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Histological study of a case of recurrent olecranon bursitis with mixed calcium pyrophosphate dihydrate and apatite crystal deposits*

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Summary. This is the report of a light and transmission electron microscopic study of an olecranon bursitis and of the adjacent distal tricipital tendon in an 83 year-old man. The data are compared with those of a similar study in the same patient performed 2 years ago.

Calcium pyrophosphate dihydrate crystals were observed in the bursal fluid, in the inner part of the bursal wall (extracellular localization and intracellular phagocytosis) as well as in the peripheral part of the tendon. In addition, small apatite deposits were observed in the bursa and tendon by electron microscopy. The origin of these bursal deposits is discussed; it is suggested that they may be related to an exchange from the tendon to the remodelled bursal wall.

Key words: Bursitis – Calcium pyrophosphate dihydrate crystals – Apatite – Chondrocalcinosis – Electron microscopy

Juxtaarticular calcium pyrophosphate dihydrate (CPPD) crystal deposits permit the study of an important problem in rheumatology in an unusual situation, i.e., outside the cartilage-synovial membrane couple. The present observation gives the opportunity to compare the histological changes in a case of recurring olecranon bursitis with CPPD crystals with those observed a little more than 2 years previously (Gerster et al. 1982). It also provides data of a new case of mixed CPPD and apatite crystal deposits.

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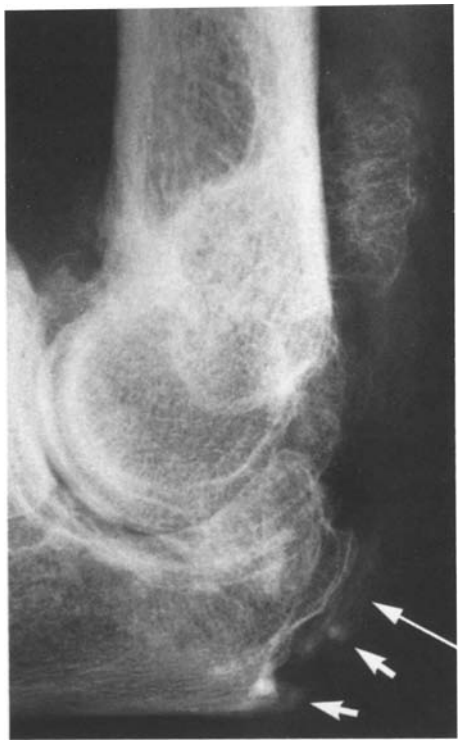


Fig. 1. Right elbow, lateral view (7 June 1983). The long arrow indicates a lamellar structure suggesting CPPD deposits. The 2 short arrows indicate rounded images interpreted as apatite deposits. The upper bone mass was already observed on an X-ray taken before surgery in 1981 and presumably related to the previous trauma at the age of 50

