Distribution of 99mTc-phosphate compounds in osteonecrotic femoral heads

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We examined the distribution of 99mTc-MDP in 12 late-stage nontraumatic necrotic femoral heads by autoradiography and compared this to the histology of adjacent sections. A widespread fibrocartilaginous metaplasia, and enchondral ossification was observed in the demarcation zone. The highest uptake of the isotope was seen at the provisional calcification in areas with enchondral ossification in the demarcation zone. We concluded that the uneven distribution of 99mTc-MDP was mainly due to the remodeling processes.

In very early stages of necrosis of the femoral head, uptake of 99mTc-methyldiphosphanate (99mTc-MDP) in the head might be decreased (Strömquist 1983, Miki et al. 1987), but usually an increased uptake is noticed (D'Ambrosia et al. 1978, Conklin et al. 1983, Bonnarens et al. 1985, Spencer and Maisey 1985).

Only a few studies have compared the topographic location of an isotope in osteonecrosis with the histologic morphology (Cameron 1969, Morscher and Fridrich 1971, Bohr and Heerfordt 1977, Hirano et al. 1987). This is, however, important for interpreting the scintigrams.

We made scintigraphic and histologic examinations of the femoral heads from patients who underwent total hip replacement for nontraumatic necrosis of the femoral head.

Material and methods

Twelve femoral heads of patients with late-stage nontraumatic necrosis of the femoral head planned for total hip replacement were examined. The patients were included only after informed consent.

Two to 3 months prior to surgery, all the patients were examined by 99mTc-MDP scintigraphy, and they were given 500 mg tetracycline twice daily for 2 days followed by 500 mg twice daily for 4 days a fortnight later.

One to two hours before removal of the femoral head, 550 mBq 99mTc-MDP (Institutt for energiteknikk, Kjeller, Norway) was given intravenously. After removal the femoral head was immediately cut in the coronal plane, and a radiograph of the two halves was obtained.

One half of the femoral head was embedded in carboxymethyl cellulose and frozen immediately by immersion in hexane cooled to –75 °C with solid carbon dioxide. Using the technique described by Christensen and Arnoldi (1980), sections of 10 µm of the frozen block were cut with a heavy-duty microtome, fixed in formol-calcium for 5 min and stained with hematoxylin and eosin and according to Burstone (1962) to show the alkaline phosphatase activity. Further, the distribution of mineral and osteoid tissue was demonstrated by von Kossa's stain for calcium deposits.

Autoradiography was performed by placing the frozen block on a sensitive film (X-omat MA, Kodak) for about 20 h. The autoradiography was compared with the different stained frozen sections neighboring the newly sectioned surface of the block used for autoradiography.

The block was defrosted, embedded in methylmethacrylate, ground down to 70-µm slices, and examined for fluorescence from the tetracycline labeling in ultraviolet light.

The other half of the femoral head was fixed in neutral formalin, decalcified, and stained with hematoxylin and eosin, safranin-O, and toluidine blue to show areas with fibrocartilaginous metaplasia.

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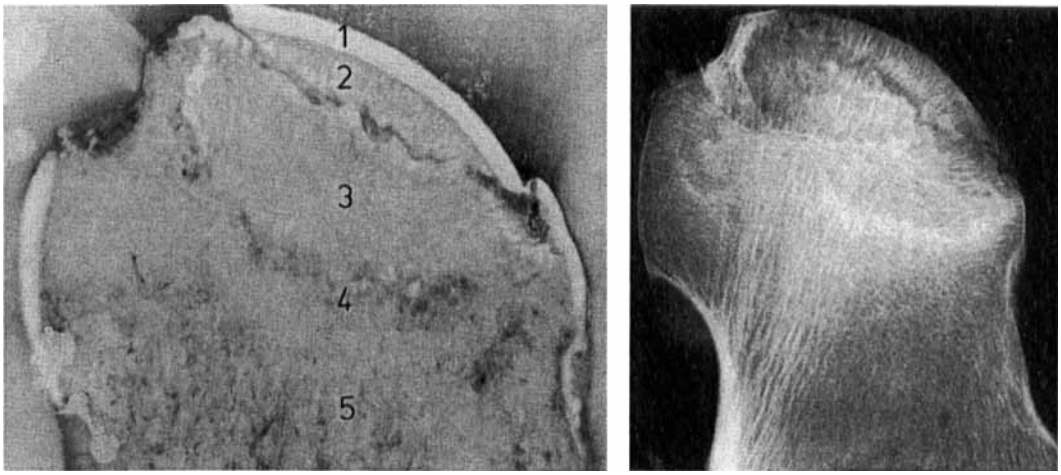


