TWO CLINICAL VARIANTS OF
SPONYLO-EPIPHYSIAL DYSPLASIA CONGENITA

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Seventeen patients with congenital spondylo-epiphysial dysplasia from six centres in Britain have been investigated and two variants delineated. There is wide clinical and radiological variability in each group with overlap between them, but 12 of the patients had very short stature and grossly disorganised hips with severe coxa vara, and the five remaining patients were less seriously affected with height only a little below the third percentile and only mild coxa vara. Both groups can be diagnosed at birth but the two cannot be differentiated on clinical and radiological grounds until after the age of three to four years when the developing severe coxa vara and difference in stature become apparent. All cases were sporadic with the exception of a concordant twin-pair.

Spondylo-epiphysial dysplasia congenita was first described by Spranger and Wiedemann (1966), with a further review of 29 patients by Spranger and Langer (1970). Bach et al. (1967) and Fraser et al. (1969) also described the disorder, the latter noting particularly the association with a high degree of myopia, detached retinas and deafness. More recently Kozlowski, Masel and Nolte (1977) described 17 cases, noting more than one clinical variant but finding it impossible to delineate them in the young infant. The condition can be diagnosed at birth and is characterised by short stature associated with a short trunk, which is partly due to platyspondyly and partly to coxa vara, hidden flexion at the hips and the accompanying lumbar lordosis. Pectus carinatum is usual, and superficially there is a resemblance to Morquio’s disease. Adult height may be as little as 84 centimetres.

Radiological features are striking, particularly of the hips where ossification of the capital femoral epiphyses may be retarded and accompanied by varying degrees of coxa vara. There is platyspondyly with posterior wedging of the vertebral bodies resulting in characteristic “pear-shaped” vertebrae in childhood and variable changes later. Radiological changes at the extremities of the limbs are not usually of great severity. Associated deformities include cleft palate and talipes equinovarus or other deformities of the foot. Most cases are sporadic but autosomal dominant inheritance has been reported and Spranger and Langer (1974) have noted a possible recessive form.

Spondylo-epiphysial dysplasia congenita is a rare disorder and no accurate figures for prevalence are available. However, by comparing the numbers of patients with this disorder with two other conditions diagnosed at birth, classical achondroplasia and congenital osteogenesis imperfecta, for which data are available, it is likely that the prevalence of spondylo-epiphysial dysplasia congenita is approximately 3.4 per million (Wynne-Davies, unpublished data).

The aim of the current survey was to review cases of spondylo-epiphysial dysplasia congenita from six centres in Britain, identifying clinical variants and noting the growth, the body proportions and the natural history, as well as attempting to establish the mode of inheritance.

MATERIAL AND METHOD

Seventeen cases of spondylo-epiphysial dysplasia congenita were available for review: seven from the Hospital for Sick Children, Great Ormond Street, London; four from the Princess Margaret Rose Orthopaedic Hospital, Edinburgh; three from the Harlow Wood Orthopaedic Hospital, Nottingham; and one each from the Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, the Rowley Bristow Memorial Hospital, Pyrford, and the Western Infirmary, Glasgow.

The patients were examined clinically and radiologically, and information relating to the birth and family history was obtained. Body proportions were noted including the standing height, span, and length from
head to pubis and pubis to heel when supine. Case records from infancy were also reviewed. Many of the patients have been seen annually and their growth charted for up to five years. Ten of the 17 patients were under 10 years of age when first examined, five were between 10 and 20 years, and two were between 20 and 30 years. The age of the patients at presentation ranged from nine months to 29 years.

RESULTS

It was apparent from the outset that there were two clinical variants of the congenital form of spondyloepiphyseal dysplasia in this series (Figs 1 and 2), one being more severe than the other with marked dwarfism and grossly disorganised hips; there were 12 patients, five male and seven female, in this group. The other group of five patients, consisting of three males and two females who were twins, had some shortness of stature and only mild coxa vara. Both groups had presented with similar signs at birth and appeared to be clinically and radiologically indistinguishable for the first three or four years of life.

Clinical features and complications. The presenting signs in the two groups, although similar, were variable, for example a short trunk at birth, sometimes with deformities of the foot. Pectus carinatum was present in most cases but the principal feature was stiffness and limitation of the movement of the hips.

