Spondyloenchondrodysplasia

H MENDER*, K KRUSE†, AND J SPRANGER*

From the Departments of Pediatrics, Universities of Mainz* and Würzburg†, West Germany.

SUMMARY Spondyloenchondrodysplasia is a rare autosomal recessive skeletal dysplasia with vertebral dysplasia and enchondroma-like lesions in the pelvis and long bones. The vertebral bodies show dorsally accentuated platyspondyly with disturbance of ossification. Clinical abnormalities such as short stature, rhizomelic micromelia, increased lumbar lordosis, barrel chest, facial anomalies, and clumsy movements may be present. We report on four patients, three of them from one family, who showed a wide range of clinical and radiological changes to document considerable variability of expression of the mutated gene.

In 1976 Schorr *et al*¹ reported two brothers with a condition they called spondyloenchondrodysplasia because of enchondromatosis with marked involvement of the spine including platyspondyly. Two additional cases were published by Sauvegrain *et al*.² On the basis of these and three further reports,³⁻⁵ the condition is now thought to be a distinct entity with autosomal recessive inheritance. Here we report an isolated case, two brothers, and a distantly

related third boy with markedly different manifestations of this syndrome.

Case reports

CASE 1

RP, a boy born in 1972, was the first child of healthy parents who were 25 and 22 years old at his birth. Pregnancy was uncomplicated. The boy was born at term with a length of 41 cm and a weight of 2400 g. Short limbs were noted immediately.

At 12 years (fig 1) the boy was 108 cm tall (-6

Received for publication 31 March 1988.
Accepted for publication 28 May 1988.

FIG 1 The brothers case 1 (12 years) and case 2 (nine years), showing short limbed dwarfism, accentuated lumbar lordosis, short neck, oval shaped face, short nose, and long philtrum. Note the similarity between the two.

FIG 2 Growth curves of the four patients. For comparison, measurements from published patients are shown. Note wide variability in body length.

SD) (fig 2) and weighed 28.4 kg. He had rhizomelic micromelia with an arm span of 104 cm and an upper segment/lower segment ratio of 1.3 (+11 SD). His hands and feet were short and plump with broad thumbs. Calcaneovalgus deformity and clinodactyly of the fourth and fifth toes were noted, and the right foot was internally rotated. There was genu valgum, cubitus valgus, barrel chest, pectus carinatum, increased lumbar lordosis, a short neck, and relative macrocephaly (52.5 cm). The face was oval shaped and expressionless with a prominent premaxillary region, frontal bossing, depressed and broad nasal bridge, short nose, anteverted nostrils, and long philtrum. Body movements were clumsy and the gait was waddling.

Laboratory findings included normal serum levels of growth and thyroid hormone, urinary acid mucopolysaccharides, and normal parameters of calcium metabolism.

Radiographs were available from the age of six weeks to 12 years: at all ages the tubular bones were shortened. During infancy, metaphyseal irregularities and widening were present (fig 3a) which regressed in later childhood. Hand radiographs (fig 4a, c) showed premature ossification of the carpal bones during infancy. The basilar portions of the iliac bones were hypoplastic and the acetabular roofs horizontal. The vertebral bodies (fig 6a)

TABLE Cases of spondyloenchondrodysplasia.

	References					Present cases			
	1	6	2	3	4	5	1, 2	3	4
Patients: Male/Female	M, M	F, M	F	M	M	4 cases F	M, M	M	M
Sibs/Isolated	S	S	I	I	I	I	S	*	I
Parental consanguinity	+	-		+	-		+	+	+
Age of manifestation: Birth/Infancy/Childhood	B	I, B		I	I		B	C	C
Dwarfism	++	+++		+	++	+	++	(+)	(+)
Proportions: Limbs (rhizomelic)/Trunk shortened	L	(L)		T		T	L	-	-
Nervous system: Spasticity/Mental retardation	-	-	-	M	S	-	(M)	-	S
Skull/face: Dolichocephaly/Turricephaly/ Frontal bossing/Midface hypoplasia	-	D		-		-	F, M	(T)	-
Barrel chest	+	-, +					+	-	-
Spine: Scoliosis/increased Kyphosis or Lordosis	K, L	-, (S)			S		L	(L)	K, S
Legs: Knock knees/Bow legs	K	B		-			K	-	K
Hands shortened	†	+					+	-	-
Joints: Swollen/Painful	S	-		-	P		(S)	P	S
Metaphyses wide	++	+++	+	+	++	++	++	+	+++
Radiolucent areas in: Meta-, Dia-, Epiphyses, Pelvis, Scapula, Sternum	M, D, E	M	M	M, D, E	E	M, D	M		D, E
Pelvis: hypoplastic iliac bones	P	+	St	P, St			P		P, Sc
Vertebrae: Platyspondyly	+	+	-	-			+	-	+
Structure dorsally irregular	++	-, ++	+	++	+	++	+	++	++
Intervertebral distance increased	+++	+	(+)	++	+	++?	++	++	++
Base of skull sclerotic	++	-, ++	-	++	+	++	-	++	++
	-	-		+	-		-	-	+

*Distantly related to the brothers (present cases 1 and 2).

