Calcified tendinitis: a review

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Introduction

Calcified tendinitis is a common disorder. Many names have been used to describe it: some of them, such as 'calcific periarthritis', emphasise the extra-articular site of the deposit; others, such as 'periarticular apatite deposition', mention the nature of the compound found in the calcification; and more recent ones, such as 'calcifying tendinitis',¹⁻³ emphasise the active process that might explain the deposition. Differentiated from arthritis at the end of the nineteenth century, this syndrome has only recently been related to the presence of apatite in tendon sheaths.^{4,5} It can affect almost any tendon at its insertion and is most common around the shoulder joint. Rheumatologists and radiologists have often described this shoulder abnormality, leading to its progressive differentiation from other painful shoulder syndromes.⁶⁻¹²

This review will discuss calcific periarthritis of the shoulder as a model. Clinical features of the syndrome are variable and include pain and inflammation. The key diagnostic feature is the radiograph. Clinical evolution is simple and the condition often resolves spontaneously. Some cases are persistent and may require aggressive treatment, including surgery.

Numerous questions are still unanswered about this disorder, which is rarely associated with metabolic abnormalities of calcium and phosphorus. These include: (a) the nature of the mechanism leading to calcium salt deposition; (b) the frequent asymptomatic tolerance of such calcification, and, conversely, (c) the initiating agent of inflammatory flares; and (d) the way in which the material disperses.

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Calcified tendinitis in clinical practice

CLINICAL FEATURES

According to Welfling calcific periarthritis is responsible for 7% of painful shoulder syndromes,⁹ which have various presentations.

(1) Chronic symptoms—more or less severe pain; tenderness leading to various degrees of incapacitation. These symptoms induce the demand for radiographs, which reveal the presence of deposits.

(2) Acute inflammatory crisis with severe pain, tenderness, and local oedematous inflammation sometimes leading to restricted active and passive motion. Fever and malaise may be observed.

(3) Totally asymptomatic deposits.

According to Bosworth *et al.*, clinical symptoms occur in from 34% to 45% of patients in whom calcifications are found.⁸ Biochemical and haematological tests are not useful, and will only show non-specific evidence of inflammation.

RADIOLOGICAL FEATURES

Simple anteroposterior and lateral x-ray films are usually sufficient to see shoulder calcification, though special views in internal or external rotation may be necessary.¹² Other techniques have been described to obtain better pick up, including xerography and scanning, but many small deposits are probably missed.

The calcification is usually in the supraspinatus tendon, and various appearances have been described. The deposits may be very thin, outlining the tendon sheath, or hazy, and they vary in density and definition (Fig. 1). Only in cases of disturbance of the calcium to phosphorus ratio—for example hyperparathyroidism secondary to renal failure—is there massive calcification.¹³ The size

Fig. 1 Calcific periarthritis of the shoulder. Calcification is obvious; it has already migrated from supraspinatus region to bursa area.

usually varies between a few millimetres and about 1.5 cm.

Calcification has been described near almost every joint¹² although the precise intratendinous or paratendinous location of the stone is not always seen. The deposits may be multiple,¹⁴ which French authors identify as 'maladie des calcifications tendineuses multiples'.^{15,16} Bilateral calcification is seen in about half of shoulder cases and deposits are often seen in other locations—for example, near the hip joint—if other radiographs are taken.

Fig. 2 Acute bursitis of the shoulder (same patient). Morphological aspects of previous calcification is modified; it is less dense and probably located inside bursa.

Sequential x-ray films may show static calcification, a growing deposit, change in the location, and even spontaneous disappearance without any acute clinical flare. During the inflammatory crisis, the calcifications usually follow a very well described course. They become less defined, more cloudy, and migrate into the bursa (Figs. 2 and 3); they may or may not disappear completely within a few days or weeks. The reappearance of calcification is not well substantiated (Fig. 4). Some authors emphasise the relation of the deposit to the bone surrounding the tendon insertion point.¹⁷ Destructive changes have been reported in advanced cases, and McCarty *et al.* have described a special syndrome associating a destructive arthropathy of the shoulder, apatite deposits, and high collagenase activities in the synovial fluid. They call it the 'Milwaukee shoulder syndrome'.^{18, 19}

DIFFERENTIAL DIAGNOSIS

The diagnosis is usually easy. Other painful shoulder syndromes of osseous

or articular origin present with different symptoms. Analysis of fluid and radiological investigations are also discriminative. Extra-articular ossification is radiologically different, the deposits being trabeculated, and articular chondrocalcinosis also appears quite different on a radiograph. Tendinous calcification containing calcium pyrophosphate dihydrate may be misleading²⁰ but is usually associated with chondrocalcinosis.