After early infancy short-trunk dwarfism developed with the fingertips reaching nearly to the knee when standing (Fig. 2). All but two of the 17 patients had marked lumbar lordosis associated with hidden flexion at the hips and a waddling gait. Low back pain was common from childhood onwards. Scoliosis or kyphoscoliosis was present in all but three, but two of these were twins aged only four and a half years and may yet develop one of these conditions. All curves developed before the age of 10 years, the degree varying from mild scoliosis of little significance to very severe curves requiring bracing and operative correction. Two patients had a double primary curve and one a triple curve (see Fig. 5). Two patients in the group with severe coxa vara developed paraplegia; one aged 21 years with associated thoracic kyphoscoliosis, and the other, aged 10 years, with severe lumbar lordosis and spinal stenosis. In each case operative intervention was required. Genu valgum, varum and recurvatum were all recorded.

No patient developed symptoms or signs relating to odontoid hypoplasia, or had overt secondary osteoarthritides of the hips or any other joint, but the oldest was still only aged 29 years and these conditions could still develop. Limitation of the movement of the hips and occasional pain were common from infancy onwards, and the incongruity of joint surfaces will no doubt lead to

Figure 1—A girl aged 8½ years with spondylo-epiphyseal dysplasia congenita and severe coxa vara; height 94 centimetres.

Figure 2—A boy aged 3 years with spondylo-epiphyseal dysplasia congenita and only mild coxa vara; height 92.7 centimetres.

Figure 3—Lateral radiograph of the cervical spine showing odontoid hypoplasia. Vertebral bodies are reduced in height but have an increased anteroposterior diameter. Figure 4—Lateral radiograph of a boy aged 1 year 7 months showing the thoracolumbar spine. Vertebral bodies have abnormal oval shape ("pear-shaped") with anterior beaking. Figure 5—Anteroposterior radiograph of the thoracolumbar spine of a boy aged 14 years 3 months showing a triple curve and universal platyspondyly. The interpedicular distances in the lumbar region are parallel and not divergent. Figure 6—Lateral radiograph of the lumbar spine of a man aged 21 years showing platyspondyly with anterior wedging at T12 and L1. Vertebral bodies have an increased anteroposterior diameter with posterior wedging.
problems at a later age. The main handicap of some patients was not difficulty in walking, but due to the associated defects of sight and hearing. The estimate of the final height of the patients ranged from 104 to 127 centimetres for the group with severe coxa vara and 130 to 145 centimetres for the others. Previous reports have indicated that the face in spondylo-epiphysial dysplasia congenita is "flat" but in our series this appearance was not striking and most patients were recorded as having a normal face and head.

**Associated anomalies.** Of the 12 patients with severe coxa vara three had severe myopia, two of them with detached retinae; three had partial deafness; two a cleft palate; two talipes equinovarus; and two had inguinal herniae, one of them with generalised joint laxity. In the group of five patients with mild coxa vara, one had unilateral catact and one of the twins had talipes calcaneovalgus which was the presenting sign leading to examination and radiography of the hips.

**Radiographic features.** Both groups showed a wide range of radiographic appearances, from complete normality in some areas through minor irregularities of development to fragmented, delayed epiphyses and flared, irregular and defective metaphyses. It was only the radiological appearance of the hips after early infancy which clearly differentiated the two groups, although patients with only mild coxa vara never reached the same degree of severity in other regions of the body as did some of those with severe coxa vara. Some of the latter patients, however, had normal radiological appearances in the distal parts of the skeleton.

Anteroposterior radiograph of the left hand and wrist of a girl aged 8 years 10 months with bone maturation of 7 years 10 months. There is a pseudo-epiphysis at the base of the second metacarpal and the radial, ulnar and metacarpal epiphyses are flat and irregular. Carpal bones are small and irregular with several centres for the trapezium. The scaphoid, normally present by the age of 4 years, has not yet ossified.

