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A NEW FORM OF SKELETAL DYSPLASIA WITH AMELOGENESIS IMPERFECTA AND PLATYSPONDYLY

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ABSTRACT

We report two patients, born of consanguineous parents, affected by a disorder resulting in mild growth retardation. Hallmarks are amelogenesis imperfecta (absence of the enamel cap) associated with brachyolmia-like anomalies: platyspondyly with short pedicles, narrow intervertebral and interpedicular distances, rectangular-shaped vertebrae with posterior scalloping and herniation of the nuclei, and broad femoral necks. Inheritance appears to be autosomal recessive.

Brachyolmia is a generic name for a family of skeletal dysplasias characterized by generalized platyspondyly without significant epiphyseal or metaphyseal involvement. It has been divided into four subtypes based on vertebral shape, associated features and mode of inheritance. We report a further subtype in which mild brachyolmia is associated with amelogenesis imperfecta.

Family report

PATIENT 1

This boy was first evaluated for growth retardation at age 12. Clinical examination revealed a short boy (Fig. 1) of normal intelligence, showing no facial dysmorphia and no signs of puberty. He was 133 cm tall (-3 SD) and had an OFC of 53 cm. Sitting height was 63 cm and arm span 134 cm. His hands were 15 cm long, with a 3rd finger length of 6.5 cm. He had mild interdigital webbing, protrusion of the sternum and a limited extension of the elbows. He showed amelogenesis imperfecta and oligodontia. The milk teeth were said to be abnormal in shape, and soon decayed. The permanent teeth were yellowish and almost completely lacked their enamel cap. Panorex studies revealed missing molars (19 definitive teeth present). All erupted teeth had to be removed for early decay. Urinary excretion of' mucopolysaccharides and karyotypes were normal.

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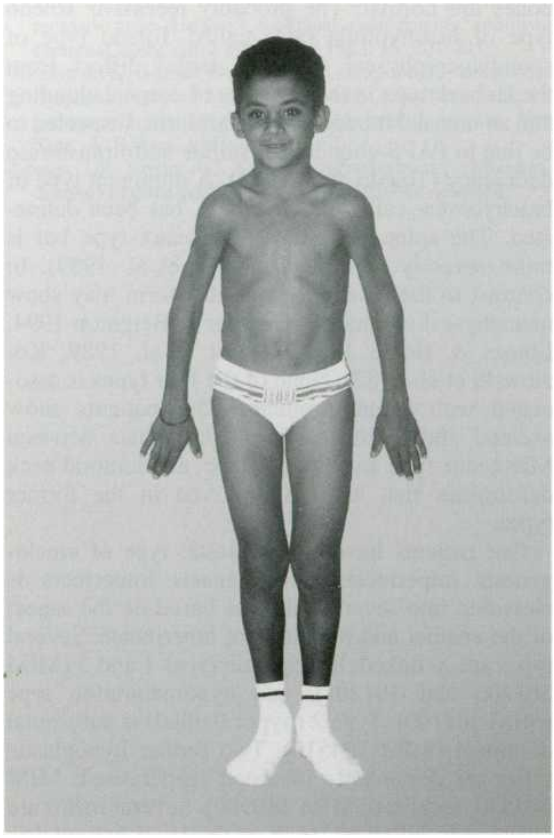
Figure 1.



Patient 1 aged 13 years: proportionate shortness of stature and pectus deformity.

PATIENT 2

This girl was the elder sister of patient 1. Menarche occurred at age 14. At age 16, she was 141 cm tall (-3.5 SD), had an arm span of 142 cm, a sitting height of 72 cm and short hands (15.5 cm; 3rd finger: 6.5 cm). She had no thoracic deformity. She was completely edentulous. Orthodontic records indicated that several molars were missing, and that all existing teeth had to be removed within a year of eruption.

FAMILY HISTORY

The patients were the two older children of healthy, first cousin-once-removed, Moroccan parents (f=1/32). The parents were of normal height and showed no dental abnormalities. Two younger sibs, aged 10 and 8 had a normal growth pattern and normal teeth. The sex-corrected midparental height was 172.5±8.5 cm for the boy and 166±8.5 cm for the girl.

