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OSTEONECROSIS IN THREE YOUNG MEN PREVIOUSLY TREATED WITH STEROID FOR APLASTIC ANAEMIA

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Zinn (1971) has submitted the results of the Swiss Multi-Centre Study Group's work on idiopathic ischaemic necrosis of the femoral head in adults. He calls the condition a multi-factorial disease, stating that its aetiology remains a matter of speculation.

Below follow brief reports on necrosis of the humeral and femoral heads in young men who had previously been treated with steroid for aplastic anaemia.

CASE REPORTS

Case 1. A farm-bailiff, born 1935. Apart from chronic otitis he had always been in good health. In April 1958 admitted with aplastic anaemia after having washed horses 6 times *inter alia* with 25 per cent arsenic trioxide, during the preceding month. Leukocyte agglutination was demonstrated in the serum on addition of arsenic trioxide and 0.037 mg arsenic (As.) (Gutzeit) per l urine.

He was treated with dimercaprol, blood transfusions, and steroid. During the first 6 months he received 50–250 mg prednisone daily, during the next 6 months 15 mg daily. Thereafter, he was off medication for 6 months. During the subsequent 4 months he was again given prednisone 15 mg daily, and then he had a year without medication. Then again for 2 months 100–250 mg daily, and the treatment was concluded (in March 1963) after 20–25 mg prednisone daily for 18 months.

In 1958 splenectomy was performed.

After the patient had suffered for some months from pain in the right shoulder and right hip joint, an X-ray examination in February 1963, revealed necrosis of the head of the right humerus and both femoral heads (Figures 1, 2, and 3). The changes progressed during the subsequent months.

In May 1964 he had a Moore arthroplasty of the left hip. On histological examination the removed femoral head showed distinct necrosis of the bone and bone marrow (Figure 4). In October 1964 a similar operation was done on the right hip. This prosthesis had to be removed in August 1965 because of osteitis with fistulation. In March 1967 the patient succumbed to cerebral haemorrhage. Autopsy showed the spine to be uniformly, maximally hypoplastic, but without collapse. The right humerus was removed for examination (Figures 5 and 6).

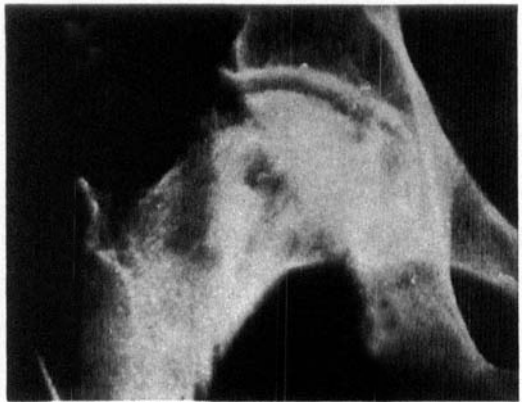

Figure 1. Right hip from Case 1, showing necrosis and collapse of the femoral head.

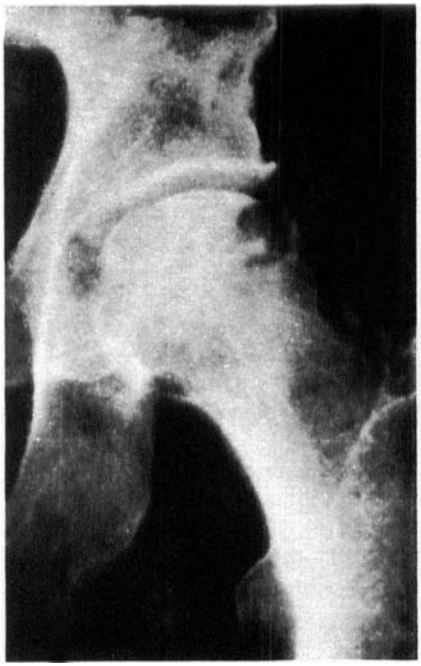

Figure 2. Left hip from Case 1, showing necrosis, but fairly well-preserved contours of the femoral head.

