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Calcifying Tendinitis, an Active Cell-Mediated Calcification

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Summary. Biopsy specimen from 18 patients suffering from calcifying tendinitis were stained with different histologic and histochemical techniques. The results of these examinations seem to indicate that we are not dealing with a dystrophic calcification, but with a cell-mediated calcification of a living tissue. The process resembles an incomplete endochondral ossification.

Key words: Calcinosis — Para-Articular Tendons — Peri-Arthritis — Tendinitis — Shoulder.

Zusammenfassung. Histologische und histochemische Untersuchungen der Supraspinatussehne von 18 Patienten mit calcifizierender Tendinitis. Der Verkalkungsprozeß wird eingeleitet durch eine Transformation der Tendinocyten in Chondrocyten begleitet von einer Anreicherung alkalischer Phosphatase. In einer zweiten Phase kommt es, unter Mitwirkung der Chondrocyten, zur granulären Verkalkung und gelegentlich auch zur Ossifikation vergleichbar der enchondralen Ossifikation. Für die Annahme einer dystrophischen Sehnenverkalkung ergeben sich keine Hinweise.

Since Codman's classic studies on the shoulder published in 1934 and 1938, it seems generally accepted that, in calcifying tendinitis, degeneration of tendon fibers precedes calcification, a process also called dystrophic calcification.

Codman believed the lesion to be traumatic in origin with degeneration occuring secondarily. Meyer on the other hand, stated that degeneration is a primary and spontaneous change. Steinbrocker, in the most recent edition of Hollander's textbook of arthritis, still adheres to these classic views. He describes the different states of calcifying tendinitis as follows: wear and tear or injury results in degeneration of tendon fibers; continuing wear leads to loss of vascularity and subsequently to tissue necrosis; this necrotic tissue, in turn is replaced by a fibrinoid mass which is surrounded by leukocytes and histiocytes; finally, this mass calcifies. McLaughlin described the necrotic tissue as resembling rice—like bodies. He thought that motion would grind them into finely pulverized material which could remain as such or calcify.

All aforementioned authors believed that the initial steps of calcifying tendinitis and of ruptures of the rotator cuff were identical. Only the last stage was thought to be different: in one case the necrotic tissue calcifies and in the other rupture occurs through the degenerated tendon. Given this apparent similarity in pathogenesis it is not surprising to find that calcifying tendinitis and ruptures of the rotator cuff are grouped together under the heading of periarthritis humeroscapularis (Schaer, Glatthaar) or of degenerative diseases of periarticular

tissues (Salter). Why in one case calcification takes place contrary to rupture in another is not explained in the pertinent literature. Indeed Steinbrocker states that "the exact method by which calcium is deposited remains obscure".

Both entities, calcifying tendinitis and rupture of the rotator cuff, also differ clinically. Patients with calcifying tendinitis are in a younger age group (30 to 45 years) and are engaged in a more sedentary work (Steinbrocker). Calcification starts 1 to 1.5 cm medial to the tendon insertion into bone ("Umbiegungsstelle" of Schaer). Radiographs do not show signs of osteoarthritis of the shoulder joint. The beginning of symptoms is acute without any known injury. The excruciating pain is responsible for the marked limitation of movements. Following disappearance or removal of the calcific deposit the patients usually remain free of symptoms.

On the other hand, patients suffering from ruptures of the rotator cuff belong to an older age group (50 to 60 years) and are laborers or factory workers (Steinbrocker). Rupture occurs at the tendon insertion into bone. Calcifications and ossifications seen at this level histologically should not be confused with calcifying tendinitis. Radiographs show signs of osteoarthritis, such as cysts, irregularities of the cortex, bony sclerosis, and/or narrowing of the acromio-humeral interval (Cotton and Rideout). A period of chronic pain precedes the rupture which occurs during an effort. Conservative or operative treatment never result in a restitutio ad integrum.

It is generally agreed that radiologically visible calcium deposits and ruptures of the rotator cuff do not appear together (DeSèze and Welfling, Friedman, McLaughlin, 1963; Neer, Ollson, Pedersen and Key). The observation of Wolfgang of eleven instances of calcification among 74 cases with tears should be carefully evaluated since this author did not differentiate between complete and incomplete tears. Firstly, tears can be incomplete, secondly, rupture of the calcium deposit into the bursa is necessarily accompanied by an incomplete tear and thirdly, no proof exists that incomplete tears will always become complete. Moreover, Wolfgang did not prove that patients showing calcification had a complete tear, which in our study is called "rupture". Respecting this distinction between incomplete and complete tears, Ollson proved through a statistic analysis that no association exists between calcifying tendinitis and cuff ruptures. McLaughlin and Asherman are of the same opinion. They state that the presence of calcification constitutes a strong evidence against a rupture.

