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*Case Reports*

# Synovial Deposit of Osmic Acid after Intra-Articular Injection

## Anatomical and Radiologic Study of a Case

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**Summary.** An anatomical and radiologic study of a synovial autopsy specimen 32 months after an intra-articular injection of osmic acid for the local treatment of a rheumatoid synovitis.

Osmium deposits are seen within peripheral cells of a fat lobule and also in a few histiocytes of the scar tissue which replaced the rheumatoid synovitis. These osmium deposits in the fat cells are present in a sufficient quantity to give a radiologic opacity.

For many years surgeons have been aware that osmic acid (aqueous solution of osmium tetroxide) induces fibrogenesis. More recently this property has been employed in the local treatment of chronic exudative synovitis – most frequently in rheumatoid arthritis – to replace an inflamed synovial membrane by cicatrization. This procedure, employed only in certain countries and almost exclusively for the knee, is one of the methods of "chemical synovectomy" or "synoviorthesis" [2].

Intra-articular injection of osmic acid produces necrosis of inflamed synovial tissue. Synovial repair is accomplished simultaneously by histiocytic phagocytosis (which could result in a storage of reduced osmium) and fibroblastic fibrogenesis. In some cases osmium is also permanently fixed in adipose tissue. The presence of this heavy metal (atomic number = 76, compared with 20 for Ca and 82 for Pb) may cause radiologic opacities described for the first time by Weston and Anttila [2, 3, 6]. If the nature of these opacities are known, confusion with calcium deposits of articular chondrocalcinosis, synovial ossifications, periostosis, or even osteogenic periosteal tumors may be avoided.

## Case Study

*Clinical History*

A female patient experienced the onset of severe rheumatoid arthritis at the age of 62 years. Despite a treatment with gold salts over a period of 9 years (total dose approx. 8–10 g) the

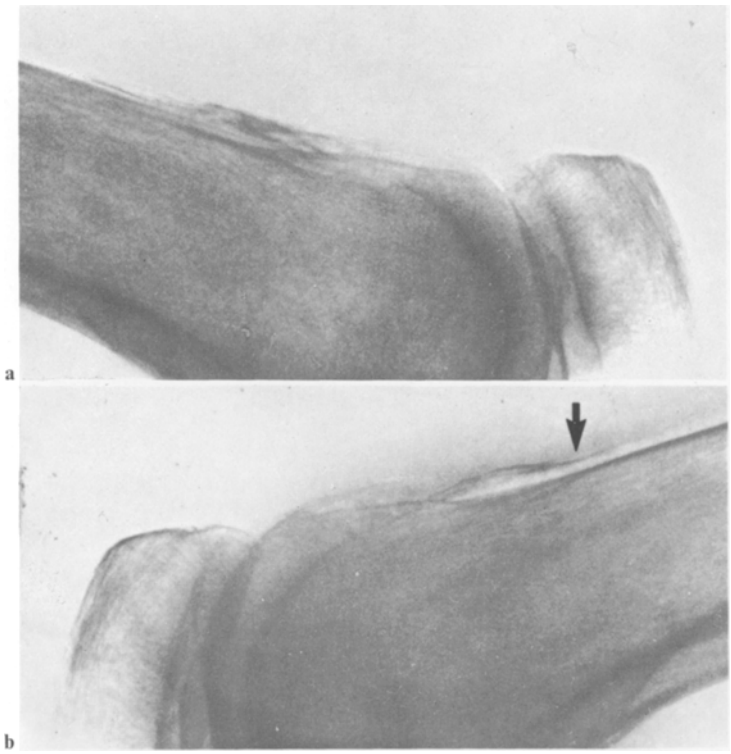



**Fig. 1a and b.** Roentgenographic profile view (April 24, 1974). **a** Right knee; **b** Left knee

patients became bedridden. The hands, wrists, and knees were involved bilaterally as well as the left shoulder and the cervical spine. Rheumatoid nodules were present. Daily oral doses of approx. 10 mg of cortisone were administered for several years up to the time of her death at the age of 75 years. Penicillamine treatment had been attempted. Death was caused by a septicemia (escherichia coli).