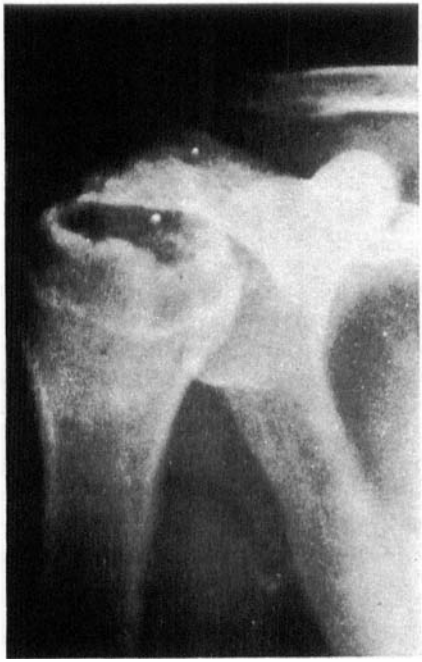

Figure 3. Right shoulder from Case 1, showing necrosis and collapse of the humeral head.

Case 2. Printer's apprentice, born 1949. Since 1965 severe abuse of alcohol, hashish, LSD, and various sedatives. Towards the end of 1967 the patient took 10 tablets of Endoxan® at a time for euphorizing purposes. In October 1967 he was admitted with aplastic anaemia. There was no evidence of lead poisoning. In October 1967 steroid therapy was instituted, prednisone 10 mg 4 times daily. At the end of one month

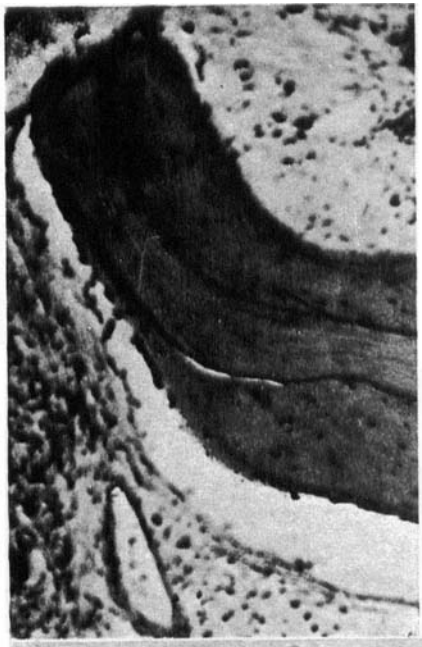

Figure 4. Histological specimen from the left hip of Case 1, showing a necrotic bony trabecula surrounded by vital bony tissue. Haematoxylin-eosin, × 125. Incidentally, the microscopic examination showed in places large necrotic areas in the bony trabeculae as well as bone marrow, peripheral proliferation of connective tissue, and widespread fibrosis. No vascular changes were observed.

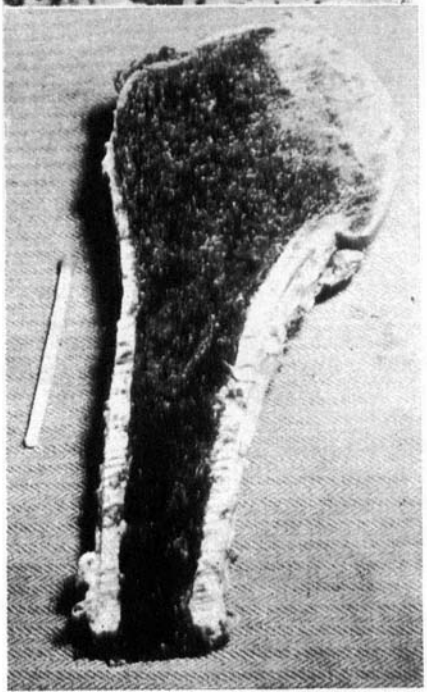

Figure 5. Photo of the cut right humerus of Case 1, showing necrosis of the head.

Figure 6. Histological specimen from the right humerus of Case 1, showing empty lacunae in necrotic bone. Haematoxylin-eosin, × 500. Moreover, there was extensive myelofibrosis with necroses and haemorrhages and in places newly formed bone.