†Only brachytelephalangy.

FIG 3 X rays of legs of (a) case 1 at nine months, (b) case 4 at two years, (c) case 2 at three years, and (d) case 3 at 12 years. The metaphyseal margins are irregular. In (a) and (c) (the brothers) the metaphyses are splayed, the epiphyses are slightly irregular, and there is proximal overgrowth of the fibulae (not seen in other cases). In (b) the metaphyses are slightly widened and cupped. Radiolucent areas are seen in the distal thirds of the femoral and tibial diaphyses and in the fibular metaphyses. The metaphyseal margins are irregular.

were flat with structural densities in their dorsal parts. In later childhood the end plates were slightly irregular. The skull was normal.

CASE 2

JP, a boy born in 1975, was the only sib of case 1. After an uncomplicated pregnancy he was born at term with a birth weight of 2500 g. Short limbs were noted immediately. At nine years (fig 1) he measured 100 cm (-6 SD) (fig 2) and weighed 21.3 kg. His arm span was 94 cm, his upper segment/lower segment ratio 1.5 ($+9$ SD), and his OFC 51.5

cm (normal in relation to body length). His physical appearance (fig 1) and laboratory and radiographical findings (figs 3c, 5b, 6c) were similar to those of his brother.

CASE 3

UP was a boy born in 1972 to parent aged 23 and 20 years. They and two younger sibs were healthy. Birth length was 51 cm and weight 3100 g. When he was four months old severe craniotabes and mild costochondral beading were noticed and a diagnosis of rickets was made, in spite of normal serum

FIG 4 X rays of the hands of (a) case 1 at nine months, (b) case 4 at six years, and (c) case 1 at 12 years. These three films show the variability of the metaphyseal irregularities which are pronounced and 'enchondromatous' in (b) but barely visible in (c).

FIG 5 X rays of the pelvis of (a) case 4 at two years and (b) case 2 at nine years. The basilar portions of the iliac bones are broad and short and the acetabular roofs are horizontal. In (a) the sciatic notches are small and there are numerous punched out lesions in the iliac crests. The femoral necks are broad and their metaphyses are slightly irregular. In (b) the right capital femoral epiphysis is flat but the normal epiphysis on the left suggests that this is a secondary phenomenon.

calcium and phosphate levels. During childhood he occasionally complained of pain in the weight bearing joints.

At 12 years (fig 7) he measured 142 cm (-1.5 SD) (fig 2) and weighed 31.5 kg. OFC was 53 cm (slightly below average), arm span 142 cm, and upper segment/lower segment ratio 0.9 (-0.5 SD). Except for an accentuated lumbar lordosis and mild turricephaly no dysplastic signs were found. Laboratory findings, including MPS urinary excretion and calcium metabolism, were normal.

Radiographs showed irregular metaphyses from infancy up to the age of 12 years; several of them were splayed and mildly clubbed (fig 3d). In later childhood the vertebral bodies (fig 6d) were flat and markedly dysplastic.

FAMILY HISTORY

Both pairs of parents were consanguineous and

related to each other (fig 8) supporting autosomal recessive inheritance.

CASE 4

AS, a boy born in 1966, was probably the incestuous product of a father-daughter union. At his birth his parents were 17 and 40 years old; they and a younger sister were reportedly healthy. Pregnancy was said to be normal but birth was complicated by premature rupture of the membranes and umbilical cord strangulation possibly causing perinatal asphyxia. Birth length was 50 cm and weight 2550 g. He learned to walk and speak at three years of age.

At six years (fig 9) he was 109 cm tall (-2 SD) (fig 2) and weighed 16.3 kg. He had spastic quadriplegia with severe foot drop, contractures of the hips and knees, and kyphoscoliosis. His joints were prominent and his hands short and broad. His face was unusual with a broad nasal bridge, a long nose,

FIG 6 X rays of the spine of (a) case 1 at nine months, (b) case 4 at two years, (c) case 2 at nine years, and (d) case 3 at 12 years. The spinal changes are quite different in these patients, three of whom (a, c, d) are members of the same family. The vertebral bodies are flat in (a), (b), and (d) but not in (c). Marked structural irregularities are seen in the dorsal third of the vertebral bodies of (b) and (d).

and slight retrognathia. Apart from slightly increased serum alkaline phosphatase and hypochromic anaemia laboratory findings were normal.

Radiographs showed slightly shortened tubular bones with wide, cupped metaphyses and radiolu-

FIG 7 Case 3 at 12 years. The physical appearance is normal and the height is on the 10th centile.

FIG 8 Partial pedigree of family P.

FIG 9 Case 4 at six years, showing short stature, contractures of the hips, knees, and ankles, and slight facial anomalies.

cent areas in the diaphyses of the humerus, femur, and tibia (fig 3b, 4b). Some epiphyses were irregular in structure or shape. The scapulae were irregular. The basilar portions of the iliac bones were hypoplastic and the pubic bones and iliac crests were studded with radiolucent lesions (fig 5a). The vertebral bodies (fig 6b) were flat and dysplastic. The base of the skull was sclerotic.

