Syndrome of the month

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Osteoglophonic dysplasia

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Osteoglophonic dysplasia is a very rare skeletal disorder characterised by gross dwarfism, severe craniofacial abnormalities, and marked changes throughout the skeleton. In childhood the long bones present a characteristic radiographical appearance with multiple lucent areas in the metaphyses. Only six case reports have been published but, in view of the bizarre manifestations and the consistency of the phenotype, syndromic autonomy is well established.

History

The 1951 edition of the classical *Atlas of general affections of the skeleton* by Sir Thomas Fairbank contained a case report headed 'Acrocephaly with abnormalities of the extremities'.¹ The clinical and radiographical details of the patient at the ages of 10 and 24 years constituted a clear and comprehensive description of the disorder now known as osteoglophonic dysplasia. It is noteworthy that the affected person had sufficient intelligence and manual dexterity to be employed as a draftsman. No family history was provided in Fairbank's report and nothing is known of the patient's antecedents or possible offspring.

The second recognisable case, a North American boy, was reported in a radiological journal under the title 'Craniofacial dysostosis with fibrous metaphyseal defects'.² Thereafter, an affected Cape Town girl, aged 10 years and of mixed ancestry, was reported by Beighton *et al.*^{3,4} The paternal age was 39 years and the possibility of a new dominant mutation was suggested. At this time Professor Jürgen Spranger of Mainz, West Germany, suggested the designation 'osteoglophonic dwarfism' on the basis of the radiographical changes; this Greek term pertains to the 'hollowed out' appearance of the metaphyses.

The mode of inheritance of the disorder was

confirmed by Kelley *et al.*⁵ when they described an affected father and son. The only other published case has emanated from Portugal, where Santos *et al.*⁶ reviewed the published reports and recorded the manifestations in a neonate who died at the age of 10 months. In accordance with current convention, the word 'dwarfism' was replaced by the more acceptable term 'dysplasia' in the title of this article.

Clinical features (figs 1 to 4)

The craniofacial manifestations of osteoglophonic dysplasia, notably mandibular prognathism, frontal

FIG 1 An affected child aged 12 years with a normal four year old girl. The patient has severe rhizomelic dwarfism.

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FIG 2 *The characteristic facies with hypertelorism and anteverted nostrils.*

FIG 3 *Profile showing frontal bossing and severe mandibular prognathism.*

bossing, and proptosis, are evident at birth. Anteverted nostrils, low set, protruding ears, macroglossia, and hypertrophy of the gums are other early features. The limbs show proximal shortening, the hands are large, and the digits stubby. Affected babies are below the 3rd centile in length but gross dwarfism is not apparent at this stage.

FIG 4 *The patient depicted in fig 1 at the age of 21 years. Her intelligence is normal and her general health is good but dwarfism is very severe.*

FIG 5 *Skull radiograph at the age of 12 years. The skull shows scaphocephaly and frontal bulging. The facial bones are hypoplastic and irregular defects are present in the mandibular rami.*

Feeding difficulties, failure to thrive, nasal obstruction, and respiratory problems occur during infancy and the death of one of the six reported patients was attributed to these latter complications. Craniostenosis necessitated craniectomy in five of the six cases.

In childhood, disproportionate dwarfism becomes increasingly apparent and the craniofacial appearance may be grotesque. The elbow and knee joints lack full extension and the teeth remain unerupted. Intelligence is within the normal range and general health is good. Apart from single instances of inguinal hernia and hypertrophic pyloric stenosis there have been no reported visceral ramifications.

Three patients are known to have reached young adulthood but the long term natural history has not been recorded. Adult heights have been 97 cm, 104 cm, and 146 cm.

Radiographical features (figs 5 to 10)

SKULL

Craniostenosis with oxycephaly and enlargement of

FIG 6 Hand radiograph, AP view. The tubular bones are short and undermodelled, with dysplastic, cone shaped epiphyses. The bones of the carpus are very dysplastic.

FIG 8 Leg radiograph, AP view. The lower femoral and upper tibial metaphyses are expanded and contain multiple lucent defects. The patellae are dislocated.

FIG 7 Arm radiograph, AP view. The long bones are porotic and undermodelled, with dysplastic epiphyses and multiple radiolucent areas.

FIG 9 AP radiograph of the pelvis and femora at the age of 21 years. The irregular cortical defects evident in fig 8 have now disappeared and the metaphyseal lucencies are less discrete.

FIG 10 AP radiograph of arm at the age of 21 years. The humerus is short and distorted. The lucencies evident in fig 7 are less discrete.

the sella turcica is a major feature. The calvarium has a 'beaten copper' appearance in affected children but this abnormality regresses by adulthood. Cystic changes are present in the mandible and the teeth are impacted.

SPINE

The vertebral bodies are flattened with anterior beaking and posterior scalloping. The vertebral canal is narrow and there is a discrepancy in the size of the thoracic and lumbar vertebrae. The spine does not usually become significantly malaligned.

LIMBS AND EXTREMITIES

The long bones show multiple metaphyseal lucencies which are maximal in the lower femora. In affected regions the external configuration and internal architecture of the skeleton may be disturbed. It is noteworthy that this 'holes in the bones' appearance resolves by adulthood. The tubular bones of the hands and feet are broad and short with cone shaped phalangeal epiphyses, and the carpus and tarsus are very dysplastic.

Differential diagnosis

Osteoglophonic dysplasia can be easily distinguished from the other dwarfing skeletal dysplasias by virtue of the unique craniofacial appearances and the characteristic radiological changes. McKusick⁷ has drawn attention to the phenotypic similarity of osteoglophonic dysplasia and hypophosphatasia; the latter disorder can be differentiated by appropriate laboratory studies.

Pathogenesis

The nature of the basic defect is not known. Cytogenetic studies and routine estimations of serum calcium, phosphorus, and alkaline phosphatase have consistently yielded normal results. In the patient studied by the author, investigations of urinary mucopolysaccharides and serum lysosomal hydrolases did not show any abnormality. Biopsy of a lucent bone lesion showed whorls of fibrous tissue.²

Genetics

The six reported patients comprise an affected

father and son, three sporadic males, and a sporadic female. Paternal age was 39, 34, and 28 years in the reported instances. These data are highly suggestive of autosomal dominant inheritance and the majority of affected persons apparently represent new mutations for the faulty gene. In view of the severity of the dwarfism and other clinical manifestations, it is probable that fitness to reproduce is compromised and it can be anticipated that the majority of new cases will be sporadic.

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