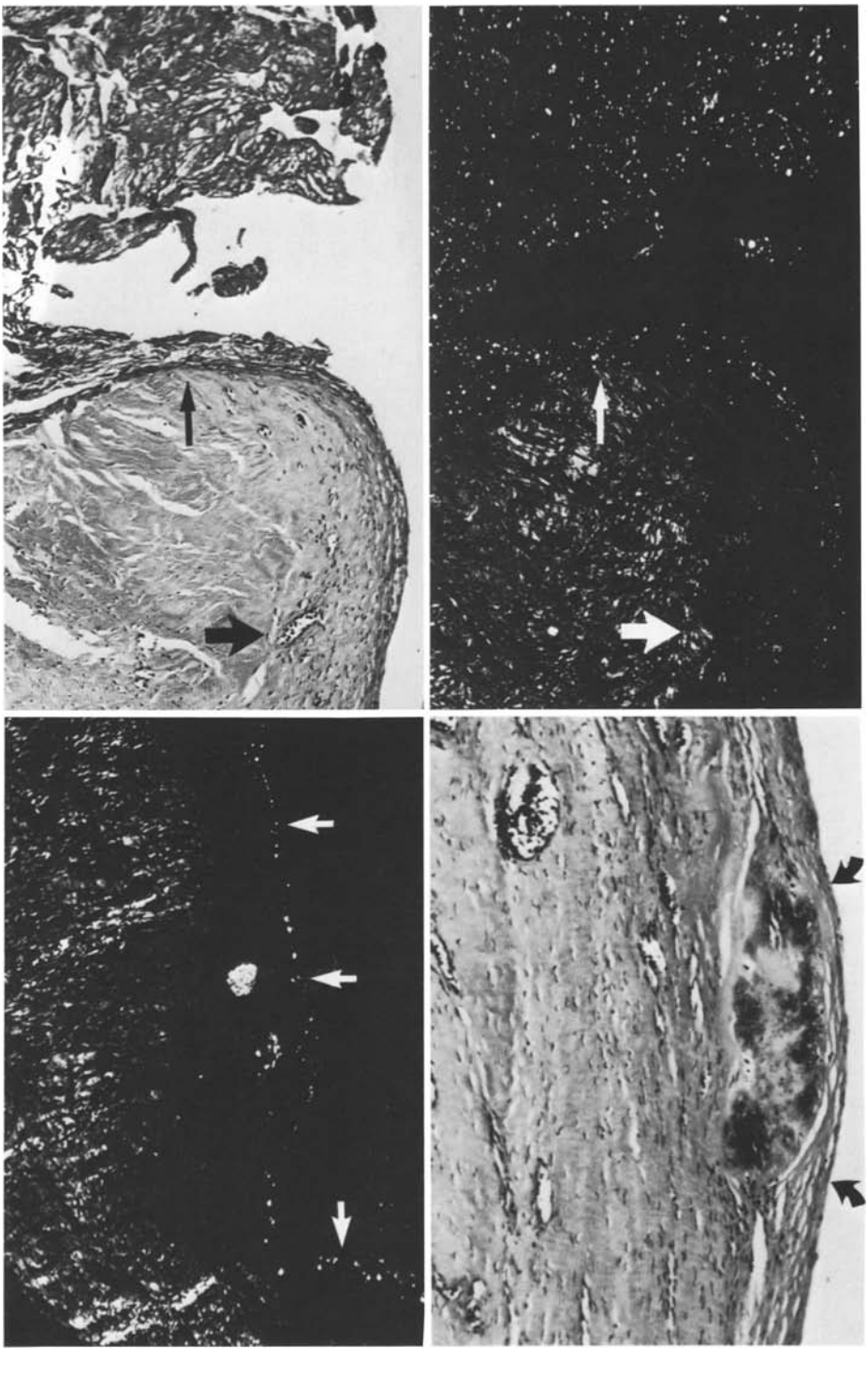
Case Report

Case history

In early 1981, without any causative trauma, an 81 year-old man presented suddenly with right olecranon bursitis containing a 10 cc viscous and sterile effusion, with 100 leucocytes/mm^3 and numerous positive birefringent crystals (both intra- and extracellular) which recurred after each of 3 bursal aspirations.

There was a history of fracture of the same elbow at the age of 50. Erythrocyte sedimentation rate was 12 mm/1st hour (Westergreen); blood glucose and uric acid levels were normal. X-rays showed chondrocalcinosis of both elbows and wrists, the right shoulder and the left hip. At surgery in April 1981 the bursitis ($3 \times 1.5 \times 1.5$ cm) was proved to be non-communicating with the elbow joint cavity and was then excised. The wall was 1 mm thick; its inner surface was smooth and non-pigmented and contained embedded CPPD crystals; its outer surface was flanked by tendon which contained separate areas of both CPPD and apatite crystal deposits.

Fig. 2a–d. Light microscopy of the bursal wall. **a)** *Lower half:* fibrous wall in which *2 arrows* indicate the inner limits of collagen bundles; the latter were in contact with fibrin deposits (*thin arrow*) and with a connective tissue pannus (*thick arrow*) which is itself covered by a thin fibrin layer. *Upper half:* fibrin deposits. HE $\times 70$. **b)** Similar field as "a", observed under polarized light, showing collagen bundles (limits indicated by *arrows*) and CPPD crystals in fibrin deposits. Unstained section $\times 70$. **c)** Another field observed with polarized light. *Left half:* collagen bundles. Three arrows indicate a festoon of CPPD crystals in the intimal layer. In front of the middle arrow, a microtophus of CPPD crystals. Unstained section $\times 90$. **d)** Elsewhere: 2 curved arrows indicate the limits of a necrotic area flanked by scar tissue on its deeper aspect and by a thin intimal fibrous layer on its outer surface (on a corresponding unstained section, CPPD crystals were seen only in the necrotic area). HE $\times 90$


