SPONDYLO-EPIPHYSIAL DYSPLASIA TARDA WITH PROGRESSIVE ARTHROPATHY

A "NEW" DISORDER OF AUTOSOMAL RECESSIVE INHERITANCE

RUTH WYNNE-DAVIES, CHRISTINE HALL, BARBARA M. ANSELL

From the Princess Margaret Rose Orthopaedic Hospital, Edinburgh, the Hospital for Sick Children, London, and the Canadian Red Cross Memorial Hospital, Taplow

An inherited skeletal dysplasia with a striking clinical resemblance to rheumatoid arthritis is described in which radiographic changes in the vertebrae are similar to those of spondylo-epiphyseal dysplasia tarda.

Fifteen patients with an inherited skeletal dysplasia which is considerably more crippling than the usual form of spondylo-epiphyseal dysplasia tarda are presented. The disorder has a striking clinical, though not radiological, resemblance to rheumatoid arthritis but with the addition of platyspondyly. It has not previously been described, although it is possible that the case referred to by Maroteaux (1974) as "les dysplasies spondylo-épiphyso-metaphysaires complexes" may be the same condition.

The 15 patients came from nine families: four families were from the United Kingdom, four from Arab countries and one from Greece. The age of the affected members ranged from 8 years to 38 years. Comparing the frequency of this disorder with other skeletal dysplasias, it is estimated that the prevalence is likely to be about one per million in the United Kingdom, although this may be an underestimate, since some patients may well have been diagnosed as suffering from atypical rheumatoid arthritis.

CLINICAL FEATURES

All 15 patients were thought to be normal for the first few years of life. Symptoms started between the age of three and eight years in all but one patient whose symptoms started at the age of 11 years. Usually several joints were affected with pain and soft tissue swelling, the commonest being the proximal interphalangeal joints of the hands and then the hips and elbows. Two patients had cystic swellings on the back of the hands and one over the hallux. One patient who presented at the age of five years had an undiagnosed febrile illness with splenomegaly at

the age of seven years. In all patients the symptoms of the joints were very similar to those of juvenile arthritis and all of them had been investigated for this, but none had shown overt synovitis, nor was there any suggestion of an inflammatory element as the erythrocyte sedimentation rates had been normal. In those cases where acute-phase proteins had been investigated, the results had been negative. There had been no known abnormalities of pregnancy.

On examination the face and head were normal. Adult height, which ranged from 1360 to 1562 centimetres, was moderately reduced, part of this reduction being due to flexion contractures at the hips and knees, and in three cases to slight scoliosis as well (Figs 1 and 2). Proportions of the body were not markedly abnormal but in six of the seven cases where measurements were available, the upper segment (head to pubis) was less than the lower segment (pubis to heel). Excluding the Arab families for whom standard body proportions are not available, the height averaged 83 per cent of normal, the head to pubis measurement 82 per cent of normal, and the span 95 per cent of normal.

One patient had clinical signs of involvement only in the hands although there were radiological changes in the spine. In all the other patients multiple joints were affected: hands, wrists, elbows, hips and knees being frequently involved, and shoulders and feet rather less so. The hands first showed a fusiform swelling of the proximal interphalangeal joints and later the terminal ones became involved (Figs 3 and 4). One patient had most joints in the body affected including the intervertebral joints but excluding the temporomandibular joints

R. Wynne-Davies, MB, PhD, FRCS

2 Dale Close, St Ebbe's, Oxford OX1 1TU, England.

C. Hall, MB, BS, FRCR, Consultant Radiologist

Department of Paediatric Radiology, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JH, England.

B. M. Ansell, MB, FRCP, Consultant Rheumatologist

Juvenile Rheumatism Unit, Canadian Red Cross Memorial Hospital, Taplow, Buckinghamshire, England.

Requests for reprints should be sent to Dr Ruth Wynne-Davies.

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Fig. 1

Fig. 3

Fig. 2

Fig. 4

Figure 1—Patient 1 aged 15 years; hips, knees and elbows are affected. Figure 2—Patient 2 (brother of Patient 1) aged 35 years; all peripheral joints are affected. Figure 3—The hands of Patient 1; the proximal interphalangeal joints are chiefly involved. Figure 4—The hands of Patient 2; all finger joints are affected.