There were a number of findings common to both groups: the skull was normal but there was delay in ossification and hypoplasia of the odontoid process (Fig. 3); vertebrae showed platyspondylpy developing during childhood (Figs 4 to 6); and the shoulder and humerus varied from being completely normal to having a varus deformity with retarded, fragmented epiphyses and metaphysial irregularity. One patient had a cyst-like appearance of the upper shaft of the humerus with a pseudarthrosis. The wrists and hands were characteristic, although showing a wide range of abnormalities (Fig. 7).
Anteroposterior radiographs of the pelvis and the hips of four children showing the development of spondylo-epiphysical dysplasia with severe coxa vara. Figure 11—A boy aged 3 years 3 months. The ilium is reduced in height and the acetabular roofs are horizontal. The capital femoral epiphyses are not visible but a small fragment of bone is present on the inferior aspect of the left femoral neck. Figure 12—A girl aged 5 years. The acetabular roofs are horizontal and irregular. There is a marked delay in the ossification of the pubic rami and the iliac wings are small. The capital femoral epiphyses are still not ossified. The femoral necks are broad with coxa vara developing. Triangular fragments of bone are present on the inferior aspect of the femoral necks. Figure 13—A boy aged 9½ years. The acetabular roofs are horizontal and there is now marked coxa vara. The femoral necks are broad with triangular fragments of bone on the inferior aspect. The capital femoral epiphyses are small and poorly ossified. Figure 14—A boy aged 14 years 2 months with severe coxa vara and discontinuity of the femoral necks. There is upward displacement of the greater trochanters with pseudoacetabular formation (compare with Figures 17 to 19). The capital femoral epiphyses are just contained within the acetabula. The "brim" view of the pelvic inlet indicates severe lumbar lordosis.

Between the ages of four and 10 years some had ragged metaphyses at the wrist which subsequently improved. Most had an epiphysis at the base of the second metacarpal, first seen between the ages of one and two years. The phalanges were usually normal. Maturation of the bones was retarded at all ages but particularly on the radial side of the wrist and there was disorganised carpal maturation with extra epiphyses sometimes being present. The knees varied from being completely normal to having marked epiphysial and metaphysiial irregularities (Figs 8 to 10). The fibulae could be abnormally long or short, but significant mechanical problems at the knee or ankle were not recorded.

In the group developing severe coxa vara, the pelvis showed irregular acetabula and retarded ossification of the pubic rami (Figs 11 to 14). There was a delay, usually of four or five years, in the appearance of the capital femoral epiphyses and they always remained small and deformed; in some patients they were never seen at all. There was considerable upward displacement of the trochanters with discontinuity of the femoral necks sometimes developing between the ages of four and seven years. Arthrography indicated that the largely unossified femoral heads were contained by the acetabula and demonstrated the very acute angle of the femoral necks (Figs 15 and 16).
In the group with mild coxa vara (Figs 17 to 19) the iliac wings were small, ossification of the pubic rami was slightly delayed and the acetabular roofs were horizontal. There was some delay in the appearance of the capital femoral epiphyses, but only by one to two years, and they then became irregular and fragmented. The femoral necks were broad and triangular bony fragments developed inferiorly but the degree of coxa vara was never marked.

**Growth and body proportions.** Figure 20 shows the reduced stature of the two groups, with and without severe coxa vara. The span was similarly reduced compared with normal values given by Provis and Ellis (1955), but the difference between the two groups with age was less marked than for height. The head to pubis measurements were reduced compared with normal values given by Tanner, Whitehouse and Takaishi (1966) and McKusick (1972), as is expected with platyspondyly; the average measurement was three-quarters of the normal value. The pubis to heel measurements were affected by the deformity of the hips and in the group with severe coxa vara averaged only 60 per cent of the normal value and was even less in older children. In those patients with mild coxa vara, the pubis to heel measurement averaged 80 per cent of the normal value.

Even allowing for the severe coxa vara and hidden flexion of the hips, which was present to some degree in nearly all of the patients, there is clearly a fundamental difference in the potential for growth of the two groups.
the difference in height being on average 20 centimetres. It is also clear that in infancy and early childhood the two groups cannot be differentiated by stature alone.

**Genetics and birth history.** All 17 cases were sporadic with the exception of the concordant twin-pair. The group with severe coxa vara included 39 first-degree relatives, 53 second-degree relatives, and 57 third-degree relatives; of the 17 sibs, eight were older and nine younger than the index patient. In the group with mild coxa vara, there were 13 first-degree relatives, 37 second-degree, and 43 third-degree. Of the five sibs, four were older and one younger than the index patient. The mean age of the mothers and fathers of the patients with severe coxa vara was 27.20 ± 2.21 years and 29.53 ± 1.97 years respectively. The mean age of the mothers and fathers of patients with mild coxa vara was 27.56 ± 0.41 years and 30.13 ± 2.61 years respectively. No significant maternal or paternal age effect could be demonstrated. The group without severe coxa vara included female twins who were both affected but who had normal parents. It is likely on clinical grounds that they were monozygous but detailed testing has not been done. The father was aged nearly 39 years and the mother 35 years at the time of their birth. In none of the 17 cases was there consanguinity.