a
b
c
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Three weeks after surgery (3 days after the removal of the plaster), the bursitis recurred and 5 cc of clear, non-viscous fluid were aspirated. The next recurrence was 14 months later and afterwards they were 4 recurrences within 9 months. On each time drainage provided approximately 15 cc of sterile fluid containing 100 leucocytes/mm^3 and positive birefringent CPPD crystals, half of which were intracellular. In the last sample (25 July 1983) scanning electron microscopy showed crystals compatible with CPPD, and microspheroids which were interpreted to be made of apatite crystals; these microspheroids were stained with alizarine. An X-ray did not show any soft tissue swelling but showed calcium deposits in the territory of the distal triceps which mostly were laminated (Fig. 1).

In August 1983 the recurrent bursitis was again excised in toto. No communication with the elbow joint cavity was observed. No recurrence was noted upon examination in July 1984.

Pathological examination

A. Methods. After gross examination a part of the material was fixed in buffered neutral 10% formaldehyde, then embedded in paraffin and cut into 10 μm thick sections which were stained with hematoxylin-eosin, van Gieson-elastin and silver impregnation (Kossa). Unstained sections were carefully deparaffinized in 56° C oven and examined under polarized light both with or without previous immersion of the preparation in a decalcifying fluid.

During surgery samples of the bursa and of the triceps tendon were fixed immediately in glutaraldehyde (5% solution buffered with 0.1 M sodium cacodylate at pH 7.2), then were post-fixed in osmium tetroxyde (1% solution with the same buffer as previously), dehydrated and embedded in Epon B. Ultrathin sections were made with an ultramicrotome equipped with a diamond knife. Both unstained (to preserve crystals) or stained (with uranyl acetate and lead citrate) sections were examined with a JEOL 100 CX II electron microscope. When it was possible the crystal deposits of the bursitis were examined by electron diffraction and diagrams were compared with ASTM standard Card (N° 9–432 for hydroxyapatite). Because of lack of calcified material, X-ray diffraction studies could not be carried out on powder or on unstained sections by Guinier's camera and/or Chesley's camera.

B. Results. The excised bursa had the size of a nut and its wall was 1–2 mm thick. The internal surface was smooth and non-pigmented but showed very rare small white spots. Its external surface was flanked by adipose tissue. The cavity contained a yellowish mucoid fluid with some fibrinous deposits.

Light microscopy showed that the bursal wall contained an outer layer of collagen bundles which were flanked on their inner aspect by a fibrous layer of scar tissue which was rather rich in capillaries in some areas, without any inflammatory cell infiltration or embedded bone, cartilage or tendinous bundles debris (at least on the numerous examined slides) (Fig. 2a–b). Under the surface a very few small areas of necrosis were observed (Fig. 2d). In these areas, as well as in inequally distributed segments of the inner layer (Fig. 2c), polarized light examination of unstained sections showed positive birefringent crystals considered to be CPPD crystals (which disappeared after decalcification). On light microscopy this inner layer, however, did not correspond to the structure of a synovial layer. No other deposits were observed. On the internal surface, i.e., in the bursal cavity, fibrin deposits were observed, associated with crystals similar to CPPD (Fig. 2a–b); a fragment of fibrocartilage with necrotic areas and embedded crystals was also observed in the cavity. Transmission electron microscopy study revealed the presence of 2 types of crystal deposits. Firstly there were electron dense prismatic crystals, rapidly damaged by the electron beam (bubbling), which were interpreted to be CPPD crystals; some of these crystals were observed in intracellular vacuoles (Fig. 4); others, of various sizes and orientation, were shown to be in an intercellular connective matrix containing occasional collagen fibrils (Fig. 5a). Secondly, there were masses of small needle-like crystals which were strictly extracellular (Fig. 4); they showed the typical electron diffraction diagram of apatite and were not associated with a network of collagen fibrils which would have suggested the presence of bone debris.

A segment of tendon (measuring 1 cm × 0.3 cm) was inserted onto a small bone fragment; it was opalescent and non-pigmented but some small, scarce white spots could be seen. By light microscopy its structure appeared normal and there was not any mineral deposit.

