Delayed ossification of the proximal capital femoral epiphysis in Legg-Calvé-Perthes’ disease

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We studied radiographs of 125 children (105 boys, 20 girls) with unilateral Legg-Calvé-Perthes’ disease to examine the epiphyseal development of the femoral head in the contralateral (unaffected) hip. The epiphyseal height (EH) and width (EW) of the unaffected hip were measured on the initial anteroposterior pelvic radiograph.

In 109 of the patients (87.2%) the EH was below the mean for normal Japanese children and a significantly small EH (below -2 SDs) was observed in 23 patients (18.4%). By contrast, the EW of most patients (95.2%) lay within ± 2 SDs of normal values except for six with a significantly small EW. A strong positive linear correlation (R = 0.87) was observed in the EH:EW ratio in the patients. A smaller EH than expected for EW in our series indicated epiphyseal flattening of the femoral head in Legg-Calvé-Perthes’ disease.

Our findings support the hypothesis that a delay in endochondral ossification in the proximal capital femoral epiphysis may be associated with the onset of Perthes’ disease.

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Legg-Calvé-Perthes’ disease is a form of avascular necrosis of the proximal capital femoral epiphysis in children. Various genetic, epidemiological, biochemical, and other factors associated with this condition have been studied, but the underlying nature of the vascular disturbance is still unknown. Some authors have suggested that intravascular thrombosis of the vessels to the femoral head may be related to a coagulopathy involving proteins C and S and hypofibrinolysis. Clinical observations, however, indicate that the disease can no longer be considered to be a focal vascular accident in the capital femoral epiphysis. Affected children have been shown to be of shorter stature than average and to have delayed skeletal maturity at the onset of the disease. This indicates that Perthes’ disease may be part of a generalised constitutional disorder associated with a disturbance of growth of bone and cartilage and of proportionate growth in various areas of the body.

Traditionally, estimation of bone age from hand and wrist radiographs has been used to document delayed skeletal maturity. Delayed hand-wrist bone age has been noted by many investigators and is a recognised part of the clinical picture of this disease. Burwell et al5-7 showed that the retardation of growth does not always affect the whole body, but mainly the distal part of the upper and lower limbs. Since Perthes’ disease occurs in the proximal femur, determination of the hand-wrist bone age may be less accurate as there may be discrepancies of development between the carpal bones and the capital femoral epiphysis.

We have examined radiologically the capital femoral epiphysis on the unaffected side to assess the growth of the femoral head. The epiphyseal height (EH) and width (EW) of the unaffected femoral head were determined based on the anteroposterior pelvic radiograph taken at the time of diagnosis, and compared with those of normal Japanese children. To our knowledge anthropometric analysis of the epiphyseal development of the unaffected femoral head in Perthes’ disease has not previously been reported.

Patients and Methods

We included in the study 125 children with unilateral Perthes’ disease. The right hip was affected in 56 and the left in 69. There were 105 boys and 20 girls. The mean age at diagnosis for the boys was 7.1 years (2.7 to 12.9) and for the girls 6.6 years (2.4 to 9.3). Figure 1 shows the distribution of the age of the patients. In all the EH and EW of the unaffected hip were measured on the anteroposterior radiograph taken at the time of diagnosis (Fig. 2). The standard measurements of EH and EW were obtained from the data of Izumida9 derived from 4000 hips of normal Japanese children.
Statistical analysis. Spearman’s rank correlation coefficients and linear regression equations were used to assess the data. The statistical analysis was performed using StatView 4.5 (Abacus Concept, Berkeley, California).

Results

In 109 patients (87.2%) the EH was less than that for normal children; in 23 (18.4%) it was below -2 SDs of the control group (Fig. 3a). There was a highly significant positive linear correlation (R = 0.724, p < 0.0001) between the EH and age and the regression equation (Y = 6.844 + 0.813 X) showed that in the patients it tended to be less than the standard value during the susceptible age for this disease. By contrast, the EW in most patients was to be found within 2 SDs of the mean and in only six (4.8%) was it significantly smaller, although a linear regression equation (Y = 12.166 + 2.306 X, R = 0.844, p < 0.0001) between the EW and age showed a significant correlation similar to that between the EH and age (Fig. 3b). In the patients there was a strong linear correlation (R = 0.87) between the EH and EW. A linear regression equation of the patients (Y = 2.464 + 0.356 X) and normal children (Y = 2.32 + 0.40 X) showed that the EH of the patients tended to be smaller than that expected for the EW (Fig. 4).

