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Case report

Osteoarthrosis and apatite synovitis

Pathological study of a metacarpophalangeal joint

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Summary. A case of metacarpophalangeal osteoarthrosis associated with synovial apatite deposits is reported. The size of the crystals indicates that they have been thickened by a recrystallisation process; the latter could have been provoked by Ca and Po^4 ions released by dissolution of some apatite crystals brought by calcified debris of bone or cartilage coming from the abraded osteoarthrotic surfaces. The role of such thickened crystals in synovial inflammation is discussed as well as their possible diagnostic value in determining origin and pathogenesis of a given synovial apatite deposit.

Key words: Osteoarthrosis – Detritic synovitis – Apatite – Crystal deposition disease

Introduction

In a previous paper a case of metacarpophalangeal osteoarthrosis (OA) with acute apatite-linked synovitis was reported (Gerster and Lagier 1985). The present paper reports and discussed the pathological findings in this case.

Case report

A 53-year old man (a right-handed upholsterer) presented, after minor trauma, with acute pain and redness in the metacarpophalangeal region of the right index finger. X-rays showed a narrowing of the corresponding joint interspace, associated with neighboring radiodense deposits (Fig. 1); arthrography showed a dilated and villous cavity. Medical history revealed that on the same site, recurrent pain had occurred during the last 10 years and that repeated juxtaarticular injections of triamcinolone hexacetonide had been performed since the last 3 years in the dorso-ulnar region. Minor occupational trauma was also reported.

Synovial fluid was sterile and contained 100000 cells/mm^3 (98% polymorphonuclears) and alizarine stained material but no birefringent crystals. Its examination by scanning electron microscopy showed an aggregation of microspheroids (8–10 μm in diameter). Dispersive X-ray analysis indicated a Ca/P ratio

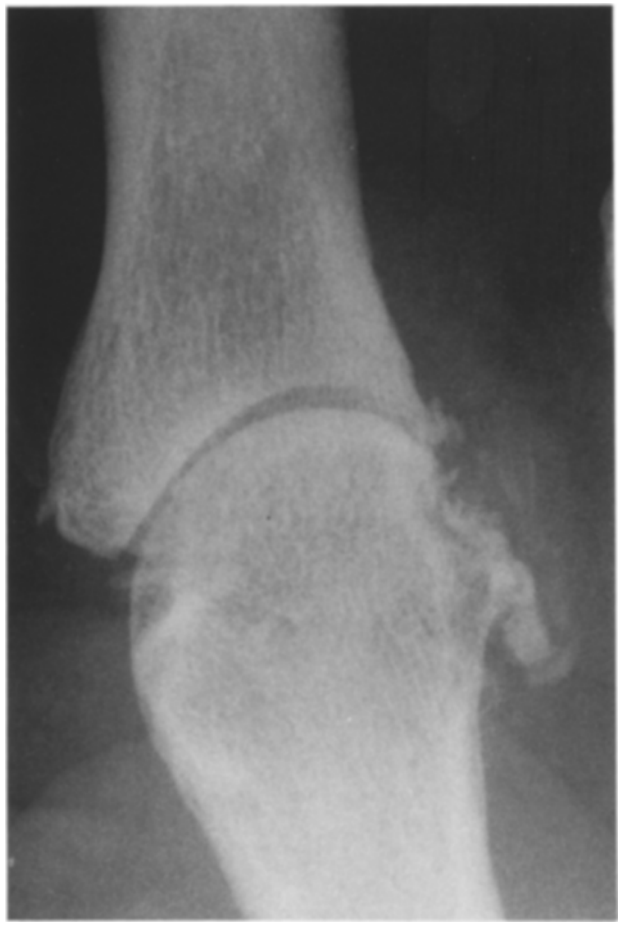

Fig. 1. Plain radiograph of the right 2nd metacarpophalangeal joint. Interspace narrowing and neighboring calcareous deposits