Discussion

Based on 12 published observations,¹⁻⁶ including two cases of 'autosomal recessive spondylometaphyseal dysplasia' reported by Gustavson *et al*⁶ and our four patients (excluding two insufficiently documented cases published by Kozłowski *et al*⁷), spondyloenchondrodysplasia can be delineated as follows (table).

Most patients are short with disproportionately short limbs in severe cases. In others, body length and proportions are in the lower normal range. Increased lumbar lordosis, kyphoscoliosis, barrel chest, genu valgum or varum, short and broad hands, dolichocephaly, turriccephaly, frontal bossing, and mild midface hypoplasia are occasional findings. Joints may be prominent or painful.

The age at manifestation varies from birth to later infancy. Clinical and radiographical abnormalities are not necessarily correlated. Thus, our case 3 had severe platyspondyly but was not short in stature.

Radiographs show mild to severe platyspondyly which is often dorsally accentuated. Localised ossification defects are sometimes present in the dorsal portions of the vertebral bodies. In adolescence, the vertebral abnormalities tend to improve.

The tubular bones are shortened and the metaphyses irregular and slightly widened with varying radiolucent lesions. Usually, the proximal fibular and distal ulnar metaphyses are more severely affected. Sometimes radiolucent areas are present in the diaphyses, epiphyses, iliac crest, scapulae, and sternum. The epiphyses may be irregular. In the pelvis, the basilar portions of the iliac bones may be short and broad with horizontal roofs.

The skeletal changes are qualitatively similar in all patients but vary in expression. They may predominate in the metaphyses or spine.

Spondyloenchondrodysplasia is a genetic disorder with autosomal recessive inheritance. Two brothers from our family had a severe form and their relative a mild form, indicating a marked degree of intra-familial variability of expression.

The disorder must be differentiated from other spondylometaphyseal dysplasias.⁷⁻¹² Most helpful in this respect are the peculiar form of the vertebral bodies and the enchondroma-like lesions of the tubular and flat bones. In their absence the exact diagnosis may be difficult. Diagnosis may be impossible in adulthood when the physes have closed and the vertebral abnormalities are less distinct.

Following the original report,¹ most authors include spondyloenchondrodysplasia in the group of enchondromatoses. However, the enchondromatous nature of the skeletal lesions has not as yet been histologically proven.

References

- Schorr S, Legum C, Ochshorn M. Spondyloenchondrodysplasia. *Radiology* 1976;118:133-9.
- Sauvegrain J, Maroteaux P, Ribier J, et al. Chondromes multiples avec atteinte rachidienne. Spondylo-enchondroplasia et autres formes. *J Radiol* 1980;61:495-501.
- Chagnon S, Lacert P, Blery M. Spondylo-enchondrodysplasie. *J Radiol* 1985;66:75-7.
- Frydman M, Preminger-Shapiro R, Bar-Ziv J. Spondylo-metaphyseal dysplasia with "enchondromatous-like" changes—a distinctive type. Personal communication, 1966.
- Schäfer E, Meinecke P. Spondylometaphysäre Dysplasie—ein besonderer Typ mit enchondromähnlichen Veränderungen; sog. Spondyloenchondrodysplasie. Personal communication, 1987.
- Gustavson K-H, Holmgren G, Probst F. Spondylometaphyseal dysplasia in two sibs of normal parents. *Pediatr Radiol* 1978;7:90-6.
- Kozlowski K, Barylak A, Middleton RW, Rybakowa M, Thomas P, Walecki J. Spondylo-metaphyseal dysplasias (report of a case of common type and three pairs of siblings of new varieties). *Australas Radiol* 1976;20:154-64.
- Fanconi S, Issler C, Giedion A, Prader A. The SPONASTRIME dysplasia: familial short-limb dwarfism with saddle nose, spinal alterations and metaphyseal striation. Report of 4 siblings. *Helv Paediatr Acta* 1983;38:267-80.
- Kozlowski K, Prokop BE, Scougall JS, Silink M, Vines RH. Spondylo-metaphyseal dysplasia (report of a case of common type and three cases of "new varieties"). *Fortschr Röntgenstr* 1979;130:222-30.
- Kozlowski K, Cremin B, Beighton P. Variability of spondylo-metaphyseal dysplasia, common type. *Radiol Diagn (Berl)* 1980;21:682-6.
- Kozlowski K, Beemer FA, Bens G, et al. Spondylo-metaphyseal dysplasia (report of seven cases and essay of classification). *Prog Clin Biol Res* 1982;104:89-101.
- Lachman R, Zonana J, Khajavi A, Rimoin D. The spondylometaphyseal dysplasias, clinical, radiologic and pathologic correlation. *Ann Radiol (Paris)* 1979;22:125-35.

Correspondence and requests for reprints to Dr J Spranger, Kinderklinik und Kinder-Poliklinik, Klinikum der Johannes Gutenberg-Universität, Langenbeckstrasse 1, 6500 Mainz, West Germany.