridge and prominent eyes. The micrognathia was less marked. Rhizomelic shortening of the limbs with anterior bowing of the thighs was still obvious but less marked. There was limitation of movement at the hip and knee joints bilaterally and skin pterygia were still present at the same joints. His chest was wide and flat with mild pectus excavatum. There was flattening of the buttocks and no natal cleft (fig 3).

X rays again showed some improvement in the bowing of the femora. In addition there was flattening and fragmentation of the right femoral epiphysis (fig 4).

There is no family history of cleft lip and palate. The proband has a normal brother born in 1986.

Prenatal ultrasonography was offered during pregnancy to exclude recurrence.

Discussion

Kyphomelic dysplasia describes a rare syndrome characterised by short, broad, bowed long bones, most striking in the femur. This generalised skeletal dysplasia includes metaphyseal flaring and irregularity in infancy, abnormal, short, flared ribs, and mild vertebral flattening. Affected subjects are short but intelligence is normal and there is a tendency for the x ray findings to improve with time. Karyotypes, where reported, are normal.^{3 4}

We present this case to illustrate in particular the good prognosis for walking and subsequent mobility despite marked femoral deformity in infancy. The improvement in x ray findings of the femur is well documented and for the first time we describe cleft lip and palate in an affected subject. The widening of the ribs in the mid-anterior portions is more extensive than previously reported, but these changes show good resolution with time although the lung volume remains small. Our patient is not markedly dysmorphic in keeping with previously reported cases. Micrognathia and midfacial hypoplasia are less marked at three years of age. The features in our patient are compared with those previously described in the table.

The differential diagnosis includes campomelic dysplasia but this can be readily distinguished by extraskelatal manifestations, the predominance of

tibial bowing, severe talipes, hypoplastic scapulae, mental retardation, sex chromosome reversal in some affected females, and severe respiratory difficulties in infancy. One other differential diagnosis of kyphomelic dysplasia is the femoral hypoplasia-unusual facies syndrome which is sporadic^{6,7} or rarely autosomal dominant⁸ and hence the diagnosis has important counselling differences. Cleft lip and palate has previously only been described in FH-UFS. It now seems that it cannot be used to differentiate the two syndromes,⁵ the major difference remaining symmetrical femoral bowing in kyphomelic dysplasia and femoral hypoplasia in the FH-UFS, which is often asymmetrical.

The prognosis appears to be encouraging, but as yet no adults have been described. Femoral angulation improves with age although adult stature is likely to remain short with some limitation of movement at the hips and knees. Cervical subluxation is the most serious complication reported³ and it must be actively sought. Osteoarthritic problems could be predicted in the future for our patient in view of the osteochondritic changes in the femoral epiphysis.

Apnoea has not previously been reported as a feature of the condition although frequent respiratory infections secondary to a small chest have been described and could be postulated as an underlying cause in our patient.

A case of two inversion (10) recombinants in a family

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SUMMARY A family is described in which the mother's four pregnancies resulted in one spontaneous abortion, one healthy boy, and a male and female sib with developmental delay and multiple minor dysmorphic features. Chromosome analysis showed a large pericentric inversion of chromosome 10, involving the region between bands p15.1 and q25.2, in the father and the healthy son: 46,XY,inv(10)(p15.1q25.2), and an unbalanced karyotype in the two affected sibs: rec(10),dup p,inv(10)(p15.1q25.2).

The unbalanced chromosome has been produced by meiotic recombination between the

This case helps to delineate further the features and natural history in this rare skeletal dysplasia.

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inversion chromosome and its normal homologue. The two affected sibs have partial duplication of 10p and partial deficiency of 10q, and share a large number of clinical features, several of which have previously been described in both of these chromosome imbalances.

We believe this to be the largest pericentric inversion of chromosome 10 reported to have produced recombinant offspring.

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CASE 1

The male proband was the third child of healthy, unrelated parents, born at term by normal vaginal delivery after an uneventful pregnancy. His birth