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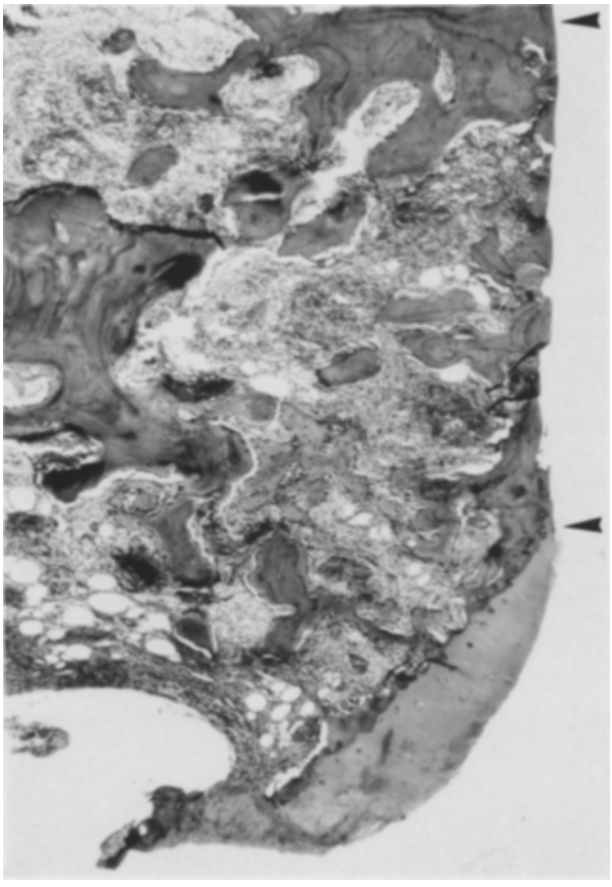

Fig. 2. Histologic aspect of the metacarpal head surface (ventral part: HE ×15). Between two *arrows*, abraded surface with burnated naked bone and underlying medullar necrotic areas. On the ventral pole, a remnant of articular cartilage

compatible with apatite. X-ray diffraction indicated apatite but after heating the sample at 900° C for 3 h the mineral was partly transformed into whitlockite, indicating an apatite deficient in calcium. The total amount of hydroxyproline in the fluid used for washing the joint (determined after hydrolysis by the Kivilico method) was 666.6 μmol/l (87.4 mg/l).

Erythrocyte sedimentation rate was 3 mm/1st h. Blood count and usual laboratory tests were normal. Rheumatoid factor was not detected in blood. Apart from some manifestations of articular discomfort including Heberden's nodes, no signs of true generalized osteoarthrosis were reported. No radiological signs of chondrocalcinosis were seen in the knee, shoulder or wrist joints.

A total arthroplasty with Swanson's prosthesis was performed as well as a dorsal synovectomy of the MCP joint. Intra-articular injection of methylene-blue did not demonstrate any link with periarticular tissues; examination of the latter by a dorso-ulnar approach did not show calcium deposits.

Pathology. Light microscopy examination of the excised material was performed after fixing in 10% neutral formalin, embedding in paraffin and staining of the slides by haematoxylin-eosin, van Gieson and Toluidin blue. The metacarpal head was decalcified in formalin-formic acid. The synovial membrane was also stained with von Kossa for calcium phosphate, with Prussian blue for iron.

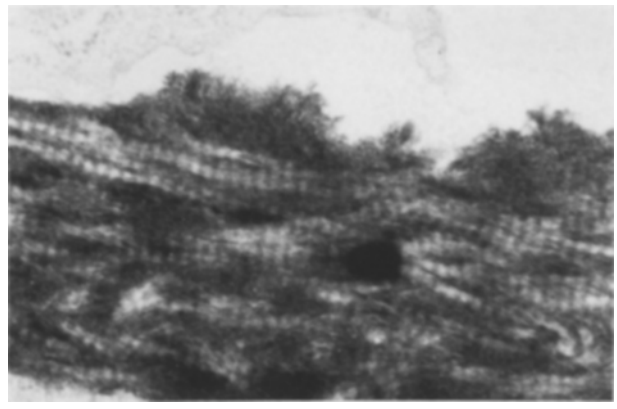

Fig. 3. Transmission electron micrograph of a bone specimen taken from the abraded articular surface. In a juxtacellular situation, apatite crystal deposition on large tightly packed collagen fibrils (unstained section, ×28500)

Some specimens were taken during surgery for particular investigation: a) from the white punctate synovial deposits for X-ray diffraction (formalin fixed material; Guinier's camera); b) from the eburnated surface and from the synovial membrane for transmission electron microscopy (TEM). The specimen of the synovial membrane was immediately fixed for two hours in 2.5% glutaraldehyde buffered with piperazine diethane sulfonate (PIPES) 0.2 M (pH 7), then washed during 12 h with PIPES, and finally embedded in a resin Epon B. The specimen of the articular surface was immediately fixed for 2 h in 2.5% glutaraldehyde buffered with sodium cacodylate 0.1 M (pH 7.2), then washed with 0.2 M saccharose in the cacodylate buffer 0.1 M (pH 7.2), post-fixed in 1% osmium tetroxide, and finally embedded in a resin Epon B. The ultrathin sections were examined with a JEOL CX 100 electron microscope for TEM with or without staining with uranyl acetate and lead citrate according to the method of Reynolds. Some of them had previously been decalcified by 1% phosphotungstic acid. Electron diffraction of mineral deposits was thus performed.

