Case reports

Journal of Medical Genetics 1987, 24, 366-377

Spondyloepiphyseal dysplasia tarda: a new autosomal recessive variant with mental retardation

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SUMMARY A new variant of spondyloepiphyseal dysplasia tarda with mild to moderate mental retardation is described in three daughters born to healthy, consanguineous parents. The mode of inheritance is compatible with that of an autosomal recessive disorder. The identification of this variant is important, as it enables more precise counselling in families in which sporadic cases with this form of presentation are found.

Spondyloepiphyseal dysplasia tarda (SED_T) is a skeletal disorder which usually presents clinically in late childhood as a short trunk type dwarfism due to progressive involvement of the spine and epiphyses.¹⁻⁴ Clinical and genetic heterogeneity is most marked in this syndrome. Although platyspondyly is universally present in SED_T, the clinical heterogeneity is due to the variable degree of epiphyseal involvement, from near normal extremities to significant deformities and limitation of movement. Intelligence is normal. Inheritance is almost always X linked recessive, although autosomal recessive and autosomal dominant inheritance have been reported.⁴

Unless there is a positive family history, the mode of inheritance in a sporadic case of SED_T cannot be determined solely on clinical or radiological findings. Therefore, for genetic counselling and in order to give more precise information to the family, it would be important if clinically well delineated specific variants of SED_T could be identified. Connor *et al*⁵ described an adult female with SED_T and short metacarpals and metatarsals which they believed

might be characteristic of a variant with autosomal dominant inheritance. This report describes yet another new variant of SED_T, characterised by mental retardation and autosomal recessive inheritance.

Case report

The proband (figs 1 and 2, III.2), a 16 year old female born in 1966, was referred to Nassr Children's Hospital Genetics Clinic for evaluation of short stature. She is the youngest born to distantly related healthy Arab (Bedouin) parents. A 23 year old sister (III.1) and a 15 year old sister (III.3) are similarly affected. She has seven healthy sisters, three healthy brothers, and a sister who died at 12 years of age of leukaemia. Her father, 60 years old, is 175 cm tall and her mother, 55 years old, is 163 cm tall. There is no family history of mental retardation other than in the affected subjects. A paternal aunt, married to first cousin, is said to have similarly affected offspring (fig 2).

The three affected sisters have similar case histories and clinical findings and will be discussed together (table). They were born after normal term pregnancies. Birth weights and lengths were not recorded but were apparently normal. The proband was said to have attained normal milestones: she sat at seven months, walked by one year, and had normal teething. Both her sisters had delayed milestones and sat at one year, walked by one and a half to two years, and had delayed teething. All three sisters did poorly in school. The proband repeated first grade three times and currently can read and write only simple sentences and do only simple arithmetic. Her sisters repeated first grade four times before dropping out of school altogether and can neither read nor write.

Received for publication 15 October 1984.

Revised version accepted for publication 15 April 1986.

FIG 1 The proband and two affected sisters.

FIG 2 Family pedigree.

Physical examination revealed dull but cooperative patients with normal facies in no acute distress. Height was below the 3rd centile. Hands and feet were of normal adult size and proportions. There was mild to moderate limitation of movement in all large joints and the gait was waddling. Complete

neurological and general examination including sensation and coordination was otherwise normal. Ophthalmological examination and audiometry were within normal limits. The following laboratory

TABLE Summary of clinical and radiographical findings.

	III.2	III.1	III.3
Age (y)	16	23	15
Mental retardation	Mild	Moderate	Moderate
Height (cm)	139	145	132
Upper segment:lower segment ratio	0.93	0.96	0.94
Large joint mobility	Limited	Limited	Limited
Hands and feet	Normal	Normal	Normal
Radiographical findings			
Dens epistrophei	Absent	Absent	Normal
Platyspondyly	Present	Present	Present
Abnormal lumbar vertebrae	Present	Present	Present
Degenerative large joint changes	Present	Present	Present
Hands and feet	Normal	Normal	Normal
Upper extremities shorter than lower extremities	Present	Present	Present

examinations were normal: serum electrolytes, liver function tests, glucose, BUN, calcium, phosphorus, alkaline phosphatase, urine analysis, urine spot test for mucopolysaccharides, and urinary amino acids. Chromosome analysis showed normal female karyotypes, 46,XX. No evidence of storage or collagen abnormalities could be found on electron microscopic examination of cultured skin fibroblasts.

