DYSPLASIA EPIPHYSIALIS HEMIMELICA

A CLINICAL AND GENETIC STUDY

J. M. CONNOR, F. T. HORAN, P. BEIGHTON

From the Johns Hopkins Hospital, Baltimore, the Cuckfield Hospital, West Sussex, and the University of Cape Town

The clinical features of nine new patients with dysplasia epiphysialis hemimelica are reported, with a long-term follow-up on a further seven patients who were described in the earliest case reports of this disease. Each of these 16 patients had only one leg involved, but 12 had multiple epiphyses affected. The distal femur, distal tibia and talus were the commonest sites and most patients presented with painless swelling or deformity. Wasting of the muscles of the affected leg was a common finding, and was occasionally disproportionate to the degree of disuse. One patient had the unique combination of involvement of the lateral and medial halves of different epiphyses in the same limb and another had unusual metaphysial changes. Diagnosis was often delayed despite typical radiographic appearances. There was no evidence for a genetic component in the aetiology nor was any common environmental factor identified. Treatment by local excision was generally effective for lesions in the vicinity of the knee, but some patients with involvement of the talus required arthrodesis around the ankle. The long-term prognosis appears to be good and so far only two of these patients have developed premature osteoarthritis.

Dysplasia epiphysialis hemimelica is characterised by asymmetrical overgrowth of one or more epiphyses in a limb or of a tarsal or carpal bone during childhood (Fairbank 1956). Although first reported by Mouchet and Belot (1926), it was delineated as a distinct entity by Trevor in 1950. Since then about 100 cases have been reported and the literature has been well reviewed by several authors (Fairbank 1956; Kettelkamp, Campbell and Bonfiglio 1966; Theodorou and Lanitis 1968). However, it is uncertain whether the condition is a single entity or whether it exhibits heterogeneity. Most reported cases have been in children and the long-term prognosis remains uncertain. The majority of cases have been sporadic, but these might represent new dominant mutations which would only become evident when the patients reproduced; Hensinger et al. (1974) described a family in which dysplasia epiphysialis hemimelica appeared to be inherited as an irregular autosomal dominant trait. Our study was designed to clear up these matters.

MATERIALS AND METHODS

The starting point for this investigation was the Fairbank Collection at the Royal National Orthopaedic Hospital, London, which contains notes and radiographs of eight patients with dysplasia epiphysialis hemimelica, seven of whom were described in Trevor's original article in 1950. There were radiographs of a further 13 patients in the Radiology Museum at this hospital and details of five of these were published by Fairbank in 1956. An attempt was made to trace and review each of these patients.

We also approached orthopaedic surgeons and radiologists in several other centres in the United Kingdom and a further six patients were identified; efforts were made to trace these patients.

There was no record of any patient with this condition at the Johns Hopkins Hospital, but the files of the skeletal dysplasia registry of the Department of Human Genetics, University of Cape Town contained details of two more.

We obtained information concerning 29 patients of whom 11 were traced, examined and radiographed. These included two of Trevor's original cases and two who were reported by Fairbank (1956). Further details were also produced about three previously reported patients who could not be traced, one new patient who is now in Iraq, and another new patient who had been lost to follow-up.

The individuals seen were evaluated paying special attention to their degree of function, the nature of the lesion and the type of treatment received. Pedigrees were drawn up and any relative with dysplasia epiphysialis hemimelica, aged five years with dysplasia epiphysialis hemimelica showing the deformity and muscle wasting.
DYSPLASIA EPIPHYSIALIS HEMIMELICA

Table I. Details of patients with dysplasia epiphysialis hemimelica that have been reported previously