TREATMENT

As both symptoms and deposits often disappear spontaneously, both clinician and patient should generally abstain from interfering. Analgesics and non-steroidal anti-inflammatory drugs (NSAID) are useful, as well as patience.

During an acute inflammatory crisis more powerful NSAID drugs such as indomethacin or phenylbutazone may

prove necessary, and some authors recommend adding colchicine as in gout and pseudogout. Aspiration of fluid may also reduce symptoms. Local injections of corticosteroids are used by some clinicians, but may themselves cause microcrystal-induced inflammation, and the risk of infection must be taken into account. Lavage between attacks has been advocated, but does not always seem rewarding. Very painful resistant cases have received x-ray treatment. Calcium inhibitors have also been tried but the results are not convincing.

Surgery may prove successful, and a few well documented cases treated by surgical removal of the deposit have been described.³

LABORATORY INVESTIGATIONS

The material aspirated from acutely painful shoulders has been studied thoroughly in a few cases, with interesting results. Firstly, they

Fig. 3 Same patient one month later. Calcification has completely disappeared, though vestigial one remains in the supraspinatus region.

Fig. 4 Same patient one year later. Calcification has reappeared, patient presents with a moderately painful shoulder.

Fig. 5 Scanning electron microscopy. Bar = 5 μ m. One globule-like structure is seen here in situ in section of a tendon sheath calcification, appearing like a stone engulfed in mortar.

allowed the identification of the material.⁴ Recent studies by our group have also isolated another compound, unidentified so far, which is different from stoichiometric apatite, and could be the result rather than the cause of the inflammation.²¹

The usual specimens obtained at operation consist of a gritty mass of sandy material or a toothpaste-like fluid. These have been recognised since Codman first described the calcifications, and in 1934 the deposits were described as 'a white amorphous mass composed of many small round or ovoid bodies'.⁶ Microscopically, at low magnification, calcifications appear as shiny amorphous coins (in a liquid phase).⁴

Physical studies first used x-ray diffraction then infrared spectrometry. McCarty *et al.*⁴ and Thompson *et al.*⁵ identified an apatite compound by x-ray diffraction, and infrared spectrometry showed that it was a carbonated apatite.²² This has been confirmed by other physical means such as thermogravimetry.²³ Our results are similar but it should be noted that all these methods consider the material as a whole and do not allow definition of individual particles.

Scanning electron microscopy allowed us to have a closer look at the external aspect of deposits²⁴⁻²⁵; we observed an extremely heterogeneous material, composed of globular bodies looking like large rocky bulks engulfed

in mortar (Fig. 5). Study of individual crystals needed even more sophisticated means. Transmission electron microscopy (TEM) allows the visualisation, on ultrathin sections, of dense globular structures among numerous isolated or clumped crystals (Fig. 6). Individual crystals may be seen in high resolution transmission electron microscopy. The crystals are much larger than classic apatite crystals, such as those observed in bone or dental enamel; some of them appear as homogeneous hexagons, the width and thickness of which can be measured. The parameters differ from one patient to another. Some of them have clear cut edges, while others seem to possess some sort of coating; defects can also be seen in several crystals (Fig. 7).

Interplanar spacings may sometimes be measured, and are consistent with these parameters in stoichiometric hydroxyapatite. These isolated crystals are, however, different from the globular material. Wavelength dispersive spectrometry in a scanning mode gave calcium to phosphorus molar ratios in both globules and isolated crystals not statistically different from control geological apatites, but similar microanalysis in a transmission mode provided lower ratios, with differences between the inside and outside of globular bodies.

All these techniques identified the material of calcific deposits as calcium

carbonate apatite,²⁶⁻²⁷ but the great heterogeneity of the material is a new feature that may open new fields of research. The differences observed between patients also deserves study.

