DEVELOPMENT OF THE HIP IN MULTIPLE EPIPHYSEAL DYSPLASIA

NATURAL HISTORY AND SUSCEPTIBILITY TO PREMATURE OSTEOARTHRITIS

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We have determined the natural history of hip development in 42 patients with multiple epiphyseal dysplasia (MED). Premature osteoarthritis was a frequent outcome and was almost inevitable before the age of 30 years in those with incongruent hips. There were two types of immature hips: type I, the more severe form, had a fragmented and flattened ossific nucleus and acetabular dysplasia, was misshapen at skeletal maturity and osteoarthritic by 30 years of age; the milder type II hip had a small, rounded, uniformly ossified nucleus and a more normal acetabulum. Type II hips were well formed at maturity and were less prone to premature osteoarthritis.

Considerable variations were noted in the manifestations of MED between families but not within families. The prognosis of a child's hip could be predicted; in sporadic cases from the type of immature hip, and in familial cases by also taking into account the outcome of affected relatives.

Multiple epiphyseal dysplasia (MED) is a genetically determined disorder characterised by abnormal ossification of multiple epiphyses (Fairbank 1947; Kaufmann 1976). The hips are usually affected and premature osteoarthritis may occur and require joint replacement at an early age (Spranger 1976). However, MED is heterogeneous with both mild and severe forms, and the susceptibility of each to premature osteoarthritis is unclear.

We report the natural history of hip development in MED, the frequency of premature osteoarthritis and a method of predicting the development of this outcome.

PATIENTS AND METHODS

Patients with MED were collected from medical records of the Department of Orthopaedics and the Bone Dysplasia Clinic of the Royal Children's Hospital.

Our criterion for the diagnosis of MED was abnormal ossification of two or more pairs of epiphyses in the absence of features suggestive of other diagnoses (Kaufmann 1976). Vertebral end-plate irregularity, especially at the thoracolumbar junction, was accepted as a feature of MED, but platyspondyly was regarded as signifying spondylo-epiphyseal dysplasia and such cases were excluded (Hulvey and Keats 1969). Patients with bilateral Perthes' disease did not have other affected epiphyses and were also excluded.

Forty-two of the 48 patients with MED were reviewed; the remaining six could not be contacted. Both clinical (Harris 1969) and radiographic assessments of the hips were made. Acetabular configuration was determined by Sharp's angle and the acetabular depth index; femoral head sphericity was measured by Mose's method and containment was quantified by the acetabular–head index (Heyman and Herndon 1950; Sharp 1961; Broughton et al 1989). Before skeletal maturity, the epiphyseal index was measured and epiphyseal ossification was recorded as being either uniform or fragmented. Mature hips were graded as being congruent, congruously incongruent or incongruent (Stulberg, Cooperman and Wallenstein 1981) and radiographic signs of osteoarthritis were recorded (Danielsson 1964).

Discriminant analysis (Statistical Package for the Social Sciences) was used to establish whether any of the radiological measurements during growth could be used as predictors of premature osteoarthritis.
The type I hip. Figure 1a – Arthrogram of the hip at five years of age. There are multiple centres of ossification and the acetabulum is mildly dysplastic. The arthrogram shows that the large femoral head is ovoid. Figure 1b – Age 10 years. Figure 1c – Age 16 years. The mature femoral head is large and ovoid and the acetabulum is small. The greater trochanter is high.

Fig. 1a  Fig. 1b  Fig. 1c

The type II hip. Figure 2a – Age nine years. The small ossific nucleus shows uniform ossification and is fully covered by the acetabulum. Figure 2b – Age 24 years. The adult hip is spherical and congruent. The joint space is narrower in the weight-bearing area than in other parts of the joint.

Fig. 2a  Fig. 2b

RESULTS

Thirty male and 12 female patients were reviewed, of whom 24 were members of eight families: 33 patients were skeletally mature and the eldest was aged 67 years. The six patients who were not reviewed did not seem to differ from the patients studied.

Patterns of epiphyseal ossification. The development of the ossific nucleus of the femoral head was abnormal. The nucleus was small, misshapen and showed abnormal patterns of ossification. It was often flatter than normal but even when it was more rounded its contour was still abnormal. Ossification occurred in either a uniform pattern with a single ossific centre or in a fragmented pattern suggesting multiple centres of ossification (Figs 1 and 2). Fragmented ossification persisted throughout childhood but towards the end of growth the multiple centres of ossification coalesced.