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Date of birth</th>
<th>Clinical presentation</th>
<th>Site of lesion(s)</th>
<th>Management</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>1939</td>
<td>At 4.5 years with a painless lump on inner side of knee</td>
<td>Medial side of the left distal femoral epiphysis</td>
<td>1944: excision</td>
<td>Reported by Trevor 1950 (Case 2) 1981: asymptomatic, normal knee both clinically and radiographically; equal leg length, no muscle wasting</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>1920</td>
<td>At 8 years with painless masses on outer side of knee and behind lateral malleolus. Pes valgus and reduced ankle movements</td>
<td>Lateral side of right distal femoral epiphysis, lateral side of right proximal tibial epiphysis, right talus</td>
<td>1928: excision of lesion from femur</td>
<td>Reported by Trevor 1950 (Case 3) 1951: normal leg length but restricted knee movements with pain; radiographic evidence of osteoarthritis of the knee with large exostosis from lateral tibial condyle 1952: lost to follow-up</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>1946</td>
<td>At 9 months with inability to fully extend knee, genu valgum and deformed right foot</td>
<td>Medial side of right distal femoral epiphysis, right talus, right navicular</td>
<td>1948: supracondylar osteotomy of femur; iron and T-strap</td>
<td>Reported by Trevor 1950 1958: able to walk well but foot in valgus; right foot enlarged, right leg 2 cm short 1982: painful knee movements for last 6 years due to osteoarthritis; right calf 4 cm smaller than left calf</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>1948</td>
<td>At 6.5 years with a painless lump on outer side of ankle and reduced ankle movements</td>
<td>Left talus, left distal fibular epiphysis</td>
<td>1970: pantalar arthrodesis</td>
<td>Reported by Fairbank 1956 (Case 5) 1968: increased pain and stiffness of ankle 1970: 15° ankle flexion, 5 cm wasting of left calf, 1 cm of left thigh, equal leg length 1971: solid ankle fusion; discharged</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>1950</td>
<td>At 3 years with a painless lump on inner side of right knee and genu valgum</td>
<td>Medial side of right distal femoral epiphysis</td>
<td>1954: excision</td>
<td>Reported by Fairbank 1956 (Case 6) 1982: no symptoms; full range of knee movements, equal leg length, no muscle wasting</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>1932</td>
<td>Pes valgus since early childhood. Intermittent painful locking of knee since the age of 14 years. Painless swelling on inner side of knee noted at 23 years</td>
<td>Medial side of right distal femoral epiphysis, medial side of right proximal tibial epiphysis, medial side of right distal tibial epiphysis</td>
<td>1942: correction of pes valgus 1955: excision of lesions from distal femur and proximal tibia</td>
<td>Reported by Fairbank 1956 (Case 9) 1955: 5 cm wasting of right calf, 1.5 cm wasting of right thigh, right leg 1 cm short 1961: asymptomatic except for symptoms of ulnar nerve compression</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>1943</td>
<td>At 9 months with a deformed foot</td>
<td>Medial side of right distal tibial epiphysis, right talus, right navicular</td>
<td>1956: excision and ankle arthrodesis 1958: triple arthrodesis of the ankle</td>
<td>Reported by Metcalfe 1950 1956: 4 cm wasting of right calf, enlarged right big toe 1960: solid fusion; discharged</td>
</tr>
</tbody>
</table>

symptoms suggestive of dysplasia epiphysialis hemimelica was also examined clinically and radiographically. A routine skeletal survey of clinically normal relatives was not considered to be justifiable.

RESULTS

A summary of the information on the seven patients who had been reported previously is given in Table I and on the nine new patients in Table II.

In all the onset of symptoms or signs had been noted in childhood, the earliest at birth and the latest at eight years of age. A painless bony swelling or localised deformity was the usual presenting complaint. Wasting of the muscle of an affected limb was also a common finding (Fig. 1), and in one case (Patient 10) led to an initial suspicion of a neurological lesion; in another (Patient 9) the muscle wasting appeared to be disproportionate to the degree of limitation of joint function. Other initial misdiagnoses included tumoral calcinosis, enchondromatosis and Perthes' disease. Inequalities of limb length were apparent in five patients, one with lengthening and four with shortening. These discrepancies were generally of a minor degree and caused few problems. Growth and development were otherwise normal.

The radiographic findings were characteristic of dysplasia epiphysialis hemimelica. Early lesions consisted of an irregular mass with multicentric ossification arising from either the lateral or the medial half of the affected epiphysis or tarsal bone; later this fused with the adjacent bone and resembled an exostosis (Figs 2 and 3).
Table II. Details of patients with dysplasia epiphysialis hemimelica that have not been reported previously