All but two of the births were normal; one was a breech malposition and the other child was born five weeks premature. The weights of all the babies at birth were normal for the length of gestation. In the maternal histories of the group with severe coxa vara it was recorded that 18 per cent of all conceptions aborted, which is slightly above the usual figure of 14 per cent. There was also one perinatal death of unknown cause. In the maternal histories of the group without severe coxa vara, four of a total of nine conceptions aborted but there were no stillbirths, perinatal deaths or other abnormalities of pregnancy.

**Differential diagnosis.** Both types of spondylo-epiphyseal dysplasia congenita are superficially similar to the mucopolysaccharide disorder of Morquio's disease (Figs 21 and 22) but the radiological differences are obvious. In Morquio's disease there is early development of epiphyses, particularly of the capital femoral epiphyses which are unusually large during the first year of life (Fig. 23), subsequently becoming smaller (Fig. 24), and finally disappearing altogether by the age of nine years. Characteristically there is coxa valga, not coxa vara, and the pelvis is also dissimilar. The radiological appearances of the hands and wrists in Morquio's disease show premature development of epiphyses in infancy with subsequent delay, and the pointed base of the second to fifth metacarpals is an invariable characteristic (Fig. 25). Morquio's disease is inherited as an autosomal recessive trait and keratan sulphate may be found in the urine.

There is more than one type of spondylo-epiphyseal dysplasia tarda; autosomal dominant, recessive and X-linked recessive forms have been described but all have
the distinguishing feature of late onset of symptoms and signs which do not become apparent until the age of 12 or 14 years or even until adult life. In general these patients are not seriously handicapped; they have some shortness of stature associated with platyspondyly and a short trunk (Fig. 26), but this is not as marked as in either of the congenital forms. The tarsal forms of spondyloepiphysial dysplasia do not have the radiographic features of congenital coxa vara but by the age of 12 or 13 years the appearance of the hips and vertebrae are very similar to those of patients with the milder form of spondylo-epiphyseal dysplasia congenita described here, although other parts of the skeleton are typically normal. Radiographs of the hips in patients with multiple epiphyseal dysplasia aged 12 years and over may also be similar, but at this age the vertebrae are normal.

Fig. 26

A man aged 26 years with spondylo-epiphyseal dysplasia tarda showing disproporitione shortening of the trunk but the deaimity is not marked; height 149.9 centimetres, head to pubis 67.3 centimetres, pubis to heel 88.9 centimetres.

Pseudo-achondroplasia is easily differentiated clinically by the characteristic short stature due to short limbs. Although these characteristics are also found in metatropic dwarfism, the long bones of patients with this condition have greatly expanded proximal and distal ends giving a distinctive “dumb-bell” shape. Another distinguishing feature is the extreme degree of platyspondyly which occurs during infancy giving rise to “paper thin” vertebrae. Kniest disease is similar to metatropic dwarfism but patients have characteristic facies and do not have platyspondyly.

DISCUSSION AND CONCLUSION

All the cases of spondylo-epiphyseal dysplasia congenita described by Spranger and Langer (1970) appear to be similar to those included here as spondylo-epiphyseal dysplasia congenita with severe coxa vara. Spranger and Langer (1974) described two sisters with a possibly autosomal recessive form of the disease which appears to be similar to that described in this paper in patients with only mild coxa vara. Kozlowski et al. (1977) noted more than one congenital form of spondylo-epiphyseal dysplasia, and felt that there were sufficient distinctive features to warrant their designation as separate entities. We agree that there are different forms of this disorder, and like these authors, note that they cannot be distinguished from each other in infancy.

Autosomal dominant and recessive inheritance has been reported in this condition but there were no affected relatives in this series, apart from the (presumed) monozygous twins. In the absence of parental consanguinity, which is likely evidence for autosomal recessive inheritance, it is possible that they are all new dominant mutations.

In the two disorders described here, the disparity in the rate of growth and differing behaviour of the developing hips becomes apparent by the age of three or four years, but apart from these distinctive features there appeared to be a wide range of clinical and radiological findings in the two groups with overlap between them. It was apparent, however, that patients with spondylo-epiphyseal dysplasia congenita and mild coxa vara were never so severely affected in any part of the skeleton as those with the very short stature and grossly disorganised hips. It is felt that it is important to distinguish between the two types of this condition in view of their differing prognosis and problems of management.

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REFERENCES


