Calcium pyrophosphate dihydrate and hydroxyapatite crystals in a patient with rheumatoid arthritis: a case report

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The association between rheumatoid arthritis (RA) and calcium pyrophosphate dihydrate (CPPD) crystal deposits can now be easily identified by MSUS, which is a noninvasive technique that can be applied to patients with painful joints and enthesis that are unexplained by rheumatoid activity. In this paper, we report an Egyptian case of a 51-year-old man who had rheumatoid arthritis since 7 years and developed bilateral knee and heel pain of 1.5 months' duration with gradual onset and progressive course. Radiography revealed features of RA in both hands, as well as features of severe osteoarthritis in both knees with no signs of chondrocalcinosis. Ultrasonography of the joints, Achilles tendon, and plantar fascia detected knee, Achilles tendon, and plantar fascia calcifications, which are characteristic of CPPD, and supraspinatus calcification, which is characteristic of hydroxyapatite (HA) deposition. Further investigations revealed no evidence of metabolic disorders. CPPD and HA crystals were identified in his synovial fluid. Subclinical affection with CPPD and HA crystals in RA can be easily detected by ultrasonography, which allows early management to prevent future attacks in RA patients that could lead to exacerbation of joint symptoms that may be missed as rheumatoid disease activity. Diet control and colchicine treatment may be more effective if started early before exacerbation.

Keywords:
calcium pyrophosphate dihydrate deposition, hydroxyapatite deposition, rheumatoid arthritis

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Introduction

Calcium pyrophosphate dihydrate crystal deposition disease (CPPD) and hydroxyapatite (HA) CPPD are characterized by deposition of insoluble crystals within the joints and periarticular soft tissues, initiating inflammatory destructive reaction [1].

Association between rheumatoid arthritis (RA) and calcium pyrophosphate dihydrate (CPPD) crystal deposits is more frequent than previously believed [2]. Gerster *et al.* [2] reported that CPPD crystals were present in 25.8% of RA patients and that a worse clinical outcome was associated with the presence of these crystals. These observations support the notion that tissue injury caused by arthritis leads to crystal formation and that crystals may worsen the primary arthritis.

In this paper, we report the case of an Egyptian male patient with RA with CPPD and HA crystals in his synovial fluid. A short review of the literature is also presented.

Case history

A 51-year-old male patient complained of gