PERTHES' DISEASE: IS THE EPiphySIAL INFARCTION COMPLETE?

A STUDY OF THE MORPHOLOGY IN TWO CASES

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A histopathological study was made of the hip joints from two children with Perthes' disease who died from unrelated causes. These cases illustrate the variability of three aspects of morphology: the extent and number of infarctions, of trabecular fractures and of the reparative process.

Despite an increasing interest in the morbid anatomy of Perthes' disease, reports on human cases remain few and their conclusions indefinite. The classification of the radiological features and natural history by Catterall (1971) led to the conclusion that the prognosis was proportional to the degree of epiphyseal involvement. This suggests that the size of the infarct is variable from case to case, and hence that the whole epiphysis is not necessarily always involved. This paper presents two cases in which detailed histological analysis has been made.

MATERIAL AND METHODS

In two cases of Perthes' disease a study was made of the radiographs and the affected hips obtained at necropsy. A coronal slab was cut from the centre of each femoral head, the anterior and posterior segments were cut into five-millimetre slabs at right angles to this plane, and fine-detail radiographs were made of all these blocks.

Case 1. Figure 1—The radiographic appearances are typical of Group 3 with a subchondral fracture line extending over more than half of the epiphysis. Figure 2—The epiphyseal bone deep to the subchondral fracture line is progressively resorbed leaving a good-sized medial and small lateral segment. Figure 3—Established healing with only mild deformity. No "at risk" signs have been present.

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Decalcified and undecalcified sections were then prepared and were stained with haematoxylin and eosin, azure blue and alcian blue (Scott).

CASE REPORTS

Case 1. This boy was aged 10 years when Perthes' disease of the left hip was diagnosed incidentally during investigation of his renal disease, and he was treated by a weight-relieving caliper for six months. He had a heavy proteinuria due to a nephrotic syndrome associated with chronic nephritis, and died of uraemia and hypertension at the age of 12. At necropsy the changes of chronic glomerular nephritis, hypertension, uraemia, pericarditis and pleurisy were found. The left femoral head and upper shaft were removed for study.

![Fig. 4](image-url)
The cut surfaces of the femoral head showing thickening of the articular cartilage particularly on the medial and lateral aspects.

Radiological findings. The serial radiographs showed Group 3 changes (Figs 1 to 3). A large central fragment had formed in the epiphysis which had been progressively resorbed. At the time of necropsy the disease process was in the established healing phase but without serious deformity of the head.

Macroscopical appearances. The superior and lateral margins of the femoral head were flattened and the cartilage here was a little fibrillated (Fig. 4).

Microscopical findings. The essential feature of the histological preparations are illustrated in Figures 5 to 9. The medial, posterior and lateral segments of the epiphysis were composed of normal trabecular bone and marrow. The articular cartilage overlying these regions was of normal histological appearance with normal endochondral ossification on its deep surface. The pathological features in the central and anterior segments varied with the depth from the surface. The articular cartilage was thick and continuous with a mass of fibrocartilage undergoing ossification at its free deep surface. Below this there were signs of appositional bone formation with remodelling and irregular thickening of the trabeculae. Bone necrosis was only seen in a few instances in the apex of the coronal section. The thickest trabecula were observed anteriorly and lay deep to the fibrocartilaginous material. The interval between the two was filled with a vascular connective tissue which was invading the cartilage (Fig. 9). In the dome of the epiphysis a subchondral fissure stretched laterally into the fibrocartilaginous mass. It was bounded above by articular cartilage and below by reactive fibrocartilage.

Case 2. This boy was aged eight years when he presented with a painful right-sided limp and radiographs revealed Perthes' disease. His erythrocyte sedimentation rate was elevated and subsequent investigations revealed a lymphocytic lymphoma which was treated by chemotherapy. The Perthes' disease remained untreated. At the time of death from uncontrolled lymphoma and bronchopneumonia the Perthes' disease was in the healing phase. Both hips were removed for further study.

Radiological findings. The initial radiograph showed Group 3 disease...
The gross appearances of both hips. On the left side the femoral head is of normal shape as is the acetabulum. On the right there is considerable deformity and adaptive alteration in the shape of the acetabulum. The overall enlargement of the femoral head compared with the normal left side may be observed.