Figure 1. Coronal section and radiogram of necrotic femoral head with five distinct zones: 1, articular cartilage; 2, subchondral necrotic bone; 3, sequester; 4, transitional area; 5, normal cancellous bone.

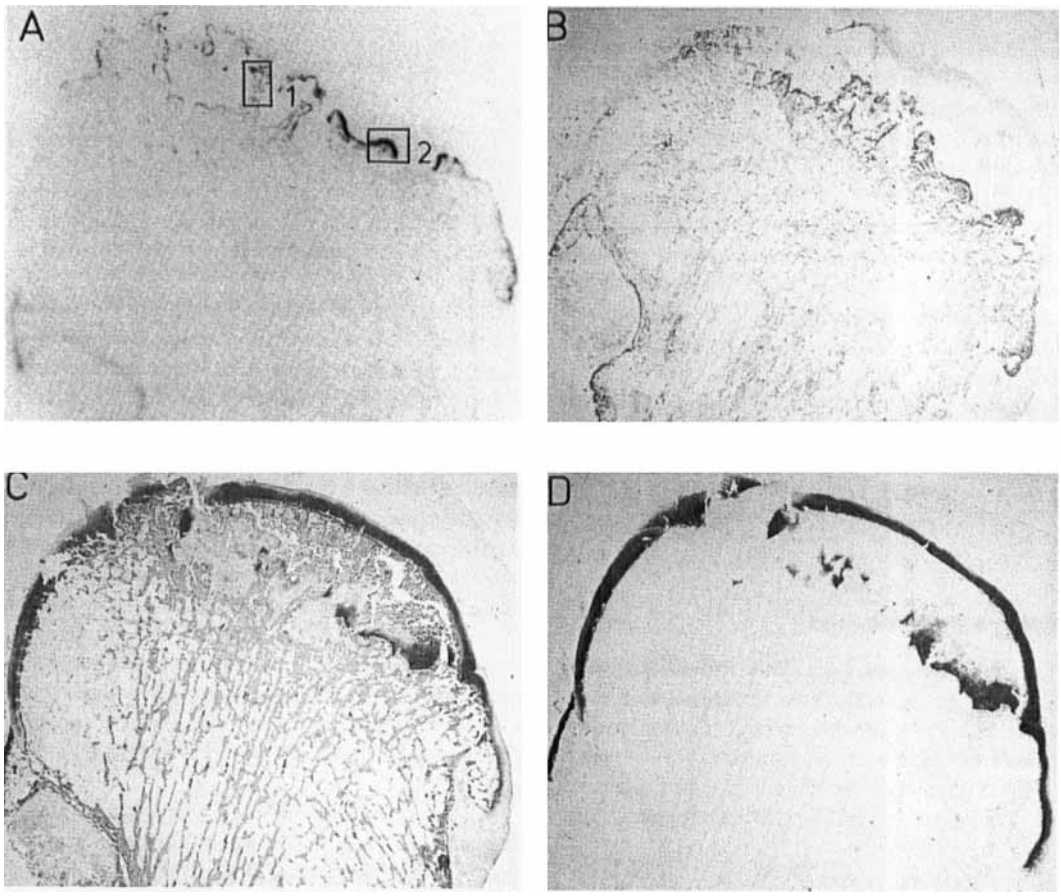


Figure 2. Autoradiography of necrotic femoral head (A; x2.5). Areas marked 1 and 2 correspond to von Kossa-stained sections in Figure 3. Adjacent sections stained with alkaline phosphatase (B), a marker enzyme for bone formation, safranin-O (C), and toluidine blue (pH 5), showing fibrocartilaginous metaplasia at the demarcation zone (D).

