A probably distinct autosomal recessive thoraco-limb dysplasia

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SUMMARY A Mexican mestizo family is reported in which two opposite sexed sibs, born to consanguineous parents, had a skeletal dysplasia. The salient features were a bell shaped thorax owing to short ribs, short limbed dwarfism, pelvic hypoplasia, dislocatable radial heads, elongated distal fibulae, and improvement with age. It is concluded that the present observation probably represents a distinct autosomal recessive thoraco-limb dysplasia identifiable at birth.

Bankier and Danks¹ have recently classified the short rib syndromes into three groups. Conditions in the second group show variable limb shortening and short ribs with a normal skull and spine. Among these, asphyxiating thoracic dysplasia and chondroectodermal dysplasia are well known types, but several other comparable disorders also exist.¹⁻⁴ We report here a previously undescribed thoraco-limb dysplasia observed in the offspring of a consanguineous couple.

Case reports

CASE 1
The proband, a Mexican mestizo girl, was the first child of consanguineous parents (F=1/256) with no family history of a similar condition. Although the 21 year old mother was 150 cm tall, she was well proportioned and, except for short femoral necks, without radiological evidence of skeletal dysplasia; the father was aged 28 and was 161 cm tall. Delivery at term required caesarean section because of breech presentation. Birth weight was 2800 g but...
length was not recorded. The neonatal period was uneventful. When first seen at four months of age (fig 1), her measurements were as follows (reference values are from Faulhaber¹): length 52 cm (5 cm below the 3rd centile), upper/lower segment ratio 1.74, arm span 44 cm, head circumference 38 cm (on the 3rd centile), and weight 3400 g. She exhibited joint hyperlaxity, round flat facies with a depressed nasal bridge, a short neck with a low hairline, a moderately narrow thorax, and shortening (mainly rhizomelic) of the four limbs. There was no respiratory distress and her muscle strength and neurological examination were normal.

Thyroid function tests at the age of five months excluded hypothyroidism. Developmental milestones have been delayed: she sat at 12 months, began to speak at 16 months, and walked without support at 24 months.

On examination at four years eight months (fig 1), her height was 87.5 cm (6.5 cm below the 3rd

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**FIG 2 Radiological changes in the proband.** At four months (top row) the bell shaped thorax, pelvic hypoplasia, and short and broad tubular bones were prominent, whereas at four years 10 months (bottom row) the shape of the pelvis and tubular bones was nearly normal; also note the overgrown distal fibulae.
centile), upper/lower segment ratio 1·50, arm span 85 cm, and head circumference 49 cm (on the 50th centile). Besides disproportionate short stature, she showed dislocatable radial heads, increased lumbosacral lordosis, bilateral genu valgum, a wide based gait, pes planus valgus, and joint hyperlaxity. The head was normal, the facial features being similar to those of her father. She had well articulated speech and seemed to be intellectually normal.

Radiographs at the age of four months (fig 2) showed a bell shaped thorax with a diminished anteroposterior width owing to short ribs; broadened costochondral junctions; short tubular bones, mainly humeri and femora, with variable diaphyseal widening and metaphyseal flaring; backward displacement of both radial heads; ossified capital femoral epiphyses; and a small pelvis with tiny sacrosciatic notches, hypoplastic ilia, and no bony projections. The skull and spine were unremarkable. At the age of four years 10 months the thoracic narrowing appeared less pronounced and the shape of the pelvis and tubular bones was nearly normal; overgrown distal tubular bones were now apparent (fig 2). There were no cone shaped epiphyses and the lumbar interpedicular distances increased caudally. Epiphyseal maturation was essentially normal.

Case 2
The only and younger sib of the proband, a male, was born at term by vaginal delivery in vertex presentation requiring forceps extraction; Apgar scores were 8 and 9 at one and five minutes. At birth, length was 45 cm (just below the 3rd centile), upper/lower segment ratio 2·0, arm span 40 cm, head circumference 34 cm (on the 3rd centile), thoracic circumference 31 cm (on the 3rd centile), and weight 2900 g (on the 10th centile). At two months of age, he showed short limbed dwarfism with maximum involvement of the proximal segments: length 48 cm (5 cm below the 3rd centile), upper/lower segment ratio 1·82, head circumference 35·5 cm, and thoracic circumference 33 cm (1·6 cm below the 3rd centile). He had a small chest and a left valgus foot. There was neither craniofacial dysmorphism nor respiratory distress and his motor activity appeared to be normal. The child died one month later from acute pneumonia; no necropsy was performed.

The skeletal changes at two months of age (fig 3) were similar to those in the proband and included a narrow, bell shaped thorax, short and broad tubular bones, particularly the humeri and femora, moderate metaphyseal flaring, displaced radial heads, and pelvic hypoplasia.

Discussion
The cardinal features of the condition described here are apparent autosomal recessive inheritance, chest narrowing owing to short ribs, and short limbed dwarfism. Additional findings in infancy

![Radiographs of case 2 at two months showing the bell shaped thorax, short ribs with broadened costochondral junctions, pelvic hypoplasia, and short and wide tubular bones.](http://jmg.bmj.com/ on June 20, 2017 - Published by group.bmj.com)
were variable diaphyseal widening and metaphyseal flaring, radial head dislocation, and a hypoplastic pelvis without spiky acetabular protrusions. With age, as noted in the proband, the radiological changes improved but the disproportionate short stature remained conspicuous. Other signs, such as increased lumbosacral lordosis, bilateral genu valgum, a wide based gait, elongated fibulae, and pes planus valgus, became manifest during childhood. Otherwise the skull and spine were normal, there was no obvious neurological or mental impairment, and there were no phalangeal cone shaped epiphyses. Although the proband had no history of respiratory difficulties, the early death of her brother may indicate that the small rib cage predisposes to pulmonary failure.

That the present disorder is distinct from the Jeune syndrome\(^ 8\) is shown mainly by the different thoracic configuration, lack of neonatal respiratory distress, and absence of acetabular spurs in infancy and phalangeal cone shaped epiphyses in childhood. Further discriminants are the noticeable short stature at birth, radial head dislocation, increased lumbosacral lordosis, genu valgum, and elongated distal fibulae. Similarly, other short rib entities such as thoracic-pelvic dysostosis,\(^ 1\) Barnes syndrome,\(^ 2\) \(^ 3\) and thoracic dysplasia-communicating hydrocephalus syndrome\(^ 4\) can also be ruled out.

To conclude, this observation expands the clinical spectrum of the thoraco-limb dysplasias and supports the notion of underlying genetic heterogeneity.

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References


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