Necrosis of the femoral head in growing rats

Occlusion of lateral epiphyseal vessels

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The cause of the vascular occlusion in necrosis of the femoral head of growing, spontaneously hypertensive rats was investigated histologically using serial sections. The lateral epiphyseal vessels, which supply the proximal femoral epiphysis, disappeared immediately before entry into the femoral heads. In fresh osteonecrosis the pathway of the vessels between the margin of the articular cartilage and the growth plate was replaced with granulation or scar tissue.

We conclude that the vascular occlusion occurs in the layer of the epiphyseal cartilage where the lateral epiphyseal vessels penetrate, and that the abnormalities of the epiphyseal cartilage might play a part in the occurrence of osteonecrosis.

Femoral head lesions, notably osteonecrosis and ossification disturbance in the epiphysis, are frequent in growing male spontaneously hypertensive rats; the condition resembles Perthes' disease and is caused by interruption of the blood supply to the proximal femoral epiphysis (Iwasaki and Hirano 1988, Hirano et al. 1988a, 1988b).

We have studied histologically the site and mechanism of the occlusion of the blood vessels feeding the proximal femoral epiphysis in spontaneously hypertensive rats.

Materials and methods

Eighty male spontaneously hypertensive rats (Okamoto-Aoki strain 1963), aged 5 weeks, were purchased from Charles River Japan Co., Ltd., Kanagawa. All of them were kept in ordinary rat cages with a standard stock chow diet at the Laboratory Animal Center for Biomedical Research, Nagasaki University School of Medicine. Groups of rats were killed with an overdose of ether at the age of 9–15 weeks, then both femurs were removed and fixed in 10 percent formalin and embedded in paraffin after decalcification. Thin coronal sections of the proximal femurs were stained with hematoxylin-eosin and Mallory's azan method. Histologic observation of the femoral heads disclosed various stages of osteonecrosis (Table 1; Hirano et al. 1988a). Of 51 femoral heads with osteonecrosis, 15 epiphyses showed fresh osteonecrosis, not yet invaded by reparative tissue (Figure 1).

For the purpose of clarifying the cause of the vascular occlusion, additional serial sections of the proximal femurs, showing normal ossification and fresh osteonecrosis, were prepared, using a microscope to trace the blood vessels feeding the epiphysis. Further, the changes of the articular cartilage and the growth plate in the femoral heads that had fresh osteonecrosis or severely impaired ossification were compared with those undergoing normal ossification.

Table 1. Number of femoral heads in spontaneously hypertensive rats showing normal ossification, osteonecrosis, and ossification disturbance

Age (wk)	Normal ossification	Osteonecrosis (fresh)	Ossification disturbance	Total
9	5	3(3)	6	14
10	8	3(3)	9	20
12	10	10(4)	14	34
15	31	35(5)	26	92

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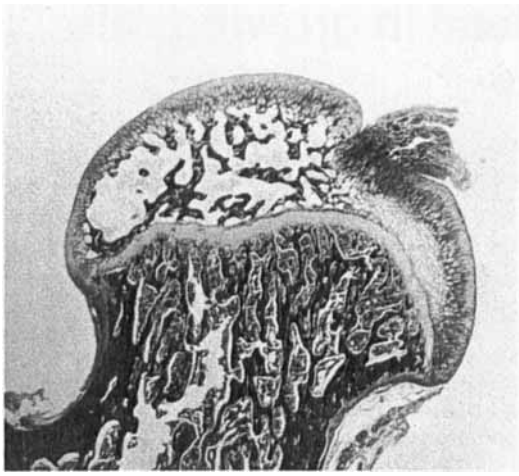

Figure 1. Complete necrosis in the ossification center of the epiphysis. HE, x18.