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Date of birth</th>
<th>Clinical presentation</th>
<th>Site of lesion(s)</th>
<th>Management</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>F</td>
<td>1960</td>
<td>At 1 year with a painless lump on inner side of knee, right genu valgum and marked valgus deformity of right ankle</td>
<td>Medial side of right distal femoral epiphysis, medial side of right distal tibial epiphysis, right talus, right first cuneiform, right navicular</td>
<td>1961: two right femoral osteotomies; excision of femoral lesion 1963: right tibial osteotomy 1965-7: stapling of distal tibial epiphysis 1966: excision of lesion from navicular</td>
<td>1981: fully active, unable to wear high heels; full knee but very limited ankle and subtalar movements, right leg 1 cm longer than left leg, 4 cm wasting of right calf and right thigh</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>1969</td>
<td>At 8 years with a painless lump behind the medial malleolus</td>
<td>Posteromedial aspect of left distal tibial epiphysis</td>
<td>1979: excision</td>
<td>1981: asymptomatic, full range of ankle movements; equal leg length, 1.5 cm wasting of left calf, 0.5 cm wasting of left thigh</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>1969</td>
<td>At 8 years with wasting of the calf of 2 years’ duration</td>
<td>Medial side of left distal tibial epiphysis, left talus</td>
<td>1960: excision of both lesions</td>
<td>Initial diagnosis: cauda equina lesion but myelographic, EMG and neural conduction studies were normal 1981: asymptomatic but very limited movement of ankle and subtalar joints; equal leg length, 3 cm wasting of left calf, 0.5 cm wasting of left thigh</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>1968</td>
<td>At 8 months with a painless lump on inner side of foot and pes planus</td>
<td>Medial side of right distal tibial epiphysis, right talus</td>
<td>1969: excision of tibial lesion 1975: talar mass excised 1976: talus excised</td>
<td>Initial diagnosis: tumoral calcinosis 1973: restricted ankle movements, equal leg length, 2.5 cm wasting of right calf 1978: right foot in good position but smaller than left foot</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>1962</td>
<td>At 2 years with a painless deformity of right ankle and a limp</td>
<td>Lateral side of right femoral capital epiphysis, lateral side of right distal femoral epiphysis, medial side of right distal tibial epiphysis, right talus</td>
<td>Right heel raise</td>
<td>Initial diagnosis: Perthes’ disease 1971: right leg 1 cm shorter than left leg, 2.5 cm wasting of right thigh, 1 cm wasting of right calf 1981: asymptomatic; normal range of movements at ankle and knee</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>1959</td>
<td>At 18 months with unilateral genu valgum and pes planus since 10 months</td>
<td>Medial side of right distal femoral epiphysis, medial side of right proximal tibial epiphysis, medial side of right distal tibial epiphysis</td>
<td>1961: excision of femoral lesion 1962: excision of lesion from distal tibia</td>
<td>1963: this Iraqi child had excellent function; small proximal tibial fragment</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>1973</td>
<td>Deformity of right ankle since birth, limp since 18 months</td>
<td>Lateral half of right distal femoral epiphysis, right distal fibula, right talus</td>
<td>1977: femoral osteotomy, corrective shoes</td>
<td>1981: right leg 6 cm shorter than the left, 3 cm wasting of right calf, metaphyseal streaking of right femur</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>1963</td>
<td>At 3 years with a painless swelling of right ankle</td>
<td>Medial side of right distal tibial epiphysis, right talus</td>
<td>1966–69: three excisions of tibial lesion, corrective shoes</td>
<td>This child was of mixed ancestry Initial diagnosis: enchondromatosis 1973: asymptomatic and fully active 1980: minor discomfort and slight limp, limited ankle movements; wasting of right calf, enlarged right big toe</td>
</tr>
</tbody>
</table>
Lesions were confined to the lower limbs; the distal femur, the distal tibia, and the talus were the commonest sites. Twelve patients had involvement in several places but only one limb was affected in any one individual.

The lesions in any particular person were confined to either the lateral or medial aspects of the affected epiphysis except for Patient 12, who had abnormalities of the capital femoral epiphysis, the lateral half of the distal femoral epiphysis and of the medial half of the distal tibial epiphysis in the same limb (Figs 4 to 7). The overall bone structure was otherwise normal apart from Patient 14 who had irregular lucent streaking in the femoral metaphyses. The results of routine haematological and biochemical investigations were within normal limits.

One patient was treated conservatively but the remainder required a variety of operative procedures (Tables I and II). Simple excision of the lesion was usually effective at the distal tibia or in the vicinity of the knee, but some patients with involvement of the talus eventually required arthrodesis around the ankle. Histopathological investigations of the early lesions showed cartilage with multiple centres of ossification, but later growths consisted of normal bone with a cap of cartilage and were indistinguishable from osteochondromata.

