A new familial skeletal dysplasia with severely retarded ossification and abnormal modeling of bones especially of the epiphyses, the hands, and feet

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Abstract. Three brothers with a constitutional skeletal dysplasia characterized by an excessively retarded ossification, principally of the epiphyses, the pelvis, the hands and the feet, are reported. In the hands and feet the retarded ossification is combined with an abnormal modeling of the bones.

All the children appeared normal at birth. At the time of examination a moderate degree of dwarfism could be predicted. There was no mental retardation. All laboratory investigations including chromosomal analyses and examination for acid mucopolysaccharides in the urine were normal. Parental consanguinity suggest an autosomal recessive inheritance. There is no resemblance of this disorder to any of the hitherto described groups of constitutional diseases of bones.

Key words: New skeletal dysplasia – Multiple epiphyseal dysplasia – Delayed maturation of hand feet pelvis sacrum

Introduction

A familial congenital skeletal dysplasia, so far not described in the medical literature, forms the basis of this presentation. The index cases are three brothers born in 1967, 1970, and 1980 to a family originating from a small village in Turkey but living in Denmark since 1979. At birth all three brothers were considered to be normal. The two older boys were admitted to the hospital because of slight, short-limbed disproportion and the suspicion of a chromosomal anomaly (Figs. 1a, b, 2). The youngest brother, born in Denmark, was carefully followed and examined primarily because of the clinical and especially the unusual radiological findings in his brothers.

Case reports

To demonstrate the progression of the skeletal changes the three boys will be presented in order of age at study.

Case 1: A boy who appeared physically normal at birth and at 3 months. The first radiological examination at the age of 1 month, including the spine and the long bones of the extremities, was normal apart from only three ossified segments of the sacral bone, short fibulae and absent epiphyseal ossification in both knees.

On physical examination, when 1 year old, only the hands and feet were noted to be short and broad. The height was 0.3 SD below the WHO standard [7]. The psychomotor development and head circumference were normal. A skeletal survey
showed a severe degree of delayed ossification, especially pronounced in the hands, the feet and the pelvis. In the hands (Fig. 8a) there was ossification of only the distal phalanges of all fingers together with a very small center in the proximal phalanx of the second and third fingers. In the feet there were small round ossification centers in the talus and calcaneus together with ossification of all metatarsal bones, with a distinct shortening of the fourth. Furthermore there was ossification of the distal phalanx of the first toe while all other ossification centers were missing. In the pelvis (Fig. 3a) ossification was markedly delayed, especially of the pubic bones, all cartilaginous areas were too wide. In the lower extremities there was an abnormal convexity of the metaphyseal borders, absence of epiphyseal ossification and shortened fibulas.

A chromosomal study showed a normal karyotype. (All chromosomal examinations were carried out by Grethe Jensen, Cytological Laboratory, Frederiksberg Hospital, Copenhagen).

Case 2: A boy, 9 years old, complained on his first admission of pain in the hips and knees after ordinary walking and reduced flexion of both elbow joints. He was of subnormal height, 3.4 SD below WHO standard [7]. The skull and dental status were normal. The facial appearance was not considered abnormal except that he looked somewhat older than his actual age. There was moderate disproportion with short arms and legs but normal length of the spine. The motion of the shoulder joints was normal but he had cubitus varus on the right arm and cubitus valgus on the left. Elbow flexion was reduced to 120° while the extension was free. Supination and pronation were unrestricted. The hands and fingers were abnormally short with slightly pointed fingertips but function was unrestricted. A slightly decreased flexion in the hip joints was observed. The knees were normal, the feet end toes short, with free movement. Investigation of neuromuscular development, vision and hearing gave normal results and there were no signs of mental retardation. No symptoms of endocrine disorders were found and the external genitalia were normally developed. The following blood analyses were normal: hemoglobin, white blood cell count, erythrocyte sedimentation rate, iron, hemoglobin electrophoresis, alkaline phosphatases, calcium, inorganic phosphorus, sodium, potassium, creatinine, aspartate aminotransferase, lactate dehydrogenase in plasma/serum, thyroxine stimulating hormone, and triiodothyronine in plasma. Acid mucopolysaccharides and amino acids in urine and lysosomal enzymes in leukocytes were normal. Chromosomal studies, including banding, showed a normal karyotype.

The radiological examination was characterized by a generally retarded ossification, combined with abnormal modeling of a great number of bones of the hands and feet. In the hand (Fig. 8b) all metacarpals were slightly fusiform with distal conical tapering and a rounded upper end. The first and second phalanges of the four ulnar fingers were also fusiform while all the third phalanges appeared short but otherwise normal. The second phalanx of the fifth finger was not ossified. In the thumb there was an increased distance between the two phalanges, suggesting the presence of a nonossified accessory phalanx. Only two of the carpals showed sporadic, irregular mineralization. The trabeculation of all bones was irregular and the cortex extremely thin. In the feet (Fig. 4a) the fourth metatarsal was short while the fifth was fusiform, with an elongated accessory bony formation along its lateral border, representing a partial duplication. The four medial metatarsals all had both proximal and distal epiphyses. The tarsal bones were represented by ossification centers in a delta-shaped talus, a calcaneus which was immature but otherwise normal and in a very small lateral cuneiform. The pelvis was narrow with a relatively increased sagittal diameter, an impression accentuated by an almost totally absent ossification of the pubic bones. The iliac wings were narrow and the acetabular roofs poorly developed. There appeared to be a partial agenesis of the sacrum (Fig. 5) with unfused ossification of only the upper three segments. The sacroiliac junction, the Y-cartilage of the acetabulum and the symphysis were all wide. The thoraco-lumbar spine was only mildly affected with an ovoid (immature) form of the vertebral bodies and coarsening of the trabecular architecture. The lum-