RADIOLOGICAL ANOMALIES

Both index children showed similar skeletal anomalies, limited to the spine and the femoral neck, more severe in the boy. There was generalized platyspondyly (Fig. 2a). On profile view (Fig. 2b), the

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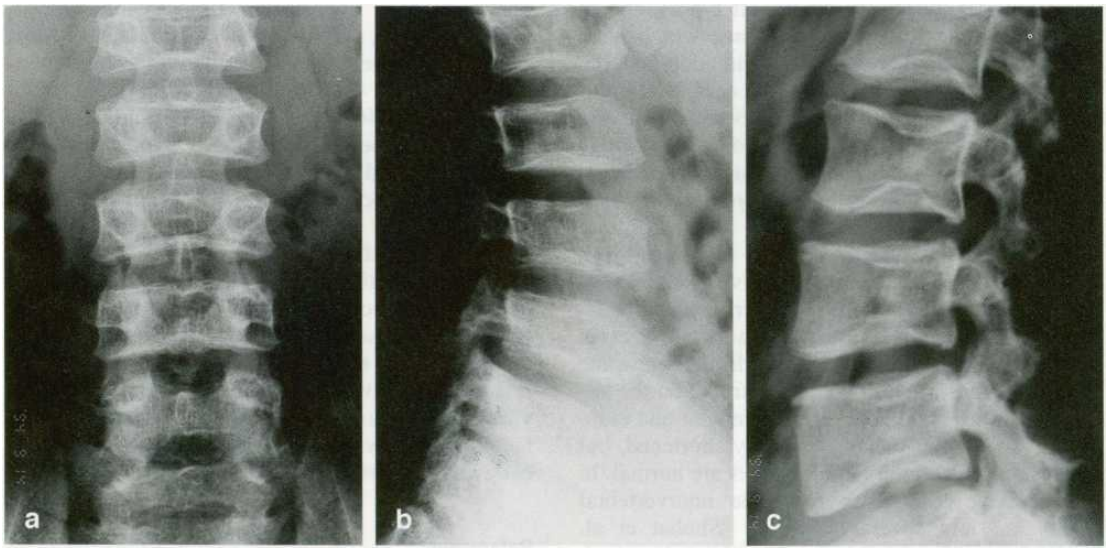
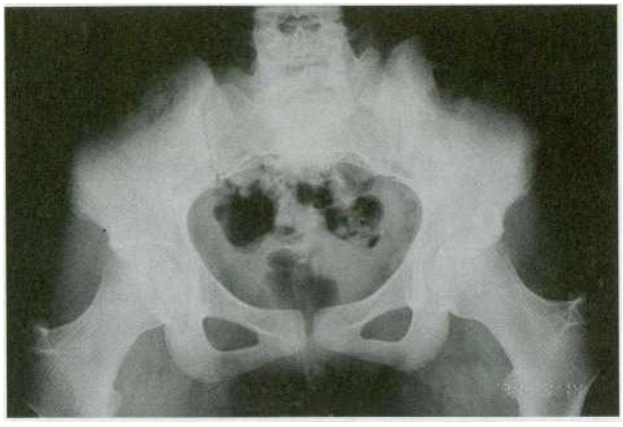
vertebral bodies appeared flattened but still rectangular, mildly elongated, and globally wedge-shaped, being higher anteriorly. There was posterior scalloping. The vertebral plates were disrupted in their posterior half by herniation of the intervertebral nucleus, which was mild in the boy (Fig. 2b) but more severe in the girl (Fig. 2c), giving her an aspect somewhat similar to that of Scheuermann disease. Intervertebral spaces were markedly narrowed. Pedicles were short. On frontal view (Fig. 2a), there was no lateral elongation; the pedicles seemed unusually wide. There was a narrowing of the interpedicular distance from L1 to L4. The pelvis appeared to be decreased in height. The femoral necks were massive but not short, this feature being more prominent in the boy (Fig. 3). There were no dysplastic changes in other long bones, in the hands, or in the skull, and there was no osteoporosis or wormian bones. Bone age in the boy was delayed 2 years.

Figure 2. *Radiological aspect of the lumbar spine.*



Patient 1: a) platyspondyly with normal intervertebral spaces (at this level) and absence of widening of the interpedicular distances; b) short pedicles and mild depression of the vertebral plates. Patient 2: c) milder platyspondyly, more severe herniation of the nuclei, and short pedicles.