At the age of 73 years an intra-articular injection into both knees of 200 mg of osmic acid was performed for recurring effusions. The resultant improvement was transitory. Then, 8 months later a synoviorthesis with yttrium 90 was performed on the left knee and was well tolerated.

*Radiological Findings*

Radiographs of the knees made 1 year following osmium injection showed a bilateral narrowing of the femoropatellar space and a suprapatellar radio-opaque image (Fig. 1).

*Pathology*

On autopsy (GE 162/75), a bilateral septic thrombosis of the iliac arteries, bilateral acute pyelonephritis, a recent anteroseptal myocardial infarction, and a vertebral luxation C6–C7 associated with spinal cord compression were found.

The *left knee joint* (32 months after osmic acid injection) showed an erosion of the cartilaginous surfaces and fibrosis of the synovial membrane. A black intra-articular deposit was scattered irregularly on the synovial membrane and particularly in the intra-articular supratrochlear fat. A specimen from this region ($3 \times 0.5 \times 0.5$ cm) showed, on sagittal section, a fat lobule containing black deposits on its endoarticular aspect (Fig. 2a). Furthermore, these deposits were covered by thick fibrous tissue whose synovial surface appeared smooth (Fig. 2a).

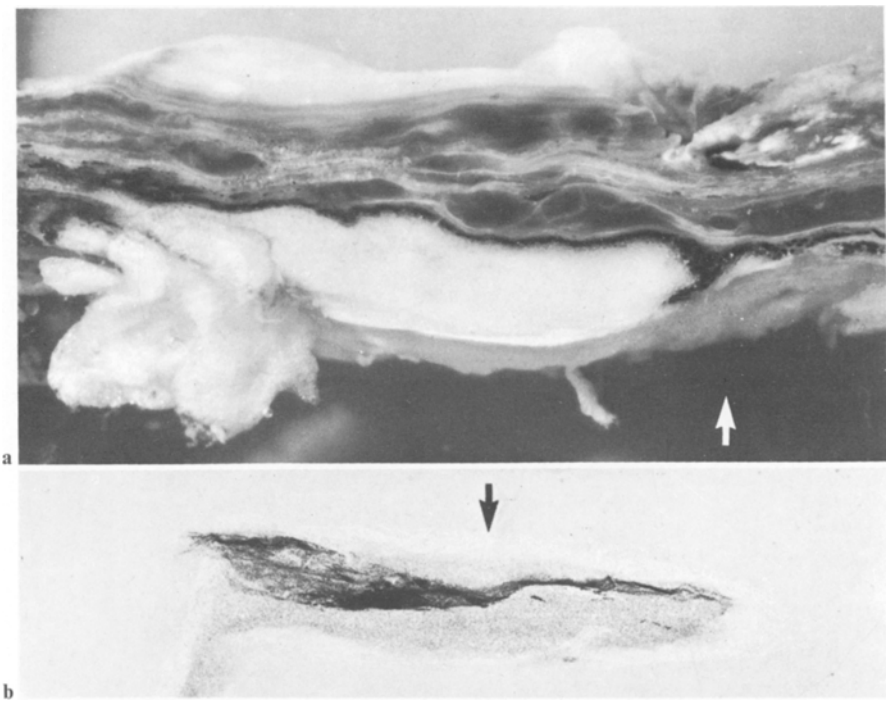


**Fig. 2a and b.** Specimen taken from supratrochlear region of the left knee (proximal pole on the right side). **a** Frontal section. From bottom to top: fat lobule – strip of reduced osmium fixed at periphery – fibrous layer of varying density – synovial surface. **b** Radiograph of frontal section, same position as seen in (a). Black arrow at the same level as black arrow in Figure 1b and as the white arrow in Figure 2a

The radiography of the specimen, on a sagittal plane, showed a forklike image. This was similar to the opacity noticed in profile view x-rays of the knee and was obviously explained by osmium deposits within the fat lobule (Fig. 2b).

Osmium deposits were not observed in lung, liver, kidney or spleen (several rare, suspicious looking black granules were controlled with the electron probe x-ray analyser).