The exact location of deposits is not well elucidated, but Welfling describes some as intratendinous and some superficial.⁹

Sandström described necrosis interpreted as being secondary to 'local anaemia and vascular changes', which favoured deposition of calcifying material.⁷ Uthoff's group favour an active mechanism of calcification, with an initial cartilage degeneration of the tendon followed by calcification of the transformed tissue.¹⁻³ They describe four stages in the calcifying process: precalcific phase; calcific phase; resorptive phase; and repair phase. These four patterns may occur concomitantly in an individual patient. This hypothesis would explain the heterogeneity and pleomorphic nature of the lesions, but the so-called 'resorptive phase' seems arguable, particularly because of the very small number of cells observed.

Using TEM, the same group studied the ultrastructural localisation of calcium in tendinitis. They found it in matrix vesicle-like structures seen either singly among collagen or in aggregates.²⁸⁻²⁹

Discussion

New light should soon be shed on calcification in several aspects: (a) better identification of the calcifying processes; (b) more knowledge on epidemiology; (c) better definition of the nature of the compounds, hopefully leading to understanding of the aetiopathological mechanisms of the disease.

The identification of deposits has improved since the features of the condition have become recognised, and should be made even easier by further technical improvements allowing visualisation of tiny calcifications. This should help define the epidemiology and explain apparent differences in the incidence and age of onset between France and Britain. So far, only one epidemiological study has been performed in the United States.⁸ The existence of a possible genetic link should also be re-evaluated,³⁰ in spite

Fig. 6 Transmission electron microscopy. Bar = 5 μ m. Dense globular structures of various size among scattered isolated crystals.

Fig. 7 High resolution transmission electron microscopy. Bar = 0.01 μ m. Single hexagonal crystal of apatite presenting a coat on its surface.

of the negative results of the HLA studies already published.¹⁶

Associations have been reported between calcifications and several diseases: diabetes, thyroid disorders, and others.³¹ A metabolic link was also noted between calcifications, uraemia, and haemodialysis.³²⁻³³ Finally, Bosworth suspected the influence of repetitive motion performed in a professional context.³⁴ The relationship between shoulder use and the appearance of calcification is not well documented and should be re-examined.

The physicochemical findings in the past few years have been rewarding. In a recent review, Legeros brings many data favouring a calcium carbonate/apatite composition for heterotopic calcifications in man.³⁴ Our results, however, made it obvious that there is a high degree of heterogeneity in these compounds and that the answer is probably not that simple. Every possible analytical and microscopical means should be used to study all types of calcification. It might be rewarding to compare idiopathic deposits with those found in other

diseases such as hyperparathyroidism, hypervitaminosis D, collagen vascular disease, and the milk alkali syndrome. The exact incidence of other types of deposits such as pyrophosphate, reported in tendons by Gerster,²⁰ should also be examined.

Several aetiopathological schemes have already been proposed.^{1 2 7 15 16 35} The classic hypothesis favours a local and initial necrosis of the tendon, leading to the deposition of calcified material. However, some calcifications obviously occur in the absence of any necrotic phenomenon. A more recent idea, based on histological and ultrastructural observations, suggests the occurrence of an initial cartilage metaplasia of the tendon, followed by an active multifocal and cell-mediated calcifying process. The intracellular or extracellular site of the first deposit is not completely clear and requires an ultrastructural or physical study of collagen fibres.

Some other mysterious features remain—for example, why should calcifications be most common around the supraspinatus tendon? How can the long-lasting tolerance of some deposits be explained, while others lead to acute crisis? What is the initiating mechanism in these acute episodes? Does it involve a modification of the physicochemical structure of the material or a change in its microenvironment? How is it that some pathological, and eventually painful, deposits disappear spontaneously?

Experimental models aid understanding of some of these problems. For instance, synthetic apatite crystals and/or natural apatites have phlogistic properties in inflammation models.³⁶⁻³⁸ A thorough study of the macrophage in such models might help us to understand how calcified material can disappear. This could also be elucidated by metabolic studies if a dissolution process takes place in these phenomena.

More sophisticated models are obviously necessary, if not to explain all the mysterious events of this syndrome, at least to define new preventive or curative treatments, or both. Special care should, however, be taken in extrapolating such results to human disease.³⁹⁻⁴² mainly because, to

our knowledge, no similar disease is described in veterinary publications, implying that metabolic pathways may be very different in man and in animals.