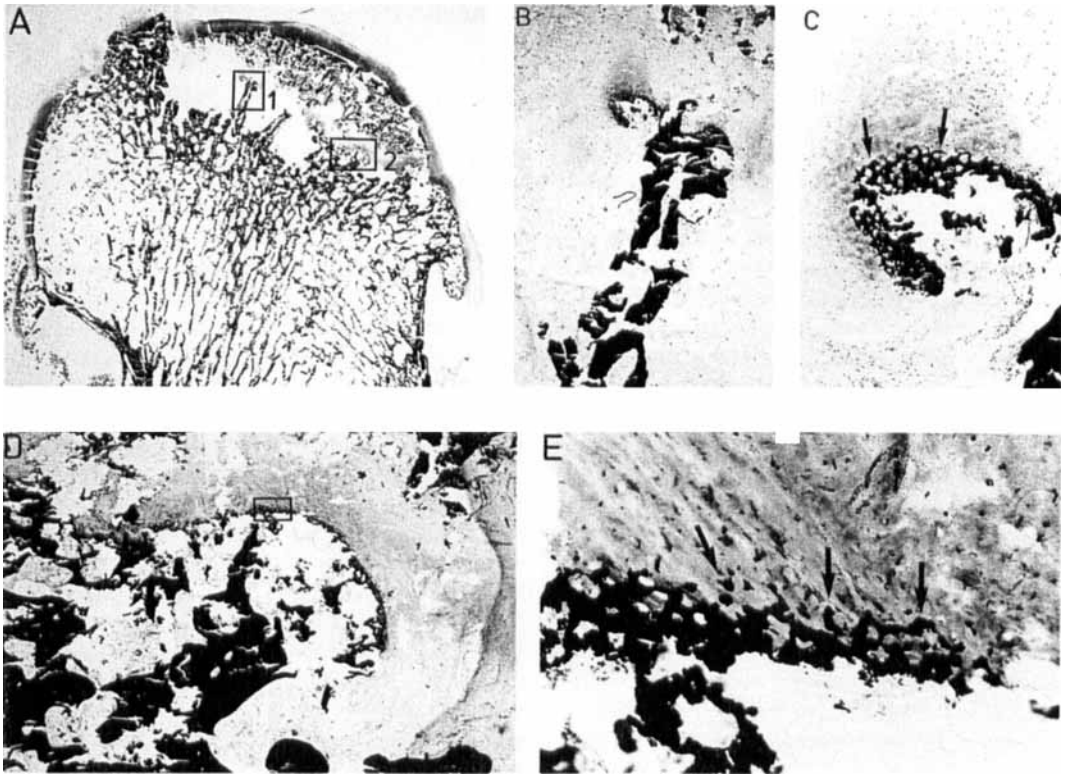
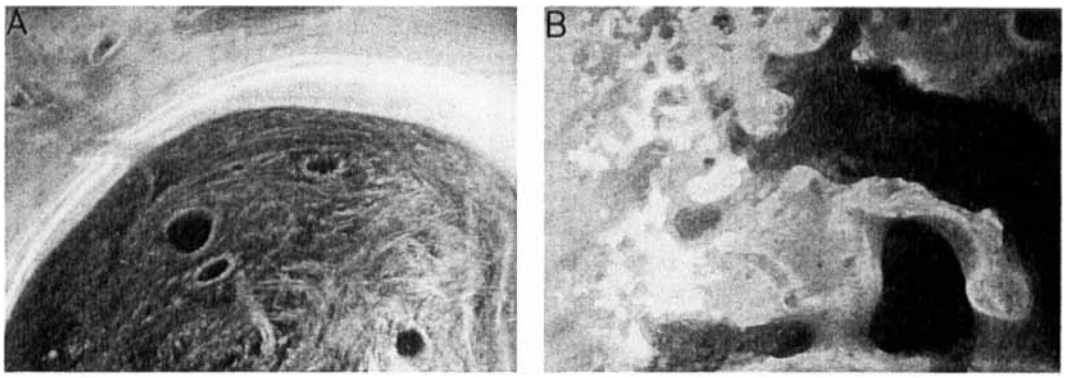


Figure 3. Accumulation of the isotope coincides with areas of enchondral ossification in the demarcation zone. Arrows indicate provisional calcification of the matrix of the metaplastic fibrocartilage.