*Histologic* examination of the formalin-fixed specimen was performed after using several staining procedures: hematoxylin-eosin, van Gieson's staining, toluidine blue, alcian blue, silver impregnation (Gomori's method), elastin staining (resorcin fuchsin), fibrin staining (Mallory's phosphotungstic acid hematoxylin method: PTAH), stain for ceroids (Ziehl's method), and stain for iron (prussian blue reaction). This examination showed:

1. Black deposits of reduced osmium in the peripheral cells of the fat lobule principally on its endoarticular aspects (Fig. 3a). The presence of osmium was confirmed by the electrom probe x-ray microanalyser.

2. Fibrosis which developed deeply between the fat cells, explaining the synovial scar thickening on the surface (Fig. 3–5). This fibrosis was red with van Gieson and nonmetachromic with toluidine blue. It was stained with alcian blue only far down between fat cells, where the rare precollagenous fibers were observed (Fig. 4). Thus it appears to be essentially a slow growing adult type.

A few black osmium deposits were observed in the cytoplasm of some histiocytes (Fig. 4). The electron probe x-ray microanalyser confirmed that these deposits were osmium. Hemosiderin deposits were exceptional. There were neither deposits of gold nor ceroid pigment. Elastic fibers were not observed. A few fragments of cartilage or collagenous bundles were embedded within the fibrous synovial layer or were associated with surface fibrin deposits (Fig. 6). These are indications of articular deterioration due to rheumatoid arthritis.

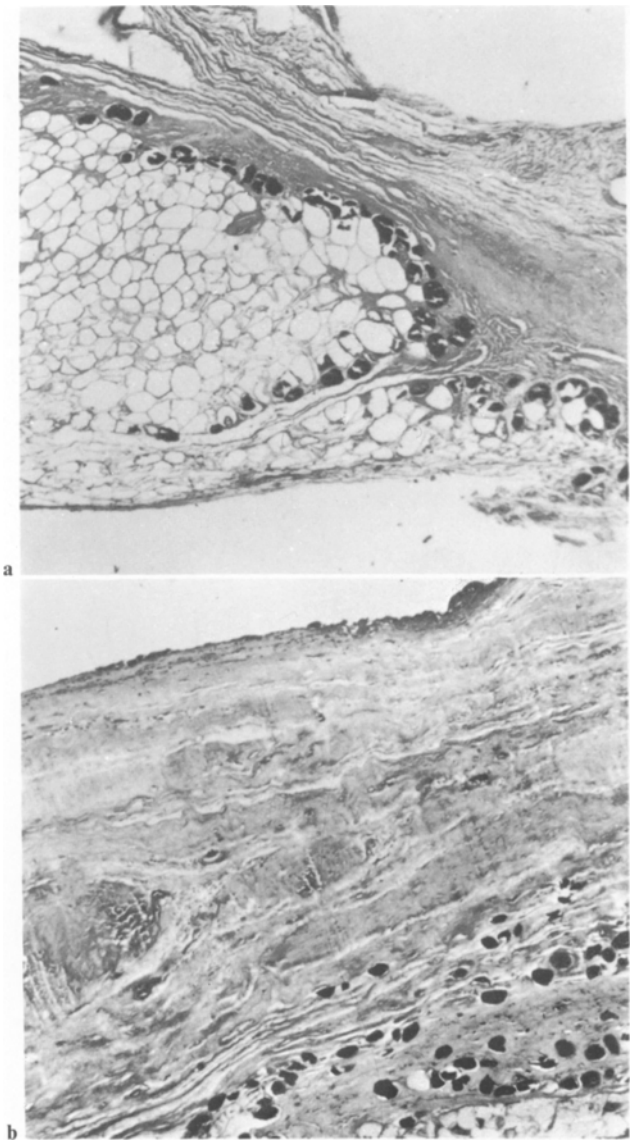



**Fig. 3a and b.** Relationship of fibrosis and osmium-impregnated adipose tissue: topography. Hematoxylin-eosin stain ×40. **a** Region indicated by white arrow in Figure 2a. Peripheral fat cells of fatty lobule impregnated with osmium, arrangement of which explains forklike image of strip seen in Figure 2a. Central fat cells still alive. **b** Segment contiguous with preceding, on same plane and at same depth in a more proximal position. In deeper layers, fixed and impregnated fat cells enclosed in the fibrous tissue. On upper border, surface of fibrosed synovium with some rare deposits of fibrin. On the left, preexisting collagenous bundles embedded in newly formed fibrous tissue