References

- Uthoff H K. Calcifying tendinitis an active cell mediated calcification. *Virchows Arch [Pathol Anat]* 1975; **366**: 51-8.
- Uthoff H K, Sarkar K, Maynard J A. Calcifying tendinitis. A new concept of its pathogenesis. *Clin Orthop* 1976; **118**: 164-8.
- McKendry R J R, Uthoff H K, Sarkar K, Hyslop P S G. Calcifying tendinitis of the shoulder: prognostic value of clinical histologic and radiologic features in 57 surgically treated cases. *J Rheumatol* 1982; **9**: 75-80.
- McCarty D J, Gatter R A. Recurrent acute inflammation associated with focal apatite crystal deposition. *Arthritis Rheum* 1966; **9**: 804-19.
- Thompson G R, Ming Ting Y, Riggs G A, Fenn M E, Denning R M. Calcific tendinitis and soft tissue calcification resembling gout. *JAMA* 1968; **203**: 464-72.
- Codman E A. *The shoulder*. Boston: Thomas Todd, 1934.
- Sandstrom C. Peridentitis calcarea. A common disease of middle life. Its diagnosis pathology and treatment. *AJR* 1938; **40**: 1-21.
- Bosworth B M. Calcium deposits in the shoulder and subacromial bursitis. A survey of 12,222 shoulders. *JAMA* 1941; **116**: 2477-82.
- Welfling J. Les calcifications de l'épaule. I Diagnostic clinique. *Rev Rhum Mal Osteoartic* 1964; **31**: 265-71.
- Swannell A J, Underwood F A, Dixon A S J. Periarticular calcific deposits mimicking acute arthritis. *Ann Rheum Dis* 1970; **29**: 380-5.
- Fam A G, Pritzker K P H, Stein J L, Hout J B, Little B J R. Apatite associated arthropathy: a clinical study of 14 cases and of 2 patients with calcific bursitis. *J Rheumatol* 1979; **6**: 461-71.
- Resnick D. Calcium hydroxyapatite crystal deposition disease. In: Resnick D, Niwayama G, eds. *Diagnosis of bone and joint disorders*. Philadelphia: W B Saunders, 1981: 1575-97.
- Smith F W, Junor B J R. Peri-articular calcification with fluid levels in secondary hyperparathyroidism. *Br J Radiol* 1978; **51**: 741-2.
- Pinals R S, Short C L. Calcific periarthritis involving multiple sites. *Arthritis Rheum* 1966; **9**: 566-74.
- Welfling J, Kahn M F, Desroy M, Paolaggi J B, de Seze S. Les calcifications de l'épaule. II. La maladie des calcifications tendineuses multiples. *Rev Rhum Mal Osteoartic* 1965; **32**: 325-34.
- Amor B, Kahan A, Cherot A, Delbarre F, Rabaud M, Aubouy G. Le rhumatisme a hydroxyapatite (la maladie des calcifications tendineuses multiples). II. Etude microscopique. Antigène HLA arthrite expérimentale. Pathogénie. *Rev Rhum Mal Osteoartic* 1977; **44**: 309-16.
- Meneghello A, Bertoli M, Romagnoli G F. Unusual complication of soft tissue calcifications in chronic renal disease the articular erosions. *Skeletal Radiology* 1980; **5**: 251-2.
- McCarty D J, Halverson P B, Carrera G F, Brewer B J, Kozin F. 'Milwaukee shoulder': association of microspheroids containing hydroxy apatite crystals, active collagenase and neutral protease with rotator cuff defects. I Clinical aspects. *Arthritis Rheum* 1981; **24**: 464.
- Halverson P B, Cheung H S, McCarty D J, Garancis J C, Mandel N. 'Milwaukee shoulder': association of microspheroids containing hydroxy apatite crystals, active collagenase and neutral protease with rotator cuff defects. II. Synovial fluid studies. *Arthritis Rheum* 1981; **24**: 474-83.
- Gerster J C, Baud C A, Lagier R, Boussina I, Fallet G H. Tendon calcifications in chondrocalcinosis. A clinical, radiologic, histologic and crystallographic study. *Arthritis Rheum* 1977; **20**: 717-22.
- Faure G, Daculsi G, Netter P, Gaucher A, Kerebel B. Apatites in heterotopic calcifications. *Scanning Electron Microscopy* (in press).