Femoral head shape in adulthood. At skeletal maturity, 40 hips were congruent, 14 were incongruent and 12 were congruously incongruent. All incongruent hips were osteoarthritic by 20 years of age and most hips with congruous incongruity were arthritic by the late 30s (Fig. 3). Congruent hips fared better, several reaching the seventh decade without arthritis; yet despite appearing congruous many still became arthritic in early adult life (Fig. 3).
Gradual flattening of the ossific nucleus during growth was observed in adults with flat femoral heads (see Figs 1a to 1c). In three patients, however, there was radiographic evidence of rapid collapse of a segment of the epiphysis in the early teens. The mature hip was flatter than the opposite hip in the unilateral case and in the bilateral cases the mature femoral heads were flatter than in other family members with MED.

**Familial patterns.** Adults from seven of the eight MED-families were studied (Fig. 4). Despite the variability observed between families, the expression of the disease was consistent within each family. This consistency was observed in the distribution of affected epiphyses, in the severity of the dysplasia and in the susceptibility to premature osteoarthritis (Fig. 4). All hips were arthritic in patients from families D and E; most were not arthritic in families B and C, whereas about equal proportions of arthritic and non-arthritic hips were observed in the remaining two families. In five of the seven families, the future development of a child’s hips could be predicted from that of affected relatives.

**The prediction of premature osteoarthritis.** Of the 66 skeletally mature hips, 30 showed radiographic evidence of premature osteoarthritis at review. Discriminant analysis was used to determine if radiographic measurements during childhood could be used to predict the development of premature osteoarthritis.

This analysis included all patients who were aged 30 years or more at review and for whom childhood radiographs were available. Of the 30 hips from this group of patients, 14 were arthritic by 30 years of age. Measurements of radiographs taken at about 10 years of age were used to establish the childhood predictors of premature osteoarthritis. The results showed that the most valuable predictors were the epiphyseal index, the acetabulum–head index, Sharp’s angle and the pattern of epiphyseal ossification. The model derived by using all four variables correctly predicted the outcome in 90% of hips. The single most useful predictor was the pattern of epiphyseal ossification which correlated with the outcome in 80% of hips.

On the basis of these findings we classified immature hips into two types (Table I). A type I hip had a flattened and fragmented ossific nucleus which was poorly covered by a dysplastic acetabulum. Of the 10 immature hips with these features, all had deformity of the femoral head at maturity; by 30 years of age, nine had clinical and radiographic signs of arthritis. In contrast, a type II hip had a rounder and more uniformly ossified nucleus which was covered by a more normally shaped acetabulum. The eight hips of this type were spherical at maturity and none were arthritic by 30 years of age. The remaining 12 hips had features of each type but behaved in accordance with the type they most closely resembled.

**DISCUSSION**

Hip development proved heterogeneous in patients with MED, but several patterns emerged. There was a milder type II pattern in which the ossific nucleus of the femur was smaller than normal but was rounded with uniform ossification and with coverage by a reasonably shaped acetabulum. In type II hips, the femoral head seemed to be sufficiently strong to prevent collapse and deformation of the ossific nucleus. In contrast, the more severe type I hips developed poorly and were more susceptible to deformation, incongruency and premature osteoarthritis.

Abnormal hip development in MED was probably due to underlying genetically determined defects of the cartilage matrix which impaired normal ossification and development of the femoral head and acetabulum. The observation of several patterns of hip development may reflect heterogeneity in the underlying mutations. Mechanical factors also contributed to the development of osteoarthritis since all incongruous hips degenerated rapidly. However, even congruous hips were prone to premature osteoarthritis. Clearly, the mutation also resulted in imperfect articular cartilage that was unable to withstand normal cyclical loading of the joint.

In only three patients was there evidence of rapid collapse of portion of the ossific nucleus which was possibly attributable to avascular necrosis. In general,
however, the pattern of development of the ossific nucleus in MED was different from that reported in Perthes' disease (Catterall 1971). First, both hips were usually symmetrically affected in MED whereas this is unusual in Perthes' disease. Secondly, in most patients with MED the ossific nucleus gradually enlarges and ossification becomes more uniform with growth but without undergoing the sequential changes that are typical of the various healing phases of Perthes' disease. As a result, the hip abnormalities in MED seem to be mainly due to primary anomalies of the epiphysis rather than to the secondary effects of avascular necrosis. Clarification of this proposal will have to await definition of the mutations and histological examination of more femoral head samples from children (Stanescu, Stanescu and Maroteaux 1985).

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REFERENCES