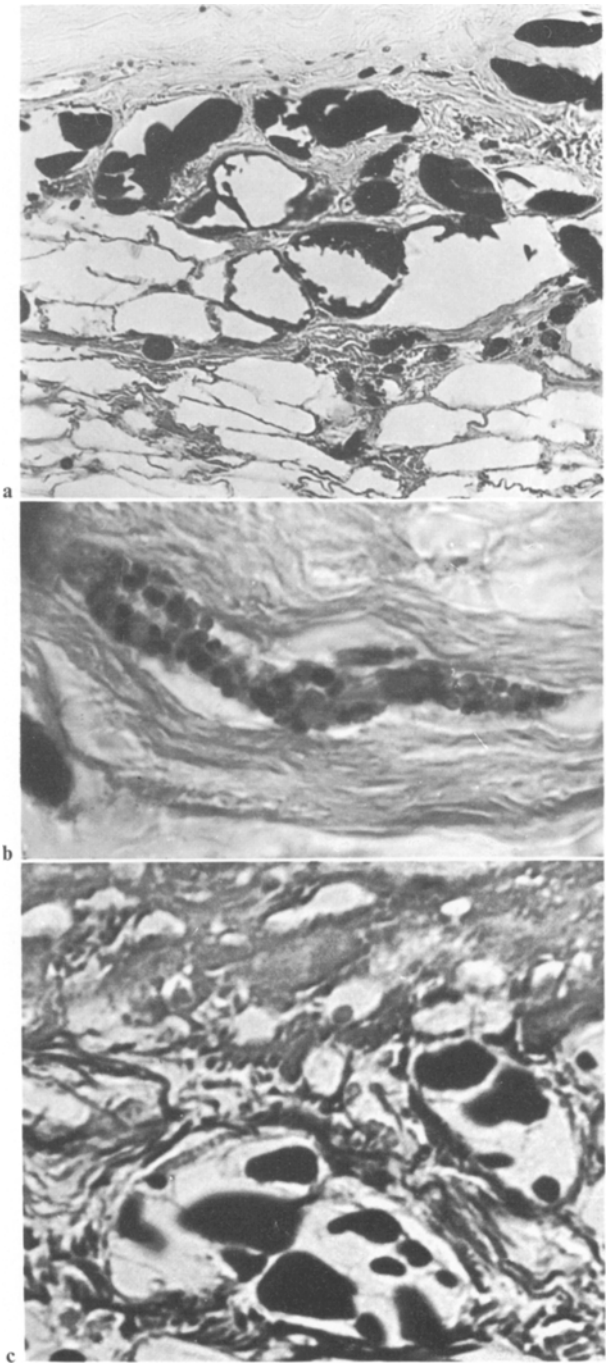
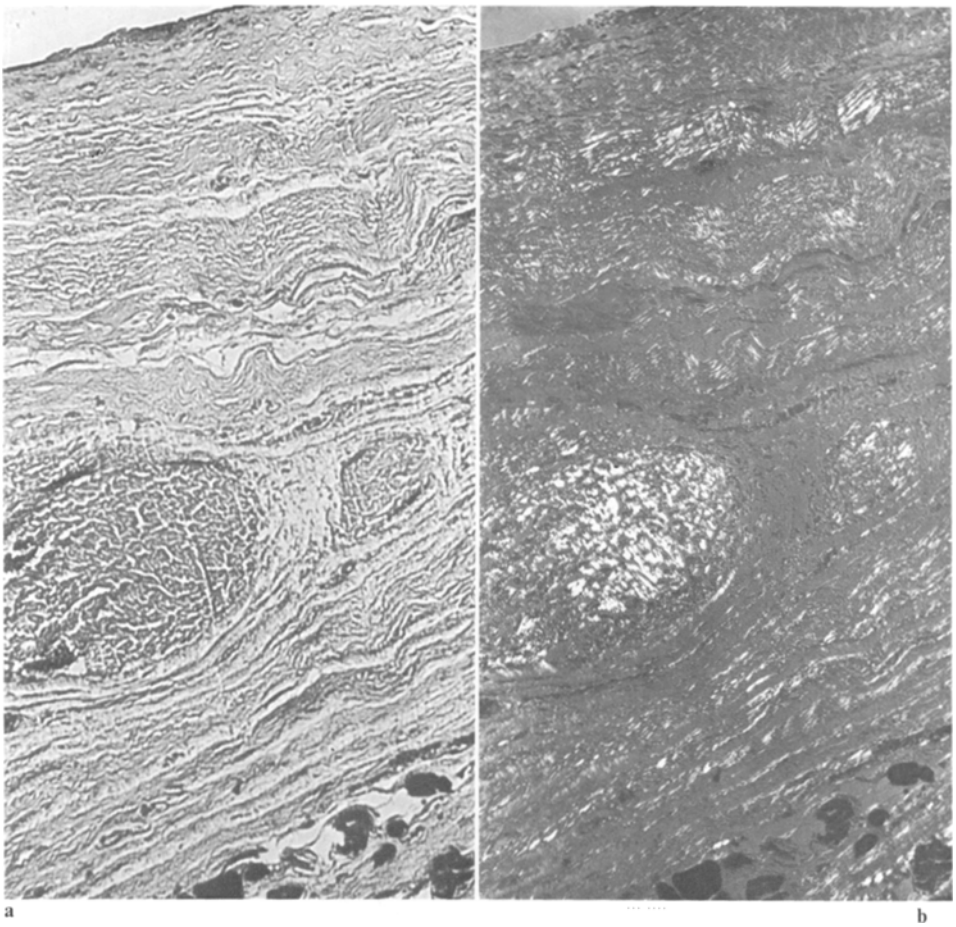



