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PYROPHOSPHATE ARTHRITIS WITH LOCAL AMYLOID DEPOSITION

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Pyrophosphate and capsular chondromatosis were demonstrated histologically in 15 cases, 14 of which also exhibited local deposition of amyloid. A systematic examination of the joint capsule in 57 consecutive hip replacement operations for osteoarthritis revealed these changes in 6 of the cases (10.5 per cent). Microscopic examination which was done if intraarticular calcifications were grossly visible at operation, showed the same changes in 8 knees, 4 with osteoarthritis and 4 with meniscal disease. The changes were also seen in the menisci. Only one patient was suffering from chronic, polyarticular pyrophosphate arthritis. In the other cases neither change had been expected *a priori*, and the patients had no signs of systemic articular disease or amyloidosis. Most of them were elderly, but in good health.

Key words: amyloid deposits; capsular chondromatosis; osteoarthritis; Pyrophosphate

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Pyrophosphate arthritis (PA) occurs especially in elderly persons as a polyarticular affection with acute episodes of effusion, tenderness, increased heat, and severe pain in several joints, the so-called pseudogout syndrome (McCarty et al. 1962). At times the condition is familial (Zitnan & Sitaj 1963: chondrocalcinosis articularis familiaris).

Pyrophosphate deposits in a few joints showing mild or uncharacteristic symptoms, or as incidental findings in histological studies, have been reported by a few authors (McCarty et al. 1966, Bjelle & Sundén 1974).

Local amyloid deposits in the joint capsules of osteoarthritic hips have been described in a previous publication (Sørensen & Christensen 1973). The combination of local pyrophosphate and amyloid deposits in the capsule of the same joint has not been reported before.

MATERIAL AND METHODS

In 1974 we found accidentally, during a meniscectomy, microscopic evidence of pyrophosphate as well as amyloid deposition, and the same deposit was found, also accidentally, in the capsule of a hip joint during a replacement operation in 1975.

By systematic microscopic examination of joint capsules removed in Charnley replacement operations on osteoarthritic hips during the period 11th October 1977 to 21st February 1978 we found 6 cases among 57 (10.5 per cent) in which there were calcium pyrophosphate deposits in the immediate vicinity of amyloid.

Since 1974 the same finding has been made in operations on knee joints for osteoarthritis or meniscal disease in 4 and 4 cases, respectively. In the knees, however, it is not possible to calculate the frequency, as tissue was sent for histological study only when grossly visible calcific deposits were present at operation.

Only one patient had clinically typical PA affecting multiple joints over a period of 7 years with frequent, acute exacerbations (Table 1, Case 1). In this patient radiography showed calcifications in the shoulders, acromio-clavicular joints, elbow joints, wrists, several finger joints, both hips (Figure 1), the symphysis, both knees (Figure 2), and several toe joints. In the lumbar spine there was severe spondylosis, but no calcification of the discs. At operation in 1974 (medial meniscectomy) and in 1976 (medial hemi-replacement) calcific deposits were widespread (Figures 3 and 4). After the replacement operation the patient developed an acute flare-up in several joints.

Among the remaining 14 patients there was no clini-

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Table 1. Details of the patients with intraarticular pyrophosphate and amyloid deposits

Case no.	M: Male F: Female Age, years	Diagnosis K: Knee H: Hip OA: Osteoarthritis		Duration, years	Calcifications visible at operation			Tissue	Histological findings		
					Synovial membrane	Cartilage	Meniscus		Pyrophosphate	Amyloid	Chondromatosis
1	M 63	K	Pyrophosphate arthritis*	7	++	++	+++(med.)	Meniscus Capsule	+++ +	+ +	 ++
2	M 46	K	Old injury medial meniscus	18			++	Meniscus Capsule	+++ +++	+ +	+++ ++
3	F 68	K	OA	10	+++		++(lat.)	Capsule	+++	+	+
4	M 39	K	Injury lateral meniscus	1/26		+	++(lat.)	Meniscus	+++	+	+
5	M 57	K	Ruptured cyst med. meniscus	10			++	Meniscus	+++	+++	++
6	F 61	K	OA	18	++	+(femur)	++(med.)	Meniscus Capsule	++ ++	+++ +++	+++ +++
7	F 57	K	OA	11	++	+(femur)	++(med.)	Meniscus Capsule	++ +++	+ +	+ +
8	M 65	H	OA	15	+			Capsule	++	++	+
9	M 71	H	OA	3				Capsule	++	++	+++
10	F 50	H	OA (congenital dysplasia)	26				Capsule	++	0	++
11	M 72	H	OA	49				Capsule	++	++	++
12	F 46	H	OA (congenital) dysplasia)	46				Capsule	++	+++	++
13	M 60	H	OA	2				Capsule	++	+++	++
14	M 71	H	OA (coxa plana)	57				Capsule	+++	+++	+++
15 –	M 75	H	OA	5				Capsule	+++	+++	+++

*Medial meniscectomy 1974, hemi-alloplasty 1976.

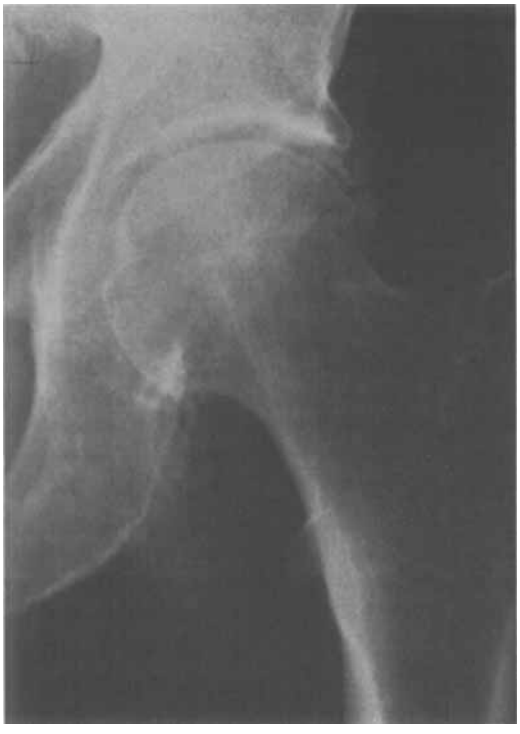

Figure 1. X-ray of the right hip (Case 1). Extensive, cloudy calcifications of the capsule.

cal suspicion of PA, and apart from two, aged 39 and 46, all were elderly, with osteoarthritic changes and a history of long-stending severe symptoms. None of the patients had hyperparathyroidism, gout, haemochromatosis, or diabetes mellitus. Renal function was normal in all cases, as evidenced by a normal serum creatinine. Serum urea was normal in 11 and negligibly elevated in 2.

Figure 3. Removed medial meniscus (Case 1, left knee) with calcifications.

Only one patient had a very brief history (Case 4). The lateral meniscus was degenerated, yellowish with white areas and a fresh injury. At re-operation 3 months later the medial meniscus was yellowish brown with an injury in the middle. However, this meniscus did not contain either pyrophosphate or amyloid. Two years previously radiography of the pelvis, lumbar spine, left knee, left shoulder, and left hand had shown no abnormalities. At the age of 32 the left knee had been opened because of a suspicion of lateral meniscal injury, but the knee proved normal. In a 57-year-old man with a ruptured meniscal cyst large quantities of pyrophosphate and amyloid were found.

Previously subcondylar tibial osteotomy was used for treating osteoarthritis of the knee, not requiring the knee joint to be opened. Since 1976 the increasing use of knee replacement operations has disclosed a number of intraarticular calcifications in the knee, but histological examination has not always been performed.

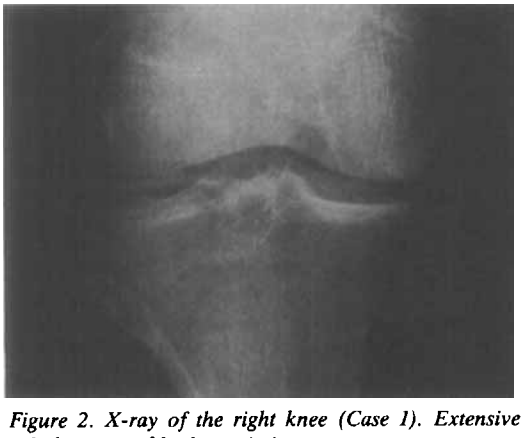

Figure 2. X-ray of the right knee (Case 1). Extensive calcifications of both menisci.

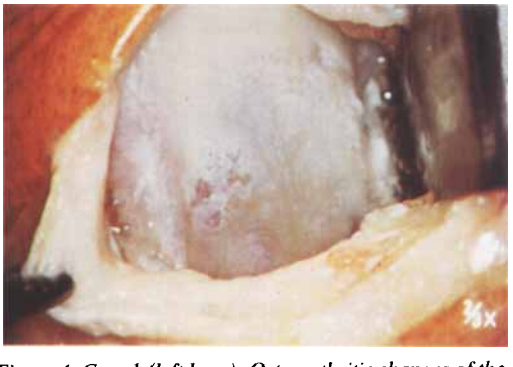

Figure 4. Case 1 (left knee). Osteoarthritic changes of the medial femoral condyle with calcifications of the cartilage.