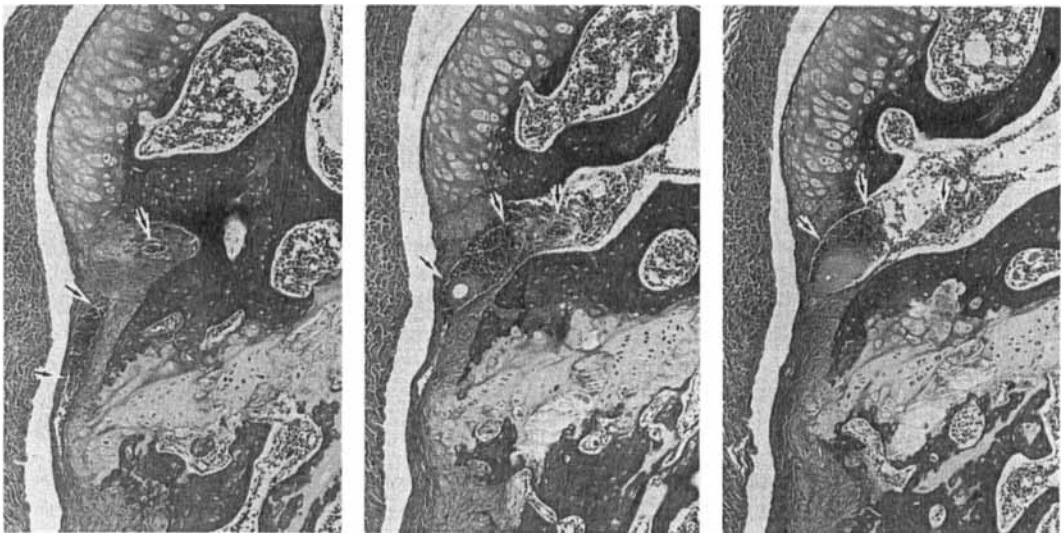

Figure 2. Serial sections demonstrate the lateral epiphyseal vessels entering the epiphysis (arrows). HE, x100.

Results

In the normal femoral heads, the blood vessels corresponding to the lateral epiphyseal vessels in man (Trueta 1957) mainly entered the epiphysis; they curved sharply just before they penetrated the epiphysis between the margin of the articular cartilage and the growth plate (Figure 2). However, in 15 femoral heads with fresh osteonecrosis, the lateral epiphyseal vessels disappeared before entering the ossification center of the epiphysis. Of those, 11 specimens showed scar tissue in the interval between the articular cartilage and the growth plate, i.e., the pathway of the lateral epiphyseal vessels (Figure 3). Slender vessels filled with red blood cells could be traced immediately before the cartilage. In the remaining four femoral heads, although the lateral epiphyseal vessels were intact before entering the femoral heads, granulation tissue was seen in the pathway within the cartilage.

With regard to the changes in the cartilage, approximately the lateral one fourth of the growth plate in almost all the femoral heads with fresh osteonecrosis lost the organized patterns, with a cluster of chondrocytes forming a nodular pattern like a rosary. Abnormal subsidence appeared near the lateral site of the articular cartilage in six femoral heads with fresh osteonecrosis (Figure 3).

The articular cartilage and the growth plate changes were more prominent in the femoral heads with severely impaired ossification than those with fresh osteonecrosis (Figure 4).