Discussion

Delayed hand-wrist bone age is recognised as a relatively common clinical feature of Perthes’ disease. If bone age is retarded, it is likely that the development of the capital femoral epiphysis may also be retarded. Loder et al evaluated pelvic bone age in children with Perthes’ disease using a series of indicators of maturity at various anatomical locations on the proximal femur and pelvis (Oxford method) and compared it with individual hand-wrist bone age. They showed that the pelvic bone age was greater than the hand-wrist bone age, but less than the chronological age in male patients. Measurements of hand-wrist bone age therefore may not be useful in evaluating the development of the entire body in an acromelic disease. We therefore focused our study on the growth of the capital femoral epiphysis in which the ischaemic necrosis occurs rather than on determination of the hand-wrist bone age.

Izumida analysed the radiographs of 4000 hips of normal Japanese children between 0 and 15 years of age and developed standard measurements for various radiological parameters of the hip including the EH and the EW. The number of children examined was considered to be sufficient to establish age-matched standard values for normal Japanese children. In our study, we used the EH and EW of the unaffected femoral head in patients with unilateral Perthes’ disease for comparison using the same technique (Fig. 2).

A reduction of the EH of the unaffected hip in most of our patients indicated that there may be abnormal development of the femoral head in this disease. Harrison and Blakemore performed a radiological analysis of the unaffected hip in children with unilateral disease and showed that 48.4% of the patients had irregularities of the surface and flattening or dimpling of the femoral head. However, anthropometric examination of the capital femoral epiphysis was not undertaken. This is the first report to our knowledge which has shown a reduced height of the unaffected proximal femoral epiphysis on the anteroposterior pelvic radiograph taken at the time of diagnosis.

A similar reduction in the EH:EW ratio which represents a flattening of the epiphysis is seen in several bone dysplasias. Van Mourik and Weerdenburg described a reduction in the EH compared with the EW of the distal femoral epi-
physis in 11 of 12 children with multiple epiphyseal dysplasia (MED) which is characterised by retardation of growth of the epiphyseal ossification in various parts of the body. Mandell et al.\textsuperscript{13} reported that avascular necrosis of the capital femoral epiphysis may be seen in MED as well as in Perthes’ disease. The similarities between the two disorders imply that the flattening of the femoral head associated with delayed maturation of the secondary ossification centre could be related to vascular disturbances.

Kikkawa, Imai and Hukuda\textsuperscript{14} performed a detailed radiological and histological analysis of the femoral heads in the spontaneously hypertensive rat (SHR) which has osteonecrosis of the femoral epiphysis resembling the clinical features of Perthes’ disease. The expression of type-X collagen during epiphyseal ossification was delayed in SHRs, and the osteonecrosis was preceded by a disturbance of mineralisation and ossification of cartilage. These observations suggested that abnormal development of the femoral epiphysis occurred much earlier than the manifestation of osteonecrosis. Ponseti et al.\textsuperscript{15} showed that the abnormal areas in the epiphyseal cartilage of patients with Perthes’ disease had different histochemical and ultrastructural properties from those of normal cartilage and fibrocartilage. They mentioned that the collapse and necrosis of the femoral head could result from the breakdown and disorganisation of the matrix of the epiphyseal cartilage, followed by abnormal ossification.

Immaturity of the capital femoral epiphysis may therefore be of aetiological significance in the onset of the disease. We did not investigate the reasons why more children do not develop bilateral disease. Lauritzen\textsuperscript{16} showed that the peak age for developing bilateral Perthes’ disease was ear-
lier than that for unilateral disease, which they attributed in part to a relatively large number of patients with dysplasia epiphysealis capitis femoris. Edvardsen, Slordahl and Svenningsen\(^\text{17}\) showed that retardation of bone age was more marked in children with bilateral disease than in those with unilateral involvement. These findings suggested that the degree of skeletal immaturity could be related to the occurrence of bilateral Perthes’ disease.

Delay in ossification of the epiphysis of the femoral head may be one of the risk factors for Perthes’ disease although the mechanism has not yet been defined. It may lead to mechanical vulnerability of the epiphysis, and the increasing mechanical stress could result in collapse of the immature epiphysis, particularly anterolaterally, where weight-bearing forces are maximum. The concomitant breakdown of the epiphysis may cause vascular occlusion.

![Scattergram of the EH and EW showing an extremely high correlation (R = 0.87) between them. The two lines represent a linear regression equation of normal children reported by Izumida\(^\text{9}\) (solid line, Y = 2.32 + 0.40 X) and of our patients (bold line, Y = 2.464 + 0.356 X). There was a relatively smaller EH than expected for EW in the affected children.](image)

References