RADIOGRAPHIC FINDINGS (TABLE, FIG 3)

Skeletal x rays showed an absent dens epistrophei in the proband and one sister (III.1). Platyspondyly was

universally present with an anterior tongue-like protrusion in the lumbar region. There was severe deformity of the pelvis with flared iliac bones, a short sacrosciatic notch, and gross acetabular deformity. The epiphyses of the femoral head were markedly deformed, as were the hip joints, resulting in bilateral coxa valga. The femoral necks were unusually narrow. The diaphyses of the lower extremities were narrowed with deformity of the condyles. There was severe deformity of the proximal and distal epiphyses of the humerus with formation of humerus varus at the shoulder joint. Extensive degenerative joint

FIG 3 (a) III.2. Lateral view of the cervical spine. The dens epistrophei is absent and platyspondyly of the cervical vertebrae is noted. (b) III.1. Lateral view of the lumbar spine showing platyspondyly with an anterior tongue-like protrusion and irregular upper and lower vertebral borders with narrow disc spaces. (c) III.3. AP view of the humerus and proximal half of the forearm showing plump proximal humeral epiphysis with humerus varus formation and epiphyseal deformity at the elbow joint with ulnar subluxation. (d) III.1. AP view of the pelvis showing 'Mickey-Mouse ear shaped' iliac bones, broad pubic bones, hypoplasia of the ischium, separated symphysis pubis, short sacrosciatic notch, bilateral deformed acetabular notches with left femoral subluxation, and bilateral coxa valga.

changes were present in the shoulder, hip, and knee joints, characterised by narrowing of the joint spaces and irregularities of the articulate surfaces. There were milder but similar changes in the ankle. The upper extremities were shorter than the lower extremities. The hands and feet were entirely normal.

Discussion

The characteristically progressive radiological findings affecting the spine and epiphyses seen in SEDT are not, in themselves, diagnostic of SEDT but are found in several of the skeletal dysplasias,⁴ and SEDT is a heterogeneous group of disorders both in clinical presentation and in genetic transmission.⁴⁻⁵ A subclassification is important in order to be able to give more specific and precise genetic counselling. Inheritance of SEDT is usually X linked recessive, but some cases of autosomal recessive and autosomal dominant inheritance are known. Occasionally, the clinical history and family pedigree can help in making a definitive diagnosis. More often, however, when confronted with a sporadic case and a negative family history, a specific diagnosis cannot be made. The dilemma occurs when genetic counselling is required. It would be of importance to the clinician if specific variants and their inheritance could be identified.

The clinical history and x ray findings in the three patients presented here establish the diagnosis of

SEDT.¹⁻² Previous reports have indicated normal mentality in SEDT. The family described here, with three affected mentally retarded daughters born to healthy, related parents, and the history of similarly affected mentally retarded first cousins also born to consanguineous parents, where all other children in the kindred are mentally normal, is most compatible with a new variant of SEDT with autosomal recessive inheritance.

The delineation of this new variant of SEDT should prove useful in the counselling of sporadic cases of SEDT. Description of new cases is important for more precise classification of variants of SEDT in the future and is essential for counselling of cases that are thought to be sporadic.

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Hypoplastic tibiae with postaxial polysyndactyly: a new dominant syndrome?

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SUMMARY A five year old boy is reported with hypoplastic, bowed tibiae and postaxial polysyndactyly. Sixteen relatives of both sexes in four generations either have bilateral syndactyly or postaxial polydactyly or both. The nature of the condition and the possible mode of inheritance are discussed.

Tibial hypoplasia associated with polydactyly has been described by several authors.¹⁻⁵ All patients

studied have had hypoplastic or absent tibiae, other craniofacial anomalies, and preaxial polydactyly. We report a case of a boy with a previously undescribed syndrome of hypoplastic tibiae with postaxial polysyndactyly.

Case report

The proband was a five year old boy delivered at term by lower caesarean section to first cousin Arab parents (father 37 and mother 33 years old). He had three older sibs (two males and one female). His birth weight was 3.8 kg, length 48 cm, and head circumference 36 cm. He had bilateral postaxial polydactyly of both hands (surgically removed), clinodactyly of