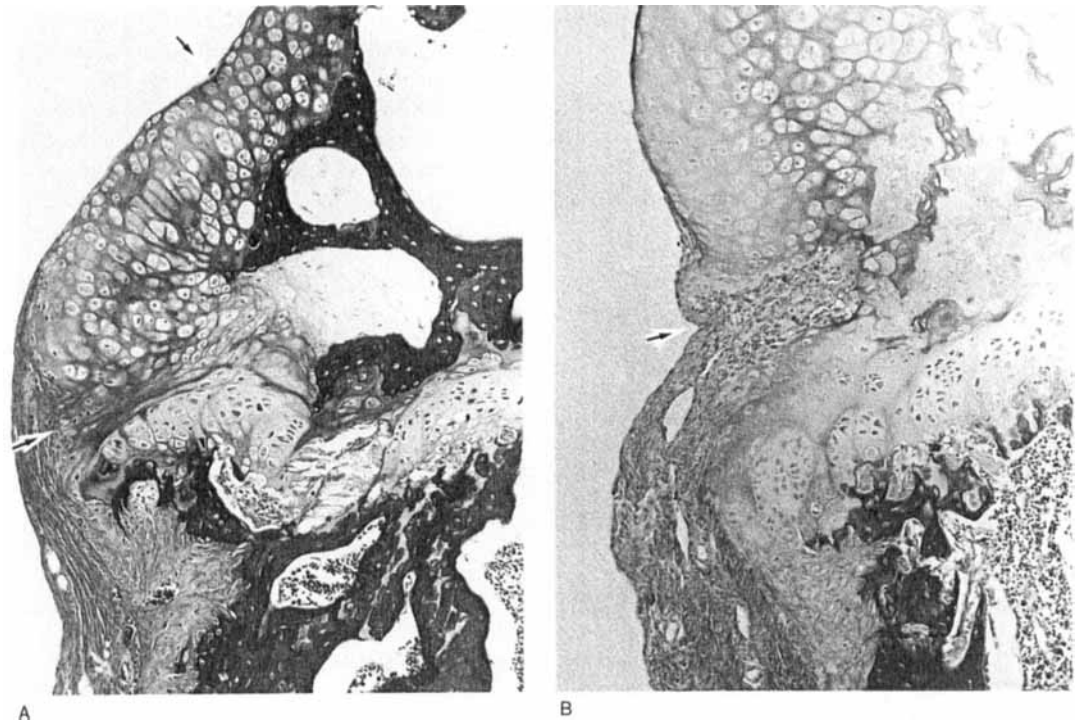

Figure 3. The lateral part of a femoral head with fresh osteonecrosis. HE, x100.

A. Note subsidence of the articular cartilage (arrow) and distortion of the growth plate. Scar tissue and proliferation of chondrocytes are seen in the interval (arrow).

B. Note granulation tissue (arrow) between the articular cartilage and the growth plate.

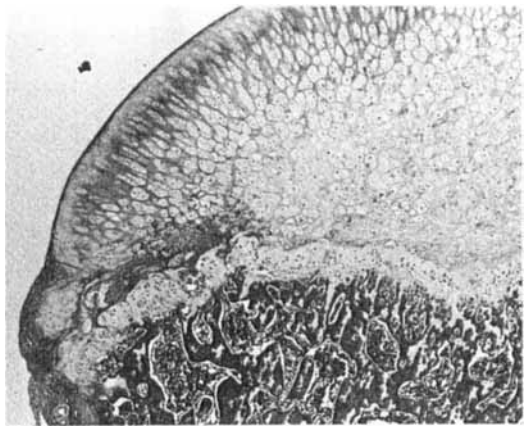

Figure 4. Femoral head with severely impaired ossification showing subsidence of the articular cartilage and rosary-like change of the growth plate. HE, x40.

Discussion

The pathologic changes of naturally occurring osteonecrosis in the femoral heads of growing spontaneously hypertensive rats resemble those of Perthes' disease in man (Iwasaki and Hirano 1988, Hirano et al. 1988a). The occlusion of the lateral epiphyseal vessels reported here would give rise to complete osteonecrosis of the ossification center in the epiphysis as that in the dog (Ljunggren 1969).

Although many hypotheses have been proposed to explain the pathogenesis of Perthes' disease in man, the cause of the interference of the blood vessels in the femoral heads still remains unknown (Caterall et al. 1982, Perugia and Ippolito 1983). Kemp (1981, 1986) supported Burrow's concept (1941) that Perthes' disease might be caused by the interruption of the venous return in the intracapsular course, namely, extraepiphyseal occlusion, because changes similar to Perthes' disease can be produced by intraarticular tamponade of the hip joints.

In contrast, Ponseti (1956) and Harrison and Burwell (1981) advocated the hypothesis that the infarction might originate in the intraepiphyseal oc-

clusion of the blood vessels. Our study may support this hypothesis.

Furthermore, Caterall et al. (1982), Ponseti et al. (1983), and Perugia and Ippolito (1983) pointed out the abnormalities in the epiphyseal cartilage of the femoral heads, and surmised that the interruption of the blood vessels might be due to the breakdown and disorganization of the epiphyseal cartilage.

The subsidence of the articular cartilage and discontinuity and distortion of the growth plate observed in our femoral heads with osteonecrosis might be secondary to mechanical forces acting on the growing hip. Further investigation of skeletal disorders, especially on an abnormality of the epiphyseal cartilage, in spontaneously hypertensive rats may contribute to the clarification of the pathogenesis of Perthes' disease.

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