In view of so many differences between calcifying tendinitis and cuff ruptures, a study was undertaken to determine whether the pathogenesis of both entities is indeed identical.

Material and Method

Biopsy material from the supraspinatus tendon was obtained from eighteen patients during removal of their calcium deposit and from four patients during repair of the tendinous cuff. Care was taken to remove a portion of the normal tendon adjacent to the lesion. Two patients with calcifying tendinitis received tetracycline pre-operatively permitting fluorescence studies. In additional four cases the supraspinatus tendon was removed in toto during autopsy. In these cases, varying from 64 to 79 years of age, no history of shoulder pain was recorded.

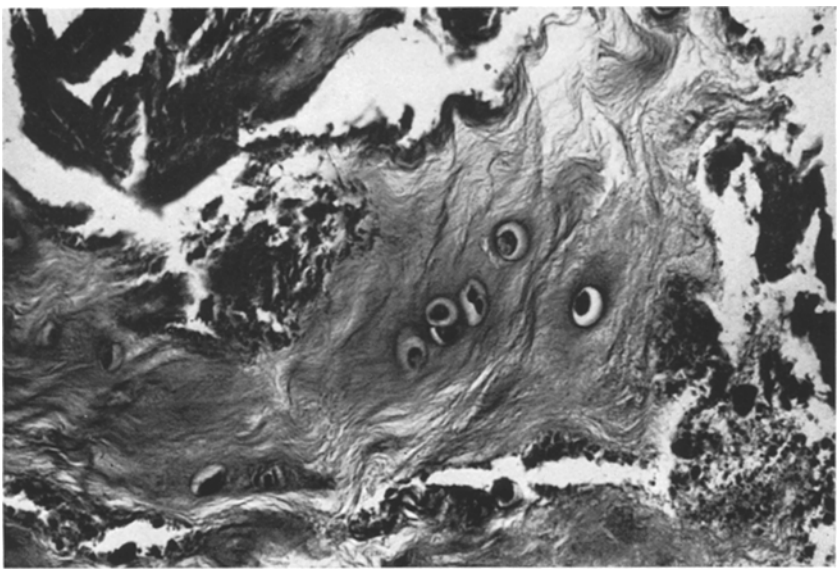

Fig. 1. Chondrocyte-like cells surrounded by a metachromatic matrix in proximity to amorphous calcified masses. Note the conservation of the fibrillar aspect of the matrix. Toluidine Blue ×500

All specimens were fixed in 70% alcohol. Decalcification with EDTA was used when the biopsy specimen included bone. In these cases half of the specimen was retained for techniques requiring undecalcified bone. The specimens were then stained with: hematoxylin-eosin, hematoxylin-phloxine-safranine, von Kossa silver stain, Toluidine Blue, Safranine O and Gomori for alkaline phosphatase.

Results

Calcifying Tendinitis

Serial sections stained with different techniques permitted the following observations: away from the site of amorphous calcium deposits, chondrocyte-like cells appeared focally instead of tenocytes. At the same time the matrix surrounding these cells became metachromatic without loosing its fibrillar aspect (Fig. 1). No calcium was present. In proximity to the site of calcium deposition, the chondrocyte-like cells hypertrophied and elaborated alkaline phosphatase. Around other hypertrophic chondrocyte-like cells pericellular granules of calcium salts appeared (Fig. 2). With increasing calcification the cells died. Calcification was always seen at multiple sites. Living tissue separated these foci. No cellular infiltration and no blood vessels were seen in the areas of ongoing calcification whereas around some sites of established calcium deposits an increased cellularity and blood vessels were noted. These cells, inside the tendon, looked like histiocytes and macrophages. Multinucleated cells were regularly present (Fig. 3). In no instance did we observe any type of leukocytes. It should be added that bursal walls were not examined. Uptake of tetracycline occured at the periphery of some calcium deposits. In two cases normal bone was present inside the tendinous