**Fig. 4a–c.** Relationship of fibrosis and osmium deposits: detail from a region in vicinity of that shown in Figure 3. **a** Boundary zone between synovial fibrosis (above) and adipose tissue (below). Osmium deposits in fat cells and histiocytes embedded in fibrous tissue. Nuclear fast red counter-stain (leaving only osmium deposits visible) ×200. **b** Osmium granules within protoplasm of histiocyte. On the left osmium deposits within two fat cells. Nuclar fast red counter-stain ×1,300. **c** Zone adjacent to the one seen in Figure 4a. Upper half: adult fibrosis. Lower half: two islets of pigmented fat cells between which there are rare precollagenous argyrophilic fibers. Silver stain ×500



a b

**Fig. 5a and b.** Detailed view of newly formed fibrous fibers from a region in vicinity of that shown in Figure 3b. Hematoxylin-eosin ×80. On upper border, synovial surface. In center, two preexisting collagenous bundles. At bottom, fixed and impregnated fat cells. **a** Normal light; **b** Polarized light

## Discussion

The present observation confirms the conclusions of a previous radiologic and anatomical joint study, performed with similar histologic techniques [2]. It also indicates the absence of visceral lesions related to osmium deposits.

The topographic relationship of synovial fibrosis with osmium deposits (in fat cells or histiocytes) indicates the role of osmic acid in the genesis of the fibrosis. It is known that osmic acid produces necrosis in normal or inflamed rabbit synovial tissue [1, 5]. The reduced osmium particles which remained free or which were already liberated after first being phagocytosed are stored by the histiocytes (sometimes also in giant cells [4], not observed in the present case). Simultaneously, intense fibroblastic activity is induced. We also observed