Fig. 5

Fig. 6

Fig. 7

Radiographs of the spine of Patient 3 at the age of nine years (Fig. 5) and 12 years (Fig. 6) showing platyspondyly throughout with increased anteroposterior diameter of vertebrae. There are varying degrees of end plate irregularity, some with wedging. Figure 7—Patient 2: marked platyspondyly and osteoporosis with fusion of posterior joints.

and was rendered virtually immobile before bilateral replacement of the hip and knee at the age of 32 years. In most other patients the principal disability arose from involvement of the hips, with increasing pain, limitation of movement and contractures. Three patients had slight scoliosis, one thoracic and two lumbar, and a fourth patient had moderate kyphosis; no spinal deformity was of sufficient severity to require treatment.

The condition appeared to be progressive, not stopping with the growth of the child nor simply merging into a degenerative arthritis. Contractures developed in all affected joints and the range of movement progressively decreased.

RADIOLOGICAL FEATURES

The skull was normal. Lateral radiographs of the spine (Figs 5 to 7) showed platyspondyly throughout, with a thoracolumbar kyphosis in the younger patients. Varying degrees of irregularity of the end plates developed with

growth, but in maturity the vertebrae, while still showing platyspondyly, were symmetrical. Between the ages of five and 10 years the capital femoral epiphysis was large. By the age of 10 years coxa vara and cyst-like irregularities in the articular surface of the femur and acetabulum had developed (Figs 8 and 9), the head of the femur was flattened, and there was progressive loss of joint space with secondary osteoarthritis (Fig. 10).

Radiographs of the hands showed enlarged epiphyses and metaphyses developing around the proximal interphalangeal joints at first and later around the terminal joints; periarticular osteoporosis also becomes apparent at a later stage (Figs 11 to 14). It was significant in the differential diagnosis from inflammatory arthritis that there were no erosions, no periostitis, nor the same degree of soft tissue swelling usually associated with inflammatory disease. The elbows and knees showed a loss of joint space with irregular articular surfaces and adjacent osteoporosis.

Fig. 8

Fig. 9

Fig. 10

Hips of Patient 3 at the age of five years (Fig. 8) and 10 years (Fig. 9). Figure 10—Radiograph showing flattened femoral heads and loss of joint space with secondary osteoarthritis in a patient aged 32 years.

Fig. 11

Fig. 12

Fig. 13

Fig. 14

Patient 2. Radiographs of the hands at the age of 5, 11, 14 and 35 years showing progressive contractures, joint space narrowing and periarticular osteoporosis. The epiphyses are large with articular irregularity at the metaphalangeal joints; there is progressive metaphysal enlargement of the distal part of the proximal phalanx and the proximal part of the middle phalanx which later affects the distal interphalangeal joints. There are no erosions and less soft tissue swelling than in rheumatoid disease.

Fig. 15

Family tree of an Arab family with a consanguineous marriage (III 15, 16) demonstrating probable autosomal recessive inheritance.

GENETICS

The sex ratio was equal. There was one known instance of consanguinity in an Arab family (Fig. 15), and it is possible this may also be a feature in the three other Arab families. No parents were affected. There was only one child of an affected individual, and she was normal. In the nine families there were three pairs of brothers affected, one pair of sisters, and one brother and sister; the other cases were sporadic. Of a total of 28 siblings from the nine families, five were known to be affected giving a ratio of 1 in 5.6 which is not too dissimilar to the expected 1 in 4 ratio of autosomal recessive inheritance.

DISCUSSION

The mode of inheritance and the platyspondyly and other radiological features distinguish this condition from juvenile arthritis. The disorder also has several distinctive features differentiating it from previously described cases of spondylo-epiphysial dysplasia tarda whether of autosomal dominant, recessive, or X-linked inheritance (Sutcliffe and Stanley 1973). In most instances of

spondylo-epiphysial dysplasia tarda symptoms do not develop until the age of 12 or 13 years and some cases are not recognised until adult life; patients are not seriously crippled, the main feature being some reduction in height with shortness of the trunk in comparison with the lower limbs; platyspondyly is present; the proximal large joints are affected but there is progressively less involvement towards the distal part of the limbs; epiphyses and metaphyses are not enlarged; and contractures and osteoporosis are not features.

By contrast, symptoms of the disorder described in this paper begin at an early age, typically in the hands with progressive crippling due to multiple and continuing involvement of the joints with associated contractures. This progressive arthropathy accompanied by enlarged epiphyses and metaphyses clearly distinguishes the disorder from other inherited skeletal dysplasias where, apart from secondary osteoarthritis due to incongruity of joint surfaces, it is usual for the condition to stabilise once the child has stopped growing. Clearly, now the clinical condition has been delineated, further research into its biochemistry and histology is required.

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