The metacarpal head was excised at 1 cm from the articular surface and showed signs of osteoarthrotic remodelling with marginal cartilaginous remnants containing no calcareous deposits (Fig. 2). Under the eburnated surface, bone remodelling was associated with marrow fibrosis containing lymphoplasmocytic infiltrates, and small areas of basophilic necrosis which possibly contained dusty calcium deposits.

TEM of specimens taken during surgery from the eburnated articular surface showed apatite deposits on collagen fibrils demonstrated by electron diffraction. This must be considered to be bone because of close packing, large diameter and the distinct cross striation of the fibrils (Fig. 3).

The synovial membrane was thickened; X-ray diffraction of the white spots seen on the surface indicated that they were made of apatite crystals (the X-ray diffraction lines were similar to those obtained previously in synovial fluid but heating for evaluation of calcium deficiency was not performed).

Histological examination showed that the fibrous capsule was flanked by a hyperplastic synovium in which collagen-rich calcified debris were embedded among fibroblasts and histiocytes and whose surface presented necrotic areas associated with a dusty non birefringent calcareous material (Fig. 4). A thrombotic vein, some haemosiderin deposits and rare deep foci of lymphocytes were observed. Circumscribed dystrophic calcinosis, synovial chondromatosis, large bone fragments, cal-

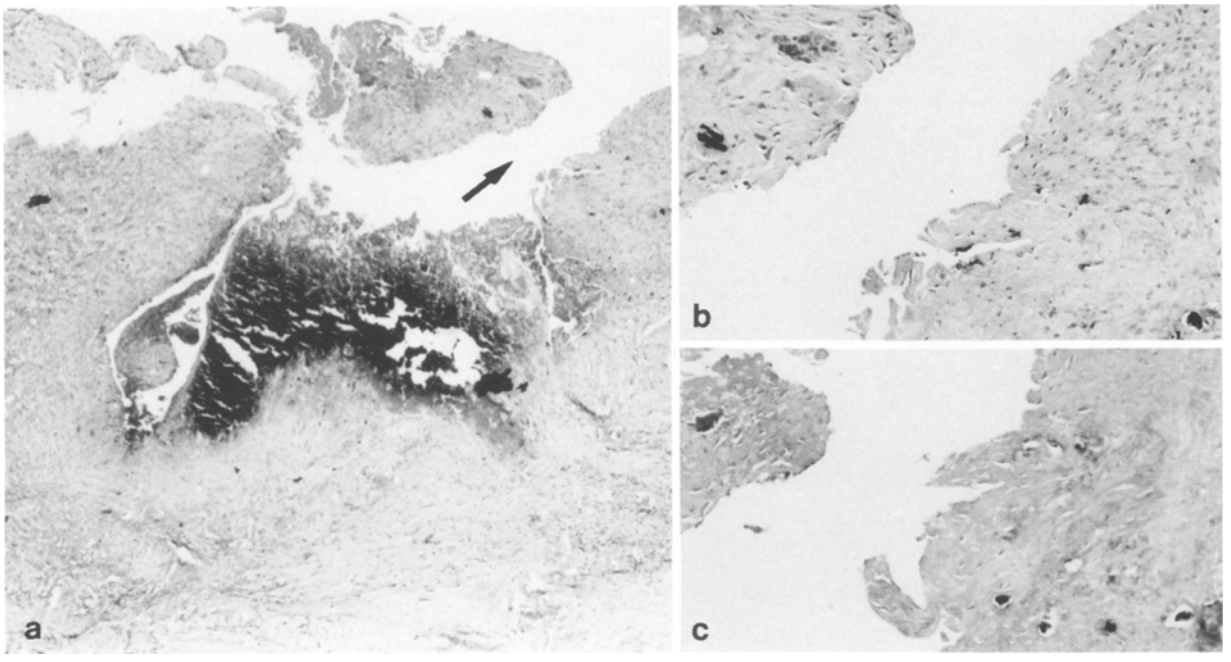

Fig. 4a–c. Histological aspect of a thickened synovial membrane. Embedded calcified debris and superficial dusty calcified necrotic areas. **a** Topographical view (von Kossa ×40). **b** and **c** Detail in the region shown by an *arrow* on **a** (×95); **b** von Kossa staining showing embedded calcified debris; **c** van Gieson staining showing embedded collagen-rich debris