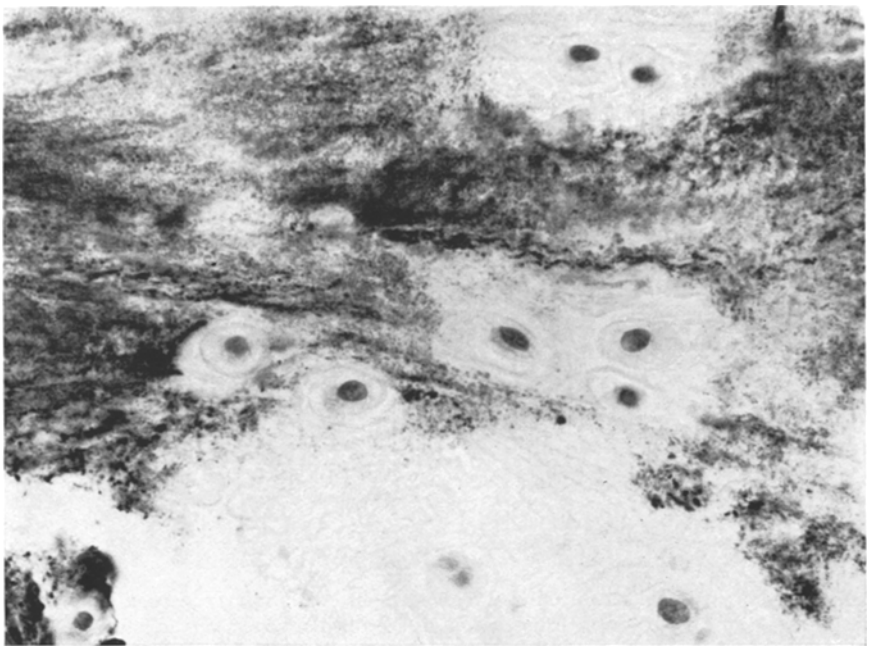

Fig. 2. Beginning of calcification around hypertrophic chondrocyte-like cells. Von Kossa ×635

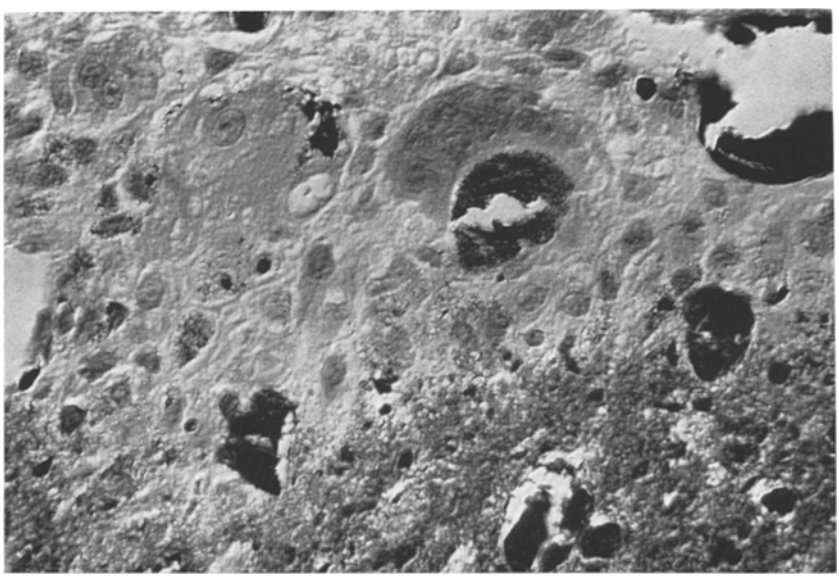

Fig. 3. Cellular infiltration bordering calcified focus. Note giant-cells surrounding broken-up calcium deposits. Von Kossa. Interference Contrast ×1350

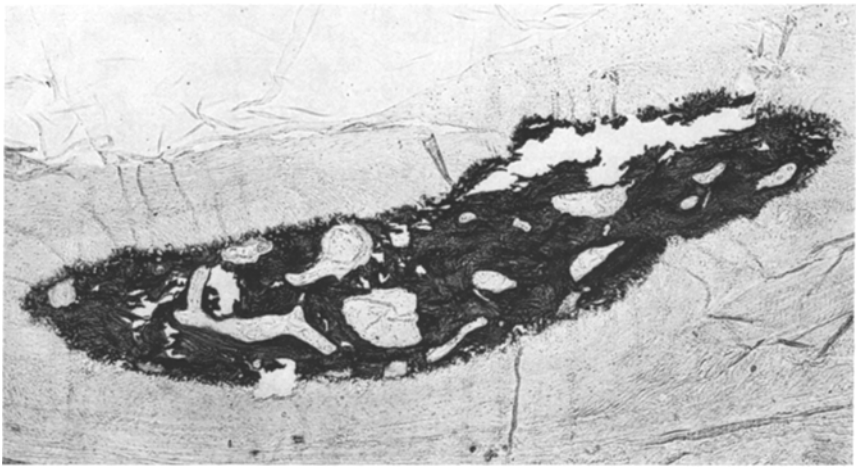

Fig. 4. Ossicle containing hemopoietic marrow inside supraspinatus tendon. Von Kossa ×40

tissue. In the first case an ossicle containing hemopoietic marrow was seen (Fig. 4). Here the uptake of tetracycline occured at two distinct sites. Firstly, in a more diffuse fashion, at the site of calcification of tendon fibers and secondly in a linear appearance, at the inner wall of the ossicle. The second case showed necrotic lamellar bone inside the tendon close to a site of amorphous calcification. Results obtained with techniques not previously used in the study of this disease seem to indicate the following sequence of events: focal transformation of tendinous tissue into cartilage with concomitant elaboration of acid mucopolysaccharides. With increasing hypertrophy of the chondrocytes an intracellular elaboration of alkaline phosphatase is seen. Later this enzyme is also seen in the matrix. Subsequently a pericellular deposition of calcium takes place. Following complete calcification degeneration into an amorphous mass occurs. At a later stage blood vessels can invade this area and phagocytosis becomes obvious. At no time did we observe leukocytes around these intratendinous calcium deposits.