HISTOLOGICAL FINDINGS

A piece of the removed joint capsule was fixed in 4 per cent neutral buffered formalin for at least 30 hours, dehydrated in ethanol and xylene, and embedded in paraffin. Sections 6 μ thick were stained with haematoxylin-eosin, van Gieson's connective tissue stain, alcian blue 8 GX, and alkaline Congo red by the method of Puchtler et al. (1962). In addition all sections were examined in polarized light.

The occurrence of pyrophosphate crystals, amyloid deposits, and chondromatosis was graded semiquantitatively as follows: None = 0, slight = +, moderate = ++, and pronounced = +++ (Table 1).

In all 15 cases typical calcium pyrophosphate crystals were observed in the subsynovial connective tissue and/or in the meniscus and were identified in polarized light as massive deposits of rhomboid or rod-like, 5–15 μ long, slightly polarizing crystals. In one case a reaction to the crystal deposits was observed in the connective tissue in the form of macrophages and multinuclear foreign body giant cells containing phagocytosed crystals in the cytoplasm. In all other cases the crystals were deposited in an inert, hyalinized collagen connective tissue staining red with van Gieson. This tissue was interspersed with slightly basophilic areas of varying size which stained red with alkaline Congo red and showed in polarized light the green dichroism characteristic of amyloid (Cohen 1975).

The layer of synovial cells superficial to the areas with calcium pyrophosphate deposits exhibited pronounced atrophy, with hyalinization of the underlying connective tissue. In these areas the amyloid deposits were often seen as a distinct ribbon running parallel with the basement membrane and just beneath it.

In all cases the subsynovial tissue exhibited chondromatosis (Table 1), consisting of a slightly basophilic, alcianophilic ground substance interspersed with small, round cells with a pale cytoplasm resembling chondrocytes and appearing in lacunae. Often, deposits of amyloid were seen in their immediate vicinity or in some instances forming a small corona around them (Stubbe Teglbjærg et al. 1979, colour illustrations).

DISCUSSION

In an autopsy material McCarty et al. (1966), investigating calcified menisci, found that in half the cases the deposits consisted of pyrophosphate dihydrate. Bjelle & Sundén (1974), among a material of 300 patients with obscure disorders of the knee collected over a period of 18 months, found 50 to have calcium pyrophosphate dihydrate crystals in the synovium, as evidenced by positive birefringence in compensated polarized light microscopy and typical calcifications on radiography. The sex ratio was equal and the mean age 70 (30–90). The symptoms varied widely.

Silcox & McCarty (1973), in 94 normal persons, found a mean plasma concentration of 1.8 ± 0.06 μM inorganic pyrophosphate. In 30 osteoarthritic patients the plasma concentration was 2.62 ± 0.12 μM, i.e. significantly elevated. In 33 patients with PA the same authors found a serum concentration of 2.34 ± 0.17 μM. In patients with osteoarthritis or gout and in patients with PA, Altman et al. (1972) observed elevated levels in synovial fluid. Among PA patients there seems to be an increased frequency of hyperparathyroidism, diabetes mellitus, hyperuricaemia, azotaemia, and haemochromatosis (cf. Bjelle & Sundén 1974).

Sørensen & Christensen (1973), in a systematic study of 60 hip joint capsules removed in the course of total Charnley replacement operations, found amyloid deposits to be common. Histological study of 51 osteoarthritic cases showed amyloid in 17, i.e. in one-third of the cases. The patients did not have diseases predisposing to generalized amyloidosis, and the amyloid deposition was a purely local phenomenon.

In the present material local deposition of pyrophosphate crystals as well as of amyloid occurred in 14 out of 15 cases, and all 15 exhibited chondromatosis. We have recently demonstrated (Ladefoged & Christensen 1980) that amyloid may be deposited in articular cartilage from the femoral head and that chondrocytes may contain one of the factors that elicit amyloid deposition.

Whether the deposition of pyrophosphate and amyloid is correlated cannot be decided on the

basis of the present findings, but the common coincidence might indicate a relationship. None of the 15 patients of the present series showed any signs of generalized amyloidosis.

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