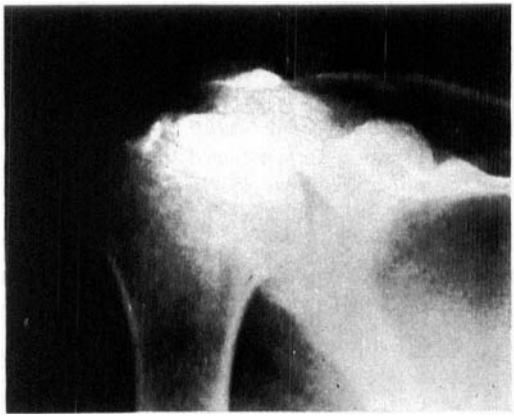

Figure 7. Necrosis of the right humeral head, from Case 2, with preserved contour of the head.

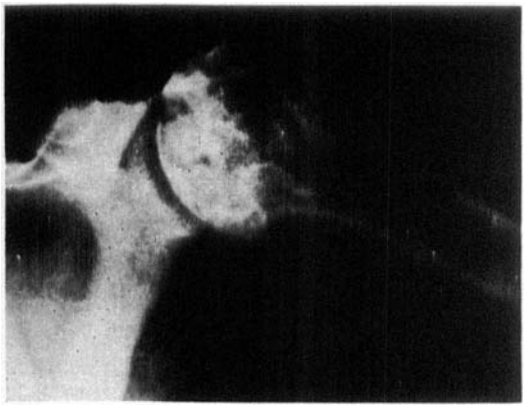

Figure 8. Necrosis of the left humeral head, from Case 2, with collapse of the humeral head.

the dose for two weeks was raised to 100 mg 3 times daily, and thereafter it was gradually lowered, first to 50 mg twice daily and then to 15 mg daily for 6 months, and thereafter the treatment was discontinued.

Splenectomy was performed in December 1967.

In March 1970 necrosis of both femoral and both humeral heads was demonstrated by radiography (Figures 7, 8, 9, and 10). At that time, the patient had been suffering from pain in all four joints for an unstated number of months.

In May 1970 exploratory arthrotomy on the right hip joint was performed. There were large, soft masses of synovial tissue overgrowing the cartilage in several places. Histological examination revealed degenerative cartilaginous changes with fibrous invasion at the periphery, and the bony trabeculae contained empty lacunae with no signs of regeneration.

In December 1970 arthrodesis of the right hip was carried out.

Incidentally, the patient continued his severe and completely uncontrollable abuse of various drugs.

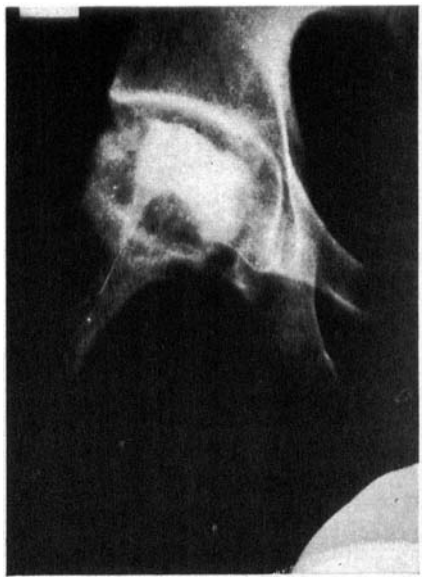

Figure 9. Right hip from Case 2 with necrosis and collapse of the femoral head.

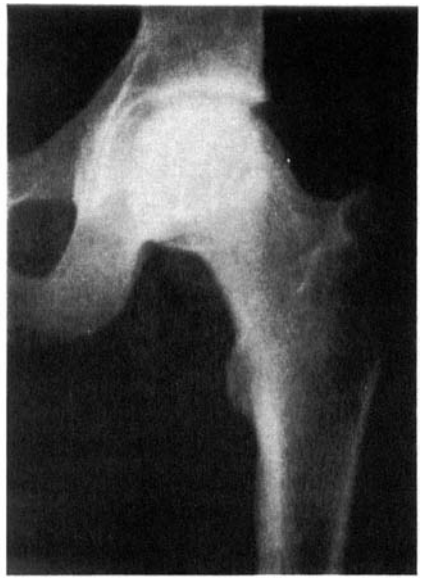

Figure 10. Left hip from Case 2, showing necrosis of the femoral head, but preserved configuration.