A. Von Kossa's stain of sections adjacent to the cut surface of the block used for autoradiography in Figure 2A (x2.5).

B and C. Enlargement of area marked 1 (x80 and x200).

D and E. Enlargement of area marked 2 (x20 and x200).



Double labeling of appositional bone growth.

Single labeling of provisional calcification in enchondral ossification in the demarcation zone.

Figure 4. Tetracycline labeling of osteonecrotic femoral head.

Results

Increased activity in all the necrotic femoral heads was found at the preoperative scintigraphy of the hip region, quite overshadowing and obscuring areas of dead bone with no uptake.

Histologically, five distinct zones were noted (Monticelli and Spinelli 1982; Figure 1):

At the distal boundary of Zone 1, a distinct basophilic line of the tidemark was noticed. In many locations, the fracture line mentioned below bordered this line.

In Zone 2 no osteocytes were found in the lacunae, and no activity was found upon alkaline-phosphatase staining or by tetracycline labeling. Usually this area was separated from the deeper layers by a fracture, which was also visible macroscopically and radiographically as the typical crescent line.

In Zone 3 no living bone was found, and no osteoblastic activity or osteoid production took place.

In Zone 4, the transitional area between the sequestered and the normal cancellous bone, two layers were usually noticed: an upper fibrous and a deeper osteosclerotic layer. In this richly vascularized zone, a vigorous osteoblastic activity was observed to cause appositional ossification. Also, widespread fibrocartilaginous metaplasia and enchondral ossification was noticed in this zone.

In Zone 5 normal cancellous bone constituted the remaining part of the femoral head.

Corresponding to these zones, comparison of the autoradiograph and adjacent histologic sections showed that the 99mTc-MDP had mainly accumulated in the demarcation zone in areas with ample metaplastic fibrocartilage (Figure 2). Notably the isotope was concentrated in areas where the von Kossa's stain showed provisional calcification in enchondral ossification of the fibrocartilaginous tissue (Figure 3). In cases with secondary arthrosis, some accumulation had also taken place in the osteophytes.

In a few cases, some diffusion of tracer from the synovium into the subchondral fracture was observed, but no uptake of the isotope was found in the subchondral bone or in the zone of sequestration.

The fluorescence from the tetracycline was mainly seen in the demarcation zone as a double labeling in areas with appositional bone growth (Figure 4). In areas with enchondral ossification, only a single band of labeling was found, which was due to the high ossification rate and the accelerated remodeling in these areas (Figure 4).

Discussion

In some of our cases, the amount of enchondral ossification was not very prominent. The cause of this difference in ossification is unknown, and we did not find any clinical correlation with this observation. However, in most cases the spotted localization of the isotope correlated closely with areas with provisional calcification in enchondral ossification of the metaplastic fibrocartilage in the demarcation zone. This supports the view that the target of the 99Tc-MDP compound is the mineralization front of the newly formed deposits of calcium phosphate in the hydroxyapatite crystals (Christensen and Krogsgaard 1981, Einhorn et al. 1986). This is further supported by the observed coincidence of high alkaline phosphatase activity and accumulation of isotope. This accumulation is probably the main factor responsible for the high tracer uptake, rather than the increased vascularity that was also noticed diffusely in the entire demarcation zone (Christensen and Krogsgaard 1981).

Passive diffusion from the synovium into the subchondral fracture line contributed in some cases to the impression of increased uptake of the isotope; but contrary to Bohr and Heerfordt (1977), we found no tracer uptake or tetracycline labeling in the subchondral bone.

Our findings parallel the findings in arthrosis, where 99mTc-MDP mainly accumulates in the weight-bearing areas and in the osteophytes. These areas are also characterized by enchondral ossification, and the mineral deposits of this tissue have been suggested as the target of the bone-seeking agent (Christensen and Arnoldi 1980).

By present techniques, it is not possible to examine the topographic localization of 99mTc-MDP in patients with early stages of nontraumatic osteonecrosis, as total hip replacement is rarely indicated in these patients.

Our observations confirm that distribution of the 99Tc-MDP isotope in late-stage nontraumatic necrosis of the femoral head reflects the remodeling processes that primarily takes place in the demarcation zone under the avascular sequester.

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