Osteoglophonic dwarfism in two generations

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SUMMARY A father and son, both affected by a skeletal dysplasia with severe craniofacial deformities, are reported and compared to three previously described isolated cases of the same dwarfism. The principal features are craniosynostosis, multiple lucent metaphyseal defects, flattening and anterior beaking of the vertebral bodies, and abnormal dentition. Autosomal dominant inheritance is suggested.

We have seen a father and son with the same severe dwarfing syndrome characterised by disproportionately short extremities, craniosynostosis (kleeblatschadel), and symmetrical lucent defects of most long bones. Clinical and radiological features of the skeletal dysplasia are similar to three previously

reported sporadic cases,¹⁻³ in one of which the lucencies were shown to be caused by fibromas. Our two patients are the first to demonstrate apparent autosomal dominant transmission of the syndrome and document the unusual natural history of this severe skeletal disorder from infancy to maturity.

Case reports

CASE 1

This boy was the 4054 g, 49.5 cm product of a term pregnancy of an 18-year-old primigravida. At birth, he had a typical kleeblatschadel deformity (figs 1 and 2), proptosis, hypertelorism, anteverted nares, maxillary hypoplasia, protruding ears, bilateral cryptorchidism, bilateral inguinal herniae, and

FIG 1 Skull films of case 1 taken at one day of age show increase in cranial volume in spite of the distortion of the vault resulting from premature closure of all sutures, the so called 'clover leaf skull'. Dentition appears delayed.

FIG 2 See fig 1.

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FIG 3 Radiograph of the infant's lower extremities on the first day of life. Note the symmetrical cortical metaphyseal defects resembling juvenile fibromatosis. The ossification of the tarsals is irregular and delayed.

somewhat short extremities. Radiography disclosed many bilaterally symmetrical corticometaphyseal defects of the long bones (fig 3). Within the first 2 months he was treated with bilateral ventriculoperitoneal shunts for obstructive hydrocephalus and partial craniectomies to release the synostoses. Other

FIG 4 The affected father and son when the latter was 21 months old.

clinical problems in the first 6 months included poor swallowing function necessitating nasogastric feedings, developmental delay, particularly gross motor, and chronic, often purulent, nasal discharge. Although he seemed only mildly dwarfed at birth, severe growth failure of his extremities was obvious by 6 months.

When admitted to the Children's Hospital of Philadelphia at 21 months for an evaluation of his dwarfism and delayed development (fig 4), he was an alert playful child who could feed himself and follow simple commands, but could not stand, crawl, or use any words. The long bone lucencies had progressed (figs 5 and 6) and many could now be palpated as hard fixed nodules. Other features of the dysplasia at this age were a dense basicranium, maxillary hypoplasia, shallow orbits, partly formed, unerupted teeth, choanal narrowing, short, broad clavicles, and beaked, flattened vertebral bodies (fig 7). Serum calcium, phosphorus, and alkaline phosphatase and urinary mucopolysaccharide excretion were normal.

CASE 2

The father of case 1 was the fourth child of normal, young parents. Although x-rays were not available, by history he had the same features at birth and the same evolution of skeletal abnormalities as his son. He had had several neurosurgical procedures in infancy to correct the multiple synostoses of his skull but, unlike his son, had no proptosis or hydrocephalus. Multiple 'holes' in his long bones appeared in the first few months, enlarged during his childhood, but later 'filled-in'. Also like his son, he had bilateral inguinal herniae and failure of eruption of any teeth. His psychomotor development was delayed in early childhood (he did not walk until 2 years or speak until 4) but he is now of apparently normal intelligence and employed as a machinist. His height at the age of 28 is 109 cm.

At the time of the son's admission to the Children's Hospital, a complete skeletal survey of the father was obtained (figs 8 to 12). This showed that the reported lucent defects had resolved leaving grossly distorted, widened, and somewhat cystic appearing metaphyses of many long bones. Other features of the skeletal dysplasia not shown here included dysplastic, dislocated humeral heads, thoracolumbar scoliosis, and brachydactyly (Bell's type B) with hypoplastic or absent middle phalanges of the feet.