Case 3. Labourer, born 1947, who had been doing various odd jobs, on land and at sea, most recently in a varnish factory.

In October 1967 the patient had idiopathic hepatitis while in prison. He was treated for 4–6 weeks with Durabolin® 25 mg daily. No further investigations were performed.

In June 1968 he was admitted with aplastic anaemia and treated with prednisone, 10 mg 3 times daily, until December 1968, when the dose was lowered to 2½ mg twice daily, to be discontinued 2 months later.

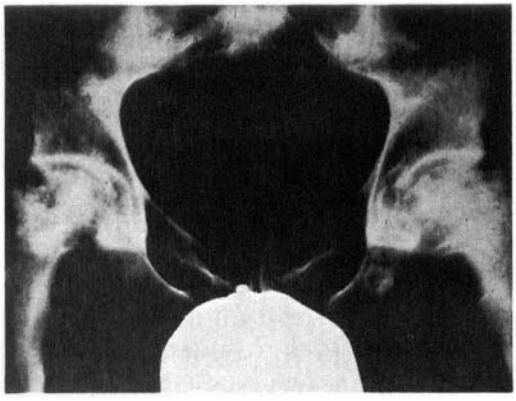

Figure 11. Right and left hips from Case 3. Necrosis of both femoral heads.

In April 1969 the patient suddenly developed pain in the region of the right hip. The pain got gradually worse in the course of the next 6 months, and at the same time pain appeared also in the left hip. X-ray examination revealed necrosis of both femoral heads (Figure 11). Operative treatment was not performed.

DISCUSSION

Necrosis of the femoral and humeral heads still remains a puzzling disease which has been increasing greatly during the past 20 years (Merle d'Aubigné et al. 1965, Fisher & Bichel 1971). Many authors have pointed out that during the same period there has been a marked increase in the use of steroids, but their role in the development of femoral and humeral head necrosis is still a matter of discussion (Boettcher et al. 1970, Sutton 1968).

That the risk of developing osteonecrosis following renal transplantations depends upon the amount of steroid administered seems to have been demonstrated by Harrington et al. (1971).

The explanations of the steroid effect have differed: Vasoconstriction (Labram 1963), emboli of hepatic fat (Jones & Engleman 1967), reduced remodelling following microtraumas (Frost 1965), or reduced protective oedema in the bone marrow (Riniker & Huggler 1971).

However, two-thirds of the idiopathic necroses of bone still occur unpreceded by steroid therapy, and have been related to numerous conditions (Zinn 1971). Riniker & Huggler (1971), on the basis of histopathological studies, have emphasized the role of the bone marrow in the development of femoral and humeral head necrosis. They state that unlike fatty tissue, haemopoietic tissue is able to distribute a pressure arising in the bone marrow without ischaemia arising in the area, a factor of decisive importance especially in the presence of osteoporosis. The risk of femoral or humeral head necrosis is said to be greatest during a rapid diminution of the thickness of the bony trabeculae, if the bone marrow does not contain haemopoietic tissue.

On the basis of X-radiation experiments and bone marrow grafting in animals, Knopse & Crosby (1971) have asked whether aplastic anaemia is a disease of the microcirculation rather than of the stem cell.

The present three cases of steroid-treated aplastic anaemia followed by osteonecrosis permit no conclusions regarding a causal relationship between the three parameters, but the two studies mentioned above might indicate such a possibility.

SUMMARY

Three young men developed osteonecrosis after having been subjected to steroid therapy:

A 28-year-old man had necrosis of both femoral heads and one humeral head. At the time he was on steroid therapy for aplastic anaemia of 5 years' duration.

A 20-year-old man had necrosis of both femoral and both humeral heads. Three years previously he had had steroid therapy for aplastic anaemia.

A 21-year-old man had necrosis of both femoral heads. One year previously he had had steroid therapy for aplastic anaemia.

These cases allow no conclusions concerning a causal relationship between aplastic anaemia and osteonecrosis, but a theoretical possibility is indicated.

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