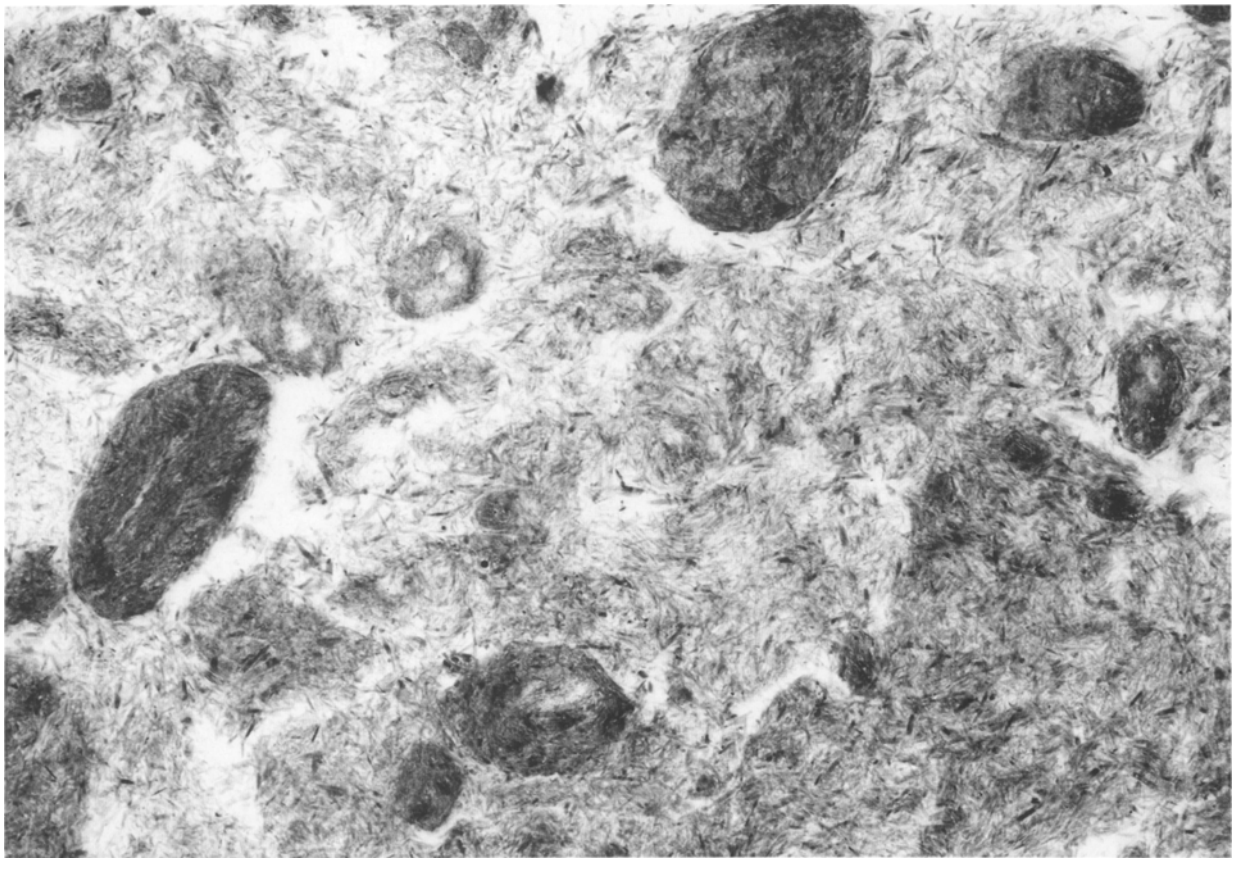

Fig. 5. Transmission electron micrograph of a synovial calcareous deposit (unstained section – ×28 500). Wide crystals or crystal aggregates, some grouped into microspheroids