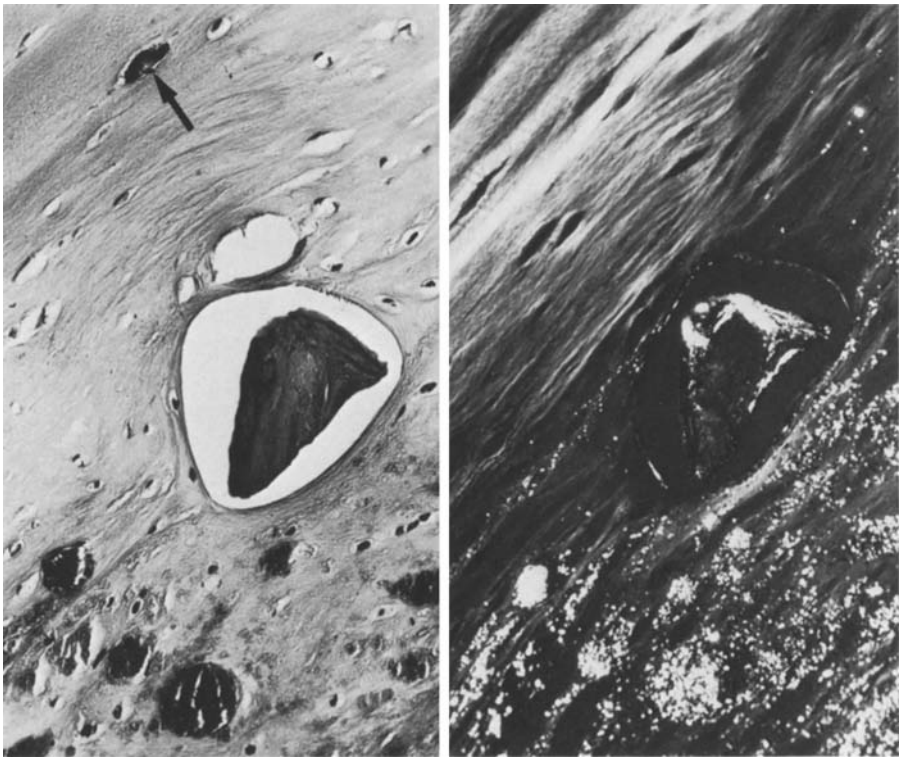


Fig. 3a, b. Light microscopy of the distal triceps tendon and epitendineum (× 60). **a)** Under ordinary light (HE) – **b)** under polarized light (unstained section). *Above and left:* tendinous bundles. *Below and right*: peritendinous scar tissue with CPPD crystal deposits. Isolated bone debris are seen amongst the tendinous bundles (a small debris is indicated by an *arrow*) and between tendon and peritendinous tissue (lamellar bone fragment in a cleft)

The zone of insertion of the tendon onto the bone did not show any histological abnormality. However, it was flanked by scarred connective tissue in which a small islet of necrotic bone was embedded and which was containing necrotic areas with CPPD crystal deposits (Fig. 3); no other mineral deposits were observed.

The study of samples by transmission electron microscopy showed, outside the areas of collagen fibrils, large electron dense CPPD crystals in clefts which were in close proximity with adjacent but structurally separate masses of apatite crystals (Fig. 5b), as proved by electron diffraction studies.

Discussion

The main finding in the present case is the observation of CPPD crystals in the fluid and wall of an inflamed olecranon bursa as well as in the epitendineum of the adjacent triceps tendon. Although diffraction diagrams could not be obtained, the microscopic images can be considered to be characteristic of CPPD crystals. Polarized light reveals positive rhomboid birefringent crystals; transmission electron microscopy shows electron dense