Figure 3. *Patient 1.*



Pelvis: broad femoral necks and reduced pelvic height.

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Discussion

Our patients appear to be affected by a skeletal disorder resulting in mild growth retardation. The syndrome consists of platyspondyly with thick short pedicles, narrow intervertebral spaces, and rectangular-shaped vertebral bodies with scalloping of the posterior wall and herniation of the nuclei. The vertebral changes were associated with dysplastic femoral neck and amelogenesis imperfecta. The skeletal anomalies appeared more severe in the boy, but as sequential follow up in infancy was not available, intrinsic variability, age or sex effects are all possible.

Platyspondyly has been observed in association with abnormal long bones in a large number of skeletal dysplasias (spondyloepiphyseal and spondylometaphyseal dysplasias of several types), and in mucopolysaccharidoses, all diagnoses which were easily discarded. Platyspondyly with cod-fish deformity is commonly observed as a complication of osteogenesis imperfecta and other osteoporotic disorders, including SPONASTRIME dysplasia. There were no signs of hypomineralisation in our affected sibs. Hence, a diagnosis of brachyolmia-like syndrome was initially suggested.

Brachyolmia is usually divided into four types (Shohat et al. 1989). In the recessive Hobaek type (Horton et al. 1983), there is universal platyspondyly, and reduced intervertebral spaces are present without nucleus herniation. On the frontal view, the margins of the vertebral bodies protrude; on the lateral view, vertebral bodies are rectangular and elongated. The tubular bones are mildly shortened, but not dysplastic, and the femoral necks are normal. In the recessive Maroteaux type, the intervertebral spaces are less severely reduced (Shohat et al. 1989). In profile, the vertebrae are less elongated, their anterior edge is rounded, and there is often a mild notching of the vertebral plates. The long bones are normal. The probably recessive Toledo type of brachyolmia (also called Toledo type of spondyloepiphyseal dysplasia tarda) differs from the Hobaek type in the presence of corneal clouding and an unusual mucopolysaccharidiuria, suspected to be due to PAPS-chondroitin sulfate sulfotransferase deficiency (Toledo et al. 1978). A dominant type of brachyolmia, called brachyrachia, has been delineated. The spine resembles Maroteaux type but is more severely deformed (Shohat et al. 1989). In contrast to the recessive type, this form may show metaphyseal anomalies (Gardner & Beighton 1994, Lomas & Boyle 1959, Shohat et al. 1989, Kozlowski et al. 1982). None of the four types is associated with dental problems. Our patients show skeletal alterations that are intermediate between Maroteaux type and Hobaek type, and femoral neck deformities that are not observed in the former types.

Our patients have a hypoplastic type of amelogenesis imperfecta. Amelogenesis imperfecta is classified into several subtypes based on the aspect of the enamel and the mode of inheritance. Several types are X-linked: hypoplastic types 1 and 3 (MIM 301200 and 301201), and hypomaturation type (MIM 301100). Type 2 (hypocalcified) is autosomal dominant (MIM 104510). Two further hypoplastic types are dominantly inherited (generalised: MIM 104530, localised: MIM 130900). Several forms are recessively inherited, such as the local hypoplastic type (MIM 204650) and the pigmented hypomaturation type (MIM 204700). Some cases of amelogenesis imperfecta occur in a syndromal context: with dentinogenesis imperfecta (Brandywine type - MIM 125500),

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with retinal dysfunction (MIM 217080), with dementia and epilepsy (Kohlschutter-Tonz syndrome - MIM 226750), with nephrocalcinosis (MIM 204690), or with ectodermal anomalies (Logic syndrome - MIM 245660). Skeletal involvement associated with amelogenesis imperfecta is observed in trichodento-osseous syndrome (MIM 190320). None of those syndromes matches the family described here.

The combination of mild brachyolmia and amelogenesis imperfecta may be due to the chance coexistence of two separate recessive disorders, but the concordance in the sibship rather supports a causal relationship between the two anomalies. With this view, we have to conclude that our probands are affected by a new type of brachyolmia, which is recessively inherited.

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