Microspherophakia-metaphyseal dysplasia: a ‘new’ dominantly inherited bone dysplasia with severe eye involvement

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Abstract
We report a father and son affected by a hitherto unpublished bone dysplasia with moderately severe dwarfism. On initial radiographs, thickening of the diaphyses of the long bones was striking. The small bones of the extremities were almost unaffected. With age, the metaphyseal deformation became more prominent. The epiphyses became irregular and their growth was delayed (particularly the femoral heads). The femoral neck showed an unusual ‘lip’ on the inner edge. Later, the stubby appearance of the long bones faded and, in adulthood, only enlarged metaphyses and deformed femoral necks persisted. The vertebrae showed moderate deformation with irregular flattening, and narrowing of the spinal canal with a shortened interpedicular distance. The eye defects consisted of high grade myopia, microspherophakia, lens coloboma, lens luxation, and retinal detachment. The name ‘microspherophakia-metaphyseal dysplasia’ is suggested for this probably autosomal dominant bone dysplasia.

Among the still growing number of bone dysplasias, brachymelia with thick diaphyses represents a puzzling and poorly classified group. We report a father and his son affected by a metaphysodiaphyseal dysplasia complicated by high myopia, which could represent an undescribed bone dysplasia.

Case reports
CASE 1
Case 1 (Genetic file no 4056) was born in 1983 to non-consanguineous parents. His mother was 30 and originated from the Philippines. Birth length was 43 cm, birth weight 2400 g, and OFC 33-8 cm. We saw him for the first time at the age of 3½ when his family was referred for diagnostic advice.

Physical examination of this boy showed micromelic dwarfism. He was 73 cm tall. The face was round and somewhat flat. The trunk was short, with pigeon breast and bell shaped thorax (fig 1). Lumbar

Figure 1 Patient 1 at 3½ years.
Figure 2 Patient 1 at 3½ years. Note femoral neck shape and probable fracture of inner tibial plates.

Figure 4 Patient 1 at 5 years. Hyperlordosis and abnormal vertebral shape.

Figure 3 Patient 1 at 3½ years. Upper limb.

Figure 5 Patient 1 at 5 years. Constraint fractures.
Figure 6  Patient 2 at 43 years. Enlarged epimeta physeal region.

hyperlordosis was prominent. The upper limbs were short but there was no limitation of movement in the joints. The lower limbs were bent. Hip extension and rotation were restricted. There was genu varum with a slight recurvatum and inward bowing of the tibiae. The hands and feet were not shortened.

Radiographs showed severe involvement of the long bones (fig 2). The femora and tibiae were very stubby and there was cortical thickening. The lower femoral, upper and lower tibial, and humeral metaphyses were enlarged and densified. Their edge was irregular and slightly convex. The epiphyses were irregular and underdeveloped. Enlargement of the femoral necks was striking. Their inner edge showed a thick, horizontal 'lip' (fig 2). The femoral heads were small and flattened. Acetabular roofs and the pelvis were normally shaped. There was hyperlordosis but the vertebrae were normally shaped. The only anomaly on hand x rays was pseudoepiphysis of the second metacarpal bone (fig 3).

Ophthalmological investigations showed a normal corneal diameter, deep anterior chamber, microspherophakia, right lens coloboma, superoexternal lens luxation on the left side and posteronasal luxation on the right side, and bilateral partial lens opacification. Visual acuity was 0.4 on the right and 0.1 on the left, and myopia was rated at −4 to −5 dioptres bilaterally.

His development was marked by progressive aggravation of the genu varum. At 5½ years, he was 80 cm tall. X rays disclosed more irregular vertebrae (fig 4), and spontaneous, bilateral, sloping fractures of the inner part of the tibial metaphyses, already suspected earlier, but probably promoted by the mechanical constraints of the varus deformity (fig 5). Small fractures of the lateral aspects of the lower femoral epiphyses were also visible. Femoral osteotomy was performed. The cataracts worsened and were surgically corrected at the same time. Psychomotor development was normal. Homocystinuria was excluded.

CASE 2
Case 2 is the father of case 1. He was born in 1946 to non-consanguineous, unaffected parents. The diagnosis of achondroplasia was suggested during childhood. He had high grade myopia, which was rated at −11 to −12 dioptres bilaterally at 11 years, when the first retinal detachment occurred. Ocular hypertension was observed at 27 years, and subtotal blindness owing to retinal detachment was present at
the age of 30. Coronal and zonular opacities of the lens were noted, but microphthalmia or spherophakia were not mentioned in the records. Recently, light perception has been improved by partial lens dislocation.

When we saw him at the age of 41, he was 139 cm tall, with micromelia and a shortened, bell shaped thorax. Limb deformation was less marked than in his son. He complained of hip pain. No prepubertal x rays could be found. On adult pictures, enlarged epimetaphyses were visible (fig 6). The pelvis was square and acetabular roofs were not horizontal. The femoral heads were enlarged with bilateral coxa vara (fig 7). The vertebral plates were irregular and the lesions were more severe at the thoracic level; vertebrae D6, D9, and L1 were wedge shaped (fig 8). The spinal canal was narrowed on side view. On front view, the interpedicular distance was narrowed and did not increase in the lower lumbar vertebrae (fig 9).

Discussion
The family reported here showed a unique pattern of bone defects. On initial radiographs, the diaphyseal thickening was striking in the long bones, though the small bones of the extremities remained almost unaffected. With age, the metaphyseal deformation became more prominent, epiphyseal irregularities occurred, and the femoral neck showed an unusual 'lip'. Later, the stubby appearance of the long bones faded and, in adulthood, only enlarged metaphyses and deformed femoral necks persisted. The vertebrae showed moderate deformation.

Few bone dysplasias are associated with lens anomalies. In Knies's spondyloepiphyseal dysplasia congenita, there is typical metaphyseal swelling and severe delay of epiphyseal ossification. Cleft palate is common. The same retardation in epiphyseal maturation is observed in 'common' spondyloepiphyseal dysplasia. Stickler syndrome, the neonatal Weissenbacher-Zweymuller syndrome, Wagner hyalidoretinal degeneration, Marshall syndrome, and micrognathic dwarfism are clinical expressions of a complex family of bone dysplasias (commonly called as a whole Stickler syndrome, although their exact nosology and delineation remains controversial). Most of them show a moderate metaphyseal involvement. A common feature is the high grade myopia with frequent retinal detachment. Weil-Marchesani syndrome associates microspherophakia and stunted growth. Bone anomalies include brachydactyly, moderate shortness of the long bones, and slight vertebral deformation. Inheritance is autosomal recessive, although shortness of stature is sometimes reported in parents. Chondrodysplasia calificans metaphysealis is characterised by short stature, progressive deformity, metaphyseal dysplasia with calcium deposit, and myopia. Myopia is also a
feature of dysosteosclerosis,\textsuperscript{13} which includes generalised osteosclerosis, platyspondyly, submetaphyseal translucencies, and ectodermal changes. The radiological pictures of our two cases do not fit any of these syndromes.

The cases reported here may be considered as expressing a ‘new’ bone dysplasia with severe eye involvement. We suggest it should be called microspherophakia-metaphyseal dysplasia. Autosomal dominant inheritance is likely.