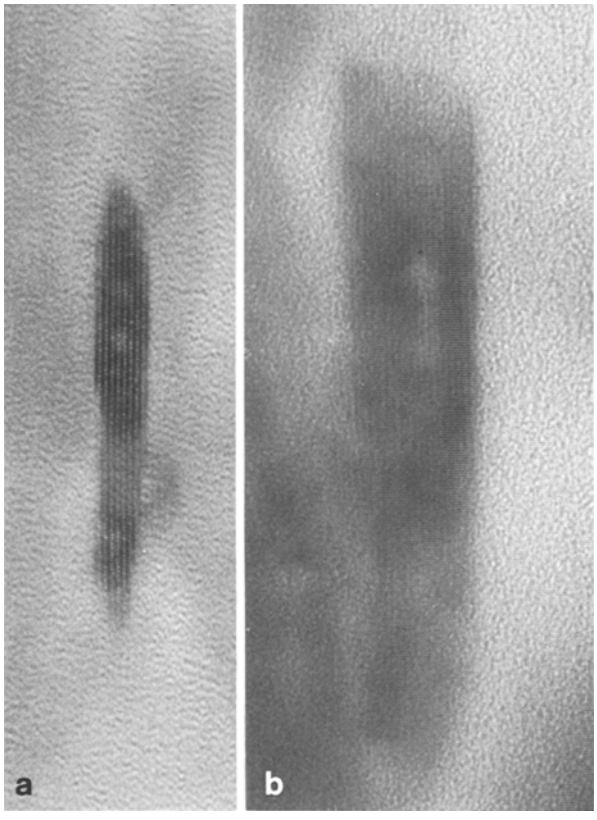

Fig. 6. High resolution transmission electron micrograph; apatite monocrystals fixed in similar conditions (non-phosphate containing fixative); unstained section ×1055000. **a** Control young crystal from a normal bone tissue. Lattice fringes and lattice defects. **b** Crystal from calcareous synovial material in the present case. Lattice fringes and, in the central core only, lattice defects

cium pyrophosphate dihydrate or sodium urate crystals deposits were not found.

TEM showed crystal microspheroids most of which measured 1.3 to 2.2 μm diameter, between which were scattered thick crystals (or crystal agglomerates) (Fig. 5). As shown by examination after decalcification these crystals were not associated with collagen fibrils. Electron diffraction showed that they were apatite.

High resolution TEM showed that – inside or outside the microspheroids – the crystals were wider than normal crystals (between 18 and 24 lattice fringes i.e. about 150 and 200 Å in their smaller dimension versus, between 6 and 8 fringes, that is to say about 50 and 65 Å, for normal controls) as illustrated in Fig. 6. The interplanar distance of 8.28 Å was compatible with apatite. Only the central part showed lattice defects (mineral deficient white zones) which are normally observed in a young apatite crystal of bone origin (Fig. 6).

Discussion

Apatite crystal deposits in the synovial membrane have rarely been reported in joints with no osteocartilaginous lesions (Schumacher et al. 1983). In contrast they have often been reported in joints with osteoarthrosis or erosive arthropathies (Dieppe et al. 1984; Hirsch et al. 1985; Lagier 1989; Resnick et al. 1977; Schumacher et al. 1981; Schumacher et al. 1983); they are thus considered to be a cause of synovial inflammation.

The origin of the associated osteoarthrosis is not clear in the present case and our purpose is not to discuss a possible relationship with repeated juxtaarticular injections of corticoids. However, a causal relationship can be established between the abrasion of the articular surfaces and the synovial apatite deposits. The embedded calcified debris are collagen-rich and thus must be considered to be fragments of calcified cartilage or of bone coming from the abraded articular surfaces. The dusty calcified material associated with superficial necrotic areas do not contain large birefringent crystals which could suggest calcium pyrophosphate deposits; thus it can be considered to be composed of crystals similar to those seen by TEM examination without an underlying collagen frame (apatite). However, these free crystals are wider than normal apatite crystals seen in bone or calcified cartilage plate (Fig. 6) and are partly agglomerated in microspheroids.

The presence of wide apatite crystals has already been reported in a pathological soft tissue calcification (Daculsi et al. 1983). As indicated by in vitro findings such crystals result from a crystal growth (Aoba and Moreno 1984; Eanes and Meyer 1977; Meyer et al. 1972) this can be due to a recrystallisation process (Okazaki et al. 1982) the growth of some crystals acting as seeds at the expense of others. It was also observed in soil bleached archeological material (Susini et al. 1988) and the process can thus explain the presence, in the central part of the wide crystals, of lattice defects due to local calcium deficiency (Featherstone et al. 1979). Such defects are seen in normal young biological apatite crystals (Fig. 6a). Their absence in the periphery (Fig. 6b) is typical of a crystal growth. It must be noted than X-ray diffraction of synovial fluid also demonstrated that apatite in the present case was deficient in calcium.