There is no other family history of short stature or bone or dental abnormalities similar to those of these two affected members. There is no known consanguinity in the family, but all are Lancaster County German in ancestry.

FIG 5 Upper extremity of case 1 at 21 months. The metaphyseal cortical defects have been displaced a short distance away from the growth plate. There is delayed appearance of the secondary ossification centres, the bone age of the hand being that of a newborn infant. The ends of the small bones of the hand are uniquely pointed and angular.

FIG 6 Case 1. AP view of the lower extremities at 21 months shows delayed ossification of the secondary centres for the hip, knee, and ankle, rhizomelic shortening of the femora, and persistence of the excentric radiolucencies in the cortices of the distal femora. The first metatarsals are broad and the middle phalanges hypoplastic.

FIG 7 Lateral view of the child's spine at 21 months of age shows beaking of the lumbar vertebrae and generalised platyspondyly reminiscent of the mucopolysaccharidoses.

Discussion

Three isolated cases appearing to be the same dwarfism have been reported previously. In the first edition of his *Atlas of general affections of the skeleton*, Fairbank¹ described a severely dwarfed male at 10 and again at 24 years with acrocephaly

FIG 8 Radiograph of the father's femora and pelvis showing symmetrical flattening and lateral migration of the femoral heads as occurs with epiphyseal dysplasias. The joint space is preserved. The femora show disturbed modelling and localised areas of radiolucency most marked distally, assumed to be the late result of the process in his son demonstrated in figs 5 and 6.

FIG 9 PA view of the father's skull showing the residua of the previous craniotomies. Disturbed dentition with several retained, unerupted teeth and multiple irregular cystic areas in both the maxillary and mandibular alveolar ridges are demonstrated.

FIG 10 Lateral view of the father's skull showing the residua of the surgery for correction of craniostenosis, increase in the volume of the cranium, and deepening of the sella.

(but not kleeblatschadel), unerupted teeth, 'epiphyseal dysplasia', and metaphyseal 'cystic' defects that resolved between 10 and 24 years of age. A second case was later reported by Keats *et al.*,² who followed from birth to the age of 7 a boy with dwarfism, oxycephaly, unerupted teeth, and progressive, 'lytic' lesions of long bone metaphyses. This patient had one of the 'lytic' lesions biopsied and it was shown to be benign, whorled, fibrous tissue. An essentially identical 10-year-old patient was described by Beighton *et al.*,³ who designated the dysplasia osteoglophonic ('hollowed-out bone') dwarfism. The involvement of both sexes, the father-to-son transmission in our patients, plus the advanced paternal age of the father of the patient described by Beighton *et al.*³ suggest that osteoglophonic dwarfism is an autosomal dominant disorder.

Osteoglophonic dwarfism cannot easily be mistaken for other forms of dwarfism. Multiple craniosynostoses or kleeblatschadel may occur in some infants with the findings of thanatophoric dwarfism,⁴ but these patients die at birth and have a very severe chondrodystrophy. Other genetic forms of craniosynostosis may be associated with mild short stature, but not the severe disproportionate dwarfism of our patients. Also, although some types of metaphyseal dysostosis or enchondromatosis may have similar metaphyseal changes,^{5,6} they lack the kleeblatschadel deformity and are clearly distinguishable by other individual criteria. The natural history of osteoglophonic dwarfism with eventual

FIG 11 Pantograph of the father showing the disturbed dentition with retention of scattered underdeveloped teeth and replacement of the alveolar ridges with disorganised non-ossified cysts. The retained teeth are notable for relatively normal crowns but abnormal to almost absent roots.

FIG 12 The father's spine showing irregular platyspondyly with residual beaking of L2.

resolution of the 'hollowed-out' areas is also distinctive. While the general features of the dysplasia are the same in all five persons there is, not unexpectedly, variability of some features, in particular the severity of craniosynostosis and the presence or absence of obstructive hydrocephalus. In addition to the many bony defects, other notable features of this

dwarfism are the bizarre disorganisation and intra-alveolar retention of the teeth and the repeated history of early psychomotor retardation with severe feeding difficulties, but later normal intelligence and nutrition. Together these features present an unmistakable phenotype of an apparently dominantly inherited skeletal dysplasia.

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