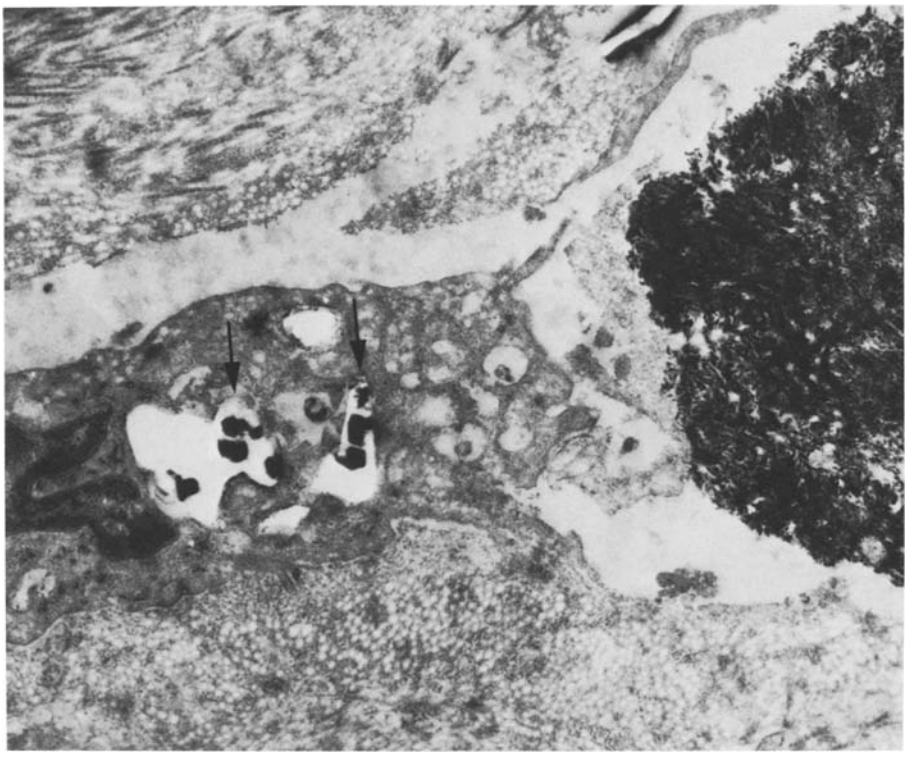
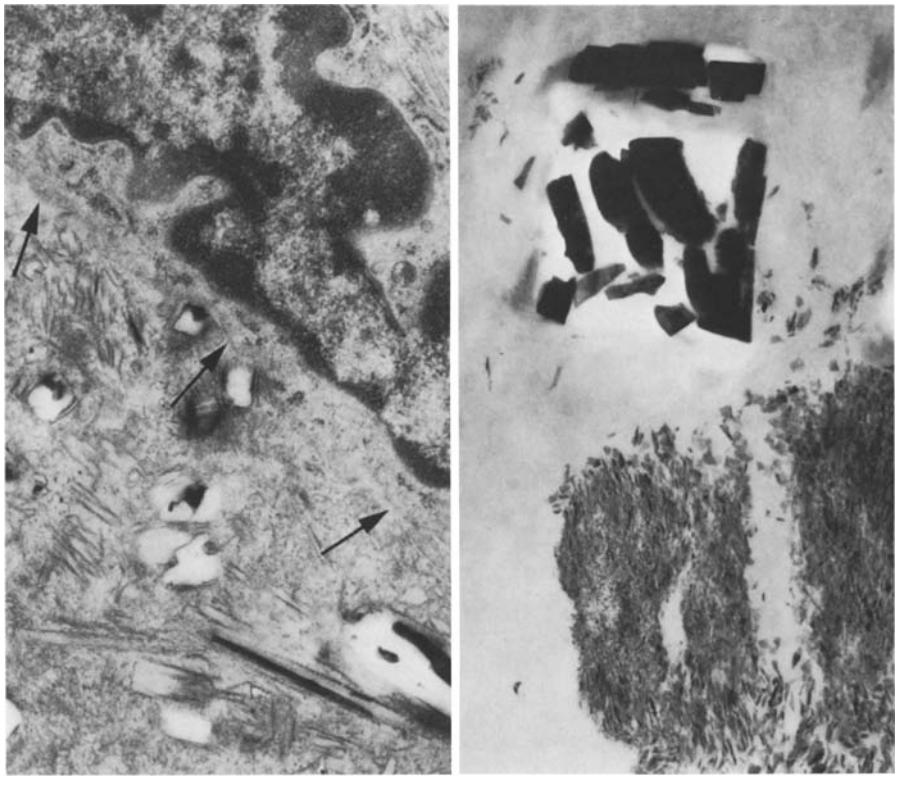


Fig. 4. Electron micrograph of the bursal wall. Electron dense fragments of CPPD crystals are observed in intracytoplasmic vacuoles (*arrows*). On the *right*, extracellular mass of apatite crystals. *Above and below*, collagen fibrils in transverse and longitudinal sections (× 16,000)

particles similar in size and appearance to those observed in CPPD crystal deposits proven by X-ray diffraction studies (Reginato et al. 1974; Bjelle and Sundstrom 1975; Gerster et al. 1982; Boivin and Lagier 1983; Lagier et al. 1984). CPPD deposits in bursitis are exceptional; apart from the previous study of this case (Gerster et al. 1982) and a personal observation in trochanteric bursitis we know of only two reports of CPPD crystal deposits in bursae: in lumbar interspinous location (Bywaters and Evans 1982) and in an infrapatellar location (Dawes et al. 1983).