Rupture of the Rotator Cuff

These specimens always included part of the bony insertion. Whereas the bone and the Sharpey's fibers looked normal, cloning of chondrocytes close to the rupture was apparent. Metachromasia was consistently absent around the clones (Fig. 5). The frayed ends of the tendon did not contain living cells.

Autopsy Specimens

Strands of poorly staining tendon were seen in which tenocytes were sparse or absent and no chondrocyte-like cells as well as no cloning were observed. In other specimens the normal structural arrangement of tendon fibers was missing. In no case was calcification seen inside the tendon.

Fig. 5. Cloning of cells bordering frayed ends of a ruptured supraspinatus tendon. H. E. ×210

Discussion

This study of calcifying tendinitis seems to indicate that we are not dealing with a dystrophic calcification but with calcification taking place in a living tissue. We, therefore, have adopted the term "calcifying tendinitis" ("tendinite calcifiante", DeSèze and Welfling) instead of calcareous or calcified tendinits.

Calcification occurs multifocally. These foci are separated by normal living tissue, a fact also observed by Ollson. The presence of cartilage in proximity to some foci of calcification was already noted by Wrede in 1912. This author stated that the appearance of cartilage cells precedes calcification. Sandström and Wahlgren also described the transformation of tenocytes into round or oval cells.

Thus, the early stage of calcifying tendinitis resembles the first steps of endochondral ossification of tendons and ligaments (Johnson; Uhthoff; Urist, De La Sierra and Strates). In this latter process invasion of blood vessels is seen following calcification of the cartilaginous matrix. In calcifying tendinitis no blood vessels are present at the moment of calcification and therefore degeneration into an amorphous mass occurs. The observation of two instances of bone formation lends support to this theory. We believe that in these two cases blood vessels had reached the hypertrophic cartilage cells at the moment of calcification prior to degeneration, so that endochondral ossification could proceed normally. Fluorescence studies confirm that mineral deposition took place at two sites as in endochondral ossification, namely at the site of calcification of the cartilaginous matrix and at the site of ossification.

In all cases of tendon rupture the frayed tendon ends showed signs of degeneration. Attempts of repair as evidenced by cloning of cells were present in close proximity to these ruptures. As had to be expected these proliferating cells did not elaborate acid mucopolysaccharides. Tendon degeneration, as seen in autopsy specimens of elderly people, did neither reveal the presence of hypertrophied chondrocytes, nor a calcified matrix nor cloning of cells.

The etiology of calcifying tendinitis is unknown. Since calcification of tendons appears in high percentage of patients in more than one location (DeSèze and Welfling) the possibility of a systemic disease can not be overlooked but was never found (DeSèze and Welfling). A process similar to Selye's calciphylaxis (Selye and Berczi) was suspected by Moseley. However, no induced systemic hypersensitivity was ever observed in patients suffering from calcifying tendinitis. Furthermore, the histology of calcareous subdeltoid bursitis (Selye, Gentile and Veilleux) induced by calcyphylaxis does not resemble that of calcifying tendinitis. The process of calcergy can also be excluded since no hypercalcemia or hyperphosphatemia (Gabbiani and Tuchweber) was ever reported in patients with calcifying tendinitis.

In summary we propose that in calcifying tendinitis vascular and/or mechanical disturbances lead to a diminished local blood flow which, in turn, is responsible for the modulation of tenocytes into chondrocytes. These cells elaborate acid mucopolysaccharides (or proteoglycans) as well as alkaline phosphatase which are essential for the subsequent calcification of the cartilaginous matrix.

The circulation of the short rotator tendons was studied by Moseley and Goldie who demonstrated that the blood supply of the supraspinatus was critical in the area one centimeter medial to its insertion into bone. Rathbun and MacNab showed that the position of the arm influenced the circulation, as in adduction blood vessels in the supraspinatus tendon close to the humerus did not fill. However, in abduction this "avascular" area showed filling of vessels.

Whereas calcification occurs in our opinion in a living otherwise normal tissue, ruptures, on the other hand, seem to take place in a degenerated tendon. Cartilage cell proliferation are expressions of an attempts by nature to repair the structurally weak tendon. We agree therefore with the current thinking that ruptures of the rotator cuff result from degeneration of tendon fibers. This degeneration is either due to wear and tear and/or injury. The histologic expression of degeneration of the tendon cuff due to ageing is somewhat different from degeneration due to wear and tear in that in the latter no attempt of repair was noticed.

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