Any seeded crystal growth needs the presence in situ of small apatite crystals and of Ca and Po^4 ions in supersaturated concentration. In the present case this cannot be explained by the solutions which have been used for the TEM embedding. This implies a recrystallisation process, a condition which could be realized by the degradation of the abraded articular surfaces. This degradation is reflected, for their collagen component, by the increase of hydroxyproline in synovial fluid

(87.4 mg/l versus 3.7–11.2 mg/l for synovial fluid in some cases of osteoarthrotic shoulders (Halverson et al. 1981) and 1.3–1.8 mg/l for normal plasma).

The release of apatite crystals from bone fragments can be considered as a possible event since few of them have been reported in the ruffled border and in the cytoplasmic vacuoles of osteoclasts (Bonucci 1981) and in macrophages and synovial cells (Kahn et al. 1978; Rifkin et al. 1979). The release of Ca ions has also been reported from apatite crystals (Elferink 1986; Evans et al. 1984) or devitalized bone (Kahn et al. 1978; Mundy et al. 1977; Rifkin et al. 1979) in contact with monocytes or synovial cells.

Agglomeration of apatite crystals in globules or microspheroids has already been reported in human extraarticular dystrophic calcifications (Dalcusi et al. 1983), in synovial fluid (Halverson et al. 1981; Schumacher et al. 1981); in human synovial calcifications (Garancis et al. 1981; Schumacher et al. 1981; Schumacher et al. 1983) as well as in experimental intraarticular calciphylaxis (Reginato et al. 1982). However it seems that, in calciphylaxis, the calcium deposits are different from those associated with an arthropathy; the crystals are radially orientated and – being not due to a recristallisation process – remain of small size (Boivin et al. 1987). A possible origin of the crystal masses from matrix vesicles was evoked; however it seems to be discarded if one notices that crystals are small and preferentially orientated radially in the calcifications of this origin reported in conditions such as those of experimental calciphylaxis (Boivin et al. 1987). Microspheroids might also be due to lysis of macrophages having previously phagocytozed apatite crystals (Cheung et al. 1981; Garancis et al. 1981).

The present case thus demonstrates the nature of a kind of detritic synovitis which we have already observed by light microscopy in hip (Lagier 1989) and in spinal facet joints (Reust et al. 1988). They are characterized by dusty apatite deposits in association with calcified debris coming from osteoarthrotic joint surfaces. Similar embedding of calcified debris has been demonstrated in other papers (Garancis et al. 1981; Reginato et al. 1977). Such detritic synovitis can be distinguished from that where there is embedding of larger bone or cartilage shards, as usually seen in some destructive osteoarthrosis. The two conditions can however be associated (Lagier 1989; Lagier et al. 1988). This apatite synovitis thus appears part of a vicious circle in which it is the consequence as well as the cause of bone erosion (via enzymatic release due to crystal phagocytosis; Alwan et al. 1988; Cheung et al. 1981; Halverson et al. 1981).

Since crystal size (Dieppe and Calvert 1983; Elferink 1986) and immunoglobulin-complement coating (Schumacher et al. 1983; Schumacher and Cherian 1984) have been reported to play a role in the inflammatory effects of crystals, it would be interesting to check if such conditions play a role in apatite synovitis. At the diagnostic level it would be interesting to distinguish these crystals, not only from other calcium crystals such as those of calcium pyrophosphate dihydrate, but also from normal apatite crystals. It may provide findings relevant to the origin and pathogenesis of a given intraarticular calcareous deposit. This implies their identification and a study of their crystallinity, i.e. of their size and their perfection. Light microscopy, Ca/P dispersive analysis, non-computerized X-ray diffraction and electron diffraction are inadequate. TEM and scanning EM might only suggest the presence of smooth (not prickly) microspheroids. The most valuable method is high resolution TEM; however, a useful approach can be made (Tochon-Danguy et al. 1983) by X-ray diffractometry (using about 10 mg of material) or with infrared absorption spectroscopy (using about 2 mg of material).

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