- Legeros R Z, Contiguglia S R, Alfrey A C. Pathological calcifications associated with uremia: 2 types of calcium phosphate deposits. *Calcif Tissue Res* 1973; **13**: 173-7.
- Saez-Clavere L, Legros R, Arlet J, Bonel G. Etude cristallographique de deux calcifications sous deltoïdiennes. *Rev Rhum Mal Osteoartic* 1980; **47**: 383-92.
- Faure G, Netter P, Coxam B, Raul P, Pourel J, Gaucher A. Place de l'apatite en pathologie microcristalline. *Annales Médicales de Nancy* 1979; **18**: 1281-4.
- Faure G, Netter P, Malaman B, Steinmetz J, Duheille J, Gaucher A. Scanning electron microscopic study of microcrystals implicated in human rheumatic diseases. *Scanning Electron Microscopy* 1980; **III**: 163-76.
- Montel G, Bonel G, Trombe J C, Heughebaert J C, Rey C. Progrès dans le domaine de la chimie des composés phosphores solides à structure d'apatite. Application à la biologie et au traitement des minéraux. *Pure and Applied Chemistry* 1980; **52**: 973-87.
- Legeros R Z. Apatites in biological systems. *Progress in Crystal Growth and Characterization* 1981; **4**: 1-45.
- Sarkar K, Uthoff H K. Ultrastructural localization of calcium in calcifying tendinitis. *Arch Pathol Lab Med* 1978; **102**: 266-9.
- Dereszewski G, Howell D S. The role of matrix vesicles in calcification. *Trends in Biochemical Sciences* 1978; **3**: 151-2.
- Cannon R B, Schmid F R. Calcific periarthritis involving multiple sites in identical twins. *Arthritis Rheum* 1973; **16**: 393-6.
- Wright V, Haq A M. Periarthritis of the shoulder. I. Aetiological considerations with particular reference to personality factors. *Ann Rheum Dis* 1976; **35**: 213-9.
- Caner J E Z, Decker J L. Recurrent acute (gouty) arthritis in patients with chronic renal failure treated with periodic hemodialysis. *Am J Med* 1964; **36**: 571-82.
- Moskowitz R W, Vertes V, Schwartz A, Marshall G, Friedman B. Crystal-induced inflammation associated with chronic renal failure treated with periodic hemodialysis. *Am J Med* 1969; **47**: 450-60.
- Legeros R Z, Legeros J P. Phosphate minerals in human tissues. In: Nriago J, Moore P, eds. *Phosphate mineral*. (in press).
- Urist R, Moss M J, Adam J M. Calcification of tendon. A triphasic local mechanism. *Archives of Pathology* 1964; **77**: 594-608.
- Denko C W, Petricevic M. Hydroxyapatite crystals-induced inflammation and prostaglandin E1. *J Rheumatol* 1979; **6**: 117-23.
- Glatt M, Dieppe P, Willoughby D. Crystals-induced inflammation, enzyme release and the effects of drugs in the rat pleural space. *J Rheumatol* 1979; **6**: 251-8.
- Cheung H S, Halverson P B, McCarty D J. Release of collagenase neutral protease, and prostaglandins from cultured mammalian synovial cells by hydroxyapatite and calcium pyrophosphate dihydrate crystals. *Arthritis Rheum* 1981; **24**: 1338-44.
- Luben R A, Sherman J K, Wadkins C L. Studies of the mechanism of biological calcifications. IV. Ultrastructural analysis of calcifying tendon matrix. *Calcif Tissue Res* 1973; **11**: 39-55.
- Bridges J B, McClure J. Experimental calcifications in a number of species. *Calcif Tissue Res* 1972; **10**: 136-49.
- McClure J, Gardner D L. The production of calcification in connective tissue skeletal muscle using various chemical compounds. *Calcif Tissue Res* 1976; **22**: 129-35.
- Doyle D V, Dunn C J, Willoughby D A. Potassium permanganate induced calcergy. A model to study the effects of drugs on hydroxyapatite crystal deposition. *J Pathol* 1979; **128**: 63-70.