In the present case, an association with apatite crystal deposits was demonstrated both by transmission electron microscopy and by X-ray diffraction. However, this bursitis cannot be considered as a classical case of "calcareous bursitis" which would have different radiological images (Vizkelety and Aszodi 1968). According to our experience classical cases of calcareous bursitis were distinct on the histological basis (i.e. necrotic material with debris of collagen fibers and dusty calcified material) as well as on the crystallographical basis (i.e. apatite crystal deposits alone, demonstrated by X-ray diffraction).



a b

Fig. 5a, b. Electron micrographs. **a)** Bursal wall. Extracellular electron dense crystals in clefts. *Three arrows* indicate the cellular limits (×19,000). **b)** Triceps tendon. *Above*, fragments of electron dense CPPD crystals in 2 clefts. *Below*, a mass of apatite crystals (×22,000)

The origin of the mineral deposits in the bursitis remains to be debated. The CPPD crystals in the bursal wall being juxtacellular – as was also observed in articular cartilage (Reginato et al. 1974; Bjelle and Sundstrom 1975; Boivin and Lagier 1983) – this suggests a local origin due to the vicinity of a cell. It does not exclude a possible relationship to more general conditions (Pritzker et al. 1978; Lust et al. 1981). Thus, phagocytosis might be secondary to the release of CPPD crystals, either within the bursal wall or the fibrinous exsudate.

However, another origin is strongly suggested, possibly in association with the *in situ* development mentioned above. The possible unequal embedding of balls of twisted preexisting collagen bundles or elastin fibers (Gerster et al. 1982), as well as the unequal distribution of crystals in the bursal wall (Fig. 2), suggest that inequally orientated movements could have occurred not only in the bursal wall but also between it and the adjacent tendon. In fact a possible embedding of CPPD crystals coming from the triceps tendon area is strongly suggested by the presence of a fragment of fibrocartilage with CPPD crystal deposits located within the central mate-

rial removed during surgery; its structure was distinct from that of the bursal wall but reminiscent of that of the triceps epitendineum (Fig. 3) or of that of a fibrocartilaginous fragment observed adjacent to the bursal wall in the previous study of this case (Gerster et al. 1982, Fig. 3). Thus, CPPD olecranon bursitis might be secondary to CPPD deposits in triceps tendon, i.e., to a condition whose lamellated X-ray images have been reported in a few rare cases (Genant 1976; Fallet in press). This "exchange" seems to be favoured by elbow mobility; indeed the first recurrence in the present case appeared after plaster removal and it is known that acute bursitis could regress after immobilization. In this context, it is interesting to note that there is an increase of intrabursal pressure during the flexion of the elbow joint (Canoso 1980).

Scarce apatite crystal deposits were also observed by electron microscopy in the bursal wall as well as in the tendon region, juxtaposed to but not intermingled with CPPD crystals. Their absence in the light microscopy study might be due not only to their rarity but also to the random selection of the surgical specimen. As for CPPD crystals one must debate a local origin and above all the existence of an exchange from the triceps tendon. Apatite deposits are normally observed in histological preparations of a tendon near its point of insertion. Some round structures seem to be apatite-type deposits in the X-rays of supra-olecranial soft tissues in the present case (Fig. 1). The role of bone debris secondarily embedded in the remodelling tissue might also be debated to explain the genesis of juxtatendinous apatite deposits as it has also been discussed for intraarticular apatite crystal deposits associated with erosive osteoarthritis (Gerster and Lagier, in press).

Thus, the study of this case of relapsing bursitis confirms the principal points which were reported after similar surgery performed 2 years ago, i.e., the role of intrabursal movements and phagocytosis of CPPD crystals whose main origin seems to be an exchange from the adjacent triceps tendinous area. Further studies of similar cases are needed to improve light and electron microscopy correlation as well as to define the etiological role of a CPPD crystal exchange between tendon and bursa. Such studies might also be of interest in a broader discussion on a possible mixed CPPD and apatite deposition disease, as well as on the possible involvement of an adjacent tendon in the development of other kinds of bursitis.

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