Figure 8—Posterior and anterior slabs. In the posterior part of the epiphysis the trabeculae appear of normal thickness and viable without evidence of central necrosis. The large mass of fibrocartilage continuous with the overlying articular cartilage is noted with a crescent of thick woven bone reaching forward into the epiphysis (Area D). In the anterior part the changes of endochondral ossification are noted in the thickened articular cartilage; these are spreading posteriorly. (Haematoxylin and eosin, x 2.5.) Figure 9—Area D. The fibrocartilaginous material observed on the right is being replaced by a vascular granulation tissue deep to which woven bone is forming. A number of giant cells are observed. (x 45.)
Pertes' Disease: Is the Epiphyseal Infarction Complete?

with an extensive infarct (Fig. 10) with normally textured bone medially and posteriorly. "At risk" signs were present. The sequential radiographs showed resorption of much of the involved segment and formation of new bone in the thickened articular cartilage laterally. In the final radiograph the viable bone on the medial, lateral and posterior aspects of the epiphysis had increased in size and height (Fig. 11).

Macroscopical observations. The affected head was broad, flat and indented by the lip of the acetabulum (Fig. 12). Both the photograph and the fine-detail radiograph of the specimen showed the reduced height of the epiphysis as well as the distortion both of the affected head and of the acetabulum. The femoral head appeared too large for the acetabulum and hinged on its lateral rim, causing a depression to develop. The acetabular roof had also lost its normal contour and become flattened (Figs 13 and 14).

Microscopical findings. The essential features of the histological preparations are illustrated in Figures 15 to 18. In the posteromedial

Case 2. Central coronal slab showing, medially, viable trabecular bone covered by thickened articular cartilage which shows some endochondral bone formation. The central portion of the epiphysis is largely composed of a fibrocartilaginous material bounded above by thickened articular cartilage and below by a small quantity of apparently viable trabecular bone. Laterally the indented area shows fibrous tissue with some new bone. The overlying articular cartilage has been partly destroyed and there is a cleft running medially between it and the fibrocartilaginous area. Thickened articular cartilage and new bone is again seen on the side of the femoral neck.

(Haematoxylin and eosin, × 2.5.)

Anterior and posterior slabs showing thickened viable trabecular bone in the posterior part of the epiphysis. Over this is a shell of endochondral new bone in the thickened articular cartilage. Anterior to this is necrotic trabecular bone which shows evidence of crushing (Area E). The marrow is also necrotic and this area is dense on fine-detail radiographs, suggesting that the marrow also is calcified. In the anterior section the large mass of cartilaginous material at the site of the previous metaphysial lesion is noticed (Area F). The trabecular bone in the anterior part of the epiphysis appears almost completely replaced by the fibrocartilage. (Haematoxylin and eosin, × 2.5.)

Figure 17—Area F showing the disorganisation of the growth plate in the metaphysial region with proliferation of the cartilaginous cells. Vascular channels are seen in the central part of this lesion (× 30). Figure 18—Area E showing (left) necrotic bone and marrow which is being actively resorbed by cellular granulation tissue, and (right) differentiation of this granulation tissue into fibrocartilage (× 50).
aspect of the epiphysis there was an area of thickened viable trabecular bone which did not show central necrosis (Fig. 15). There was evidence of remodelling in these trabeculae. Overlying this was a shell of endochondral bone which was continuous laterally with a mass of new bone formation which had formed in the thickened articular cartilage. There was a large segment of necrotic bone in the collapsed central segment of the femoral head occupying a space bounded above by articular cartilage and below by epiphyseal cartilage. It was surrounded by reactive tissue, fibrous and fibrocartilaginous in nature. This tissue extended anteriorly, laterally and posteriorly into an area where normal trabecular bone would have been expected to be observed. Over this flattened part of the epiphysis the articular cartilage was particularly thick except for the area of contact between the femoral head and the edge of the acetabulum.

The peripheral articular cartilage continued to grow and ossify. Laterally a large mass of cartilage was formed on the lateral side of the femoral neck (Fig. 13). Within this a separate mass of new bone formation was occurring, which was continuous with the shell of new bone overlying the viable bone in the posterior part of the femoral head. The growth plate was abnormal in all areas with distortion of the cartilage columns and some irregularity of the primary spongiosa. In the anterolateral aspect of the metaphysis there had been, on the initial radiographs, a large metaphyseal lesion. The histological features at that point showed that the normal organisation of the growth plate had become completely lost, the appearances being those of a mass of cartilage with no columns or endochondral ossification on its deep surface.