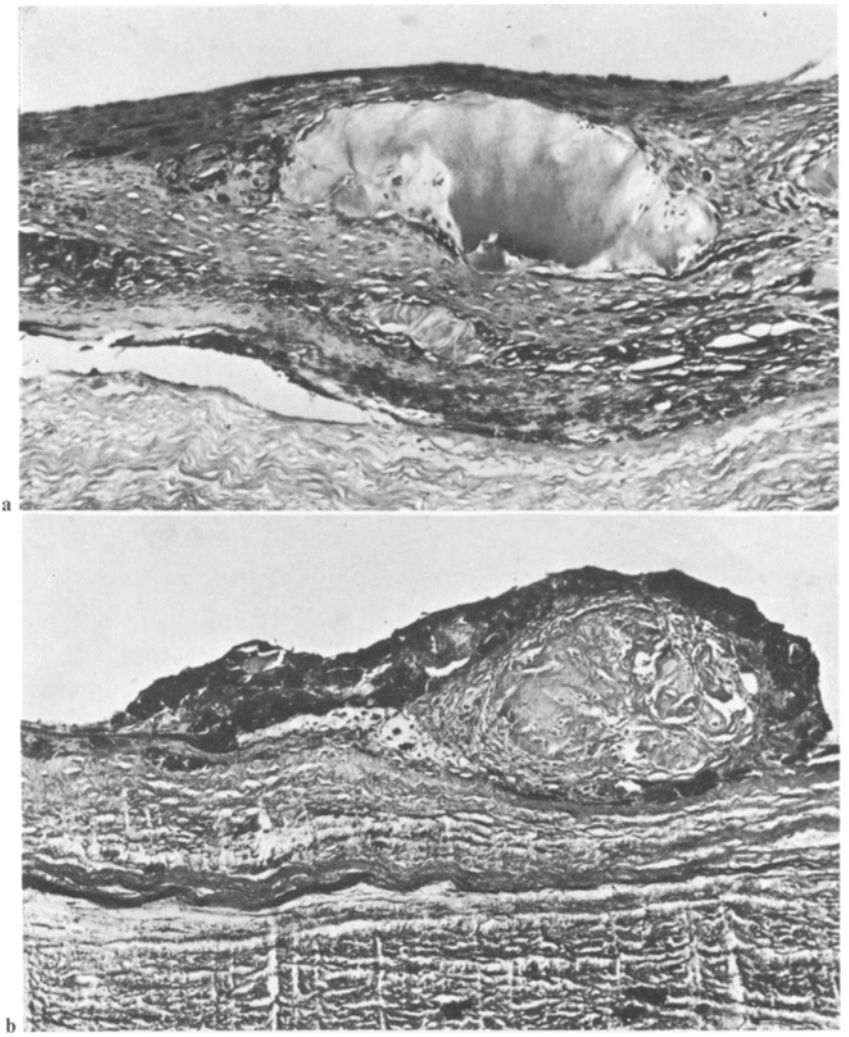


**Fig. 6a and b.** Surface of fibrous synovium taken from area in proximity of preceding. Fibrin stain PTAH ×80. **a** Cartilaginous fragment of articular origin embedded in superficial, newly formed fibrous layer. This richly cellular layer contains a few fibrin deposits (in black) and is younger than subjacent newly formed layer (in light grey). **b** Fragmented collagenous bundle applied against subjacent newly formed fibrous layer. In addition, the latter is bordered by fibrin deposits (stained in black)

this evolution in the fringes of fatty rat peritoneum impregnated with osmic acid or in granuloma pouches injected with osmic acid.

Therefore it is easy to understand why this method can bring clinical improvement to an inflamed articulation. Besides the possibility of a local recurrence of rheumatoid disease the procedure does not exclude the possibility of an iatrogenic effect or of an intensification of the previously existing arthropathy due to mechanical self-maintenance. This intensification could occur by fibrinous

exudation (minimal in the present case but rather profuse in other cases that we have observed) and/or by a worsening of a preexisting cartilaginous lesion.

This study, as well as a previous one, explains the origin of radiologic opacities which are sometimes observed after osmic acid synoviorthesis [2, 3]. Osmium deposits in the histiocytes alone are too dispersed and too rare to explain these opacities. We have verified this on human surgical synovectomy specimens and in rat granuloma pouches. These opacities (not related to the nature of the treated disease) are not observed in all cases and are more frequently seen after a 200 mg injection of osmic acid rather than a 100 mg injection [2, 3]. We presume that their occurrence is due to various factors: inequality of local concentration and penetration of osmic acid; individual variation in the amount of subsynovial fatty tissue.

These osmium deposits in fat cells seem to play by itself a role in the development of fibrosis, because many impregnated fat cells appear embedded in the deep region of the scar tissue which also contains some osmium deposits within histiocytes (Fig. 4). The latter appears principally related to the direct phagocytosis of injected osmium, but a part of this could possibly be due to a gradual release of stored osmium. This is probably very slow because fibrosis is essentially of the adult type, with only rare precollagenous fibers. However, these radiologic opacities do not seem to affect the clinical course [2].

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