The prognosis in dysplasia epiphysialis hemimelica appeared to be generally good. All of the patients examined were mobile and most had no related symptoms. Only two patients (Patients 2 and 3) had developed early osteoarthritis of an affected joint. No further lesions were seen after childhood and none increased in size after puberty. No patient, including several of the oldest recorded in the medical literature, had developed malignant change.

The sex ratio in this study was 12 boys to four girls. No parents were consanguineous and they had not been
advanced in age at the time of the birth of their affected child, as might be expected if a new dominant mutation had been responsible for the deformity. Questions pertaining to the pregnancy, delivery and early childhood of the patients with dysplasia epiphysialis hemimelica revealed no consistent environmental factor which might have been responsible for the disease. Three of the patients (Patients 1, 3 and 5) went on to have children of their own; the eight children of these patients were normal. None of the patients had an affected relative.

DISCUSSION

This study examined particularly the genetics, the clinical spectrum and the long-term prognosis of dysplasia epiphysialis hemimelica. There was no evidence to suggest an hereditary factor which was underlined by the absence of affected relatives in the older patients, including the discordant monozygotic twins studied by Donaldson et al. (1953). The family described by Hensinger et al. (1974), in which six patients in two generations had the disorder, appears to be exceptional; these patients and one other member of the family showed various combinations of intracapsular chondromata, extraskeletal osteochondromata, and typical osteochondromata which have not otherwise been seen in dysplasia epiphysialis hemimelica, suggesting that they were afflicted with a different disorder.

The usual presenting feature in this and in previous studies was a painless swelling or deformity (Trevor 1950; Fairbank 1956; Kettelkamp et al. 1966). We were impressed by the amount of muscle wasting in the affected limbs of many of the patients. Fairbank (1956) had noted secondary wasting of the muscles in some legs.

Trevor (1950) stated that the metaphyses were normal in dysplasia epiphysialis hemimelica, but three patients have since been reported with widening of the neck of the femur (Fairbank 1956, Case 3; Saxton and Wilkinson 1964; Kettelkamp et al. 1966, Case 13); two of these patients had translucent irregular areas and longitudinal striae in the metaphyses which resembled the radiographic appearance of enchondromatosis (Ollier's disease). One of our patients had similar appearances in the metaphyses of the affected limb. All who showed metaphyseal changes had involvement of multiple epiphyses but all patients with multiple epiphyseal involvement did not show metaphyseal abnormality.

Fairbank (1956) predicted that many of the abnormal joints in dysplasia epiphysialis hemimelica would later develop degenerative changes. Only two of our patients have shown evidence of this complication so far although all described in Table I have now reached middle age, suggesting that the long-term outcome is favourable. There has been one report of spontaneous regression of the clinical and radiographic features in a patient with typical dysplasia epiphysialis hemimelica (Lénárt and Aszódi 1974, Case 2).

The usual involvement of only the lateral or medial halves of the epiphyses of either the right or left limbs led to the introduction of the term dysplasia epiphysialis hemimelica (Fairbank 1956). However, exceptions to this strict laterality do occur. The entire capital femoral epiphysis has been affected in four patients (Fairbank 1956, Case 7; Saxton and Wilkinson 1964; Kettelkamp et al. 1966, Case 13; Wiedemann, Mann and von Krenzeinstein 1981), the entire proximal tibial epiphysis in another (Kettelkamp et al. 1966, Case 13), and opposite halves of different epiphyses in the same limb in one of our patients (Case 12). The occasional metaphyseal changes have been mentioned above and Wiedemann et al. (1981) noted mild abnormalities of the epiphyses of the other leg in their patient.

The fundamental defect seems to be an abnormality of the regulation of cartilage proliferation in the affected epiphyses, tarsal or carpal bones, resulting in cartilaginous exostoses and cartilage rests in the metaphyses.

We wish to thank the consultants throughout the United Kingdom who have helped with this study, and especially Mr T. J. Fairbank of Cambridge and Professor D. J. Stoker and the medical records staff of the Institute of Orthopaedics, Royal National Orthopaedic Hospital, London. We are grateful to the Academic Board of the Institute for allowing us to study the Fairbank Collection, and to the South African Medical Research Council and the University of Cape Town Staff Research Fund for their financial support.

REFERENCES


THE JOURNAL OF BONE AND JOINT SURGERY