DISCUSSION

Our interpretation of the findings in these two cases are similar. They both demonstrate an incomplete infarct of the epiphysis. This is in keeping with the findings in Case 2 reported by Jensen and Lauritzen (1976) where no evidence of bone necrosis was observed. The more markedly deformed femoral head in our Case 2 is associated with greater size of infarct, indicating that the result may be proportional to the extent of the necrosis. Repair after an infarct is partly by "creeping substitution" and partly by bone resorption by granulation tissue which subsequently and with varying success chondrifies and then ossifies. The infarct and the extent and success of the process of repair are responsible for the variable radiological appearances in the established stage of the disease. The bone necrosis and repair may be complicated by subchondral fracture and epiphyseal collapse. It is uncertain at what stage in this process these developments occur. The complex and varied tissue pattern in the femoral head thus reduces the value of core biopsy in elucidating the condition.

Incomplete infarction of the femoral head is well recognised in the adult form of avascular necrosis (Catto 1976; Inoue and Ono 1979), and the two cases reported here are similar in many respects to adult disease. A striking difference, however, is that in Perthes' disease it is possible for all the avascular bone to be removed and replaced by fibrocartilage. In the adult variety only small quantities of fibrocartilage are seen in the periphery of the infarct. There is also a difference in the extent of repair by creeping substitution (Phemister 1930) which is effectively the only remodelling process involving necrotic bone.

The extent to which the two mechanisms of remodelling, namely resorption and formation of bone, occur may well influence the final outcome. Where bone resorption predominates necrotic trabeculae will be weakened to the point of fracture. Remodelling may lead to a more or less complete replacement of the necrotic trabeculae by viable cancellous tissue.

The marrow also influences the process of repair. At the edges of the infarct where the marrow is viable it provides a route for reparative cells to invade the infarcted zone. There appositional bone will predominate. If repair is to succeed where the marrow is necrotic the tissue must be invaded by granulation tissue. It would be anticipated that this might lead to a wave of resorption of bone leading to the point of trabecular fracture.

Trabecular fracture will have important effects on the course of the disease because of the structural instability produced and hence the risk of further episodes of local infarction. Whether fracture is inevitable, given an infarct of reasonable size, is difficult to decide from the present material. Having occurred, however, it can provoke, at the margins of the infarct, a callus response which may be the reason for the fibrocartilage seen in this area. The present material suggests that fibrocartilage is observed in areas where trabecular bone has previously been crushed and removed. Its presence may be advantageous as, being less susceptible to anoxia, it is better able to survive further ischaemic episodes which would otherwise adversely affect the process of repair. However it is formed, we believe that successful "chondrification of the infarct" is a prerequisite of repair and healing.

Another feature seen in these cases is the metaphyseal lesion. This is an extensive area of cartilaginous tissue situated in the anterior and lateral aspects of the metaphysis. The growth plate in this area has lost its normal structure and there will therefore be differential rates of growth between this area and the posteromedial metaphysis where the growth plate has a more normal histological appearance. This may lead to deformity of the femoral head.

The second case reported is a striking example of the degree to which the whole joint can be shaped during the course of the disease, the acetabular remodelling presumably occurring in response to the alteration in the shape of the femoral head. To consider this as biological plasticity (Salter and Bell 1968) is to emphasise the potential for overgrowth in the cartilaginous tissue. This we believe to be great during the early phases of the disease and may be influenced by containing the femoral head within the mould of the acetabulum. Later in the disease the presence of significant degrees of ossification within the cartilage imparts rigidity to the lateral aspect of the femoral head and allows change in its shape only by subsequent growth and remodelling.

The cause and location of the vascular obstruction, which have eluded investigation, are important factors.
Both the cases in this report were in the phase of established healing and therefore did not permit conclusions to be drawn about the cause of the infarct. Some of the evidence suggests, however, that modification may be required of the accepted mechanisms of infarction by occlusion of the retinacular vessels on the side of the femoral neck. This has already been suggested by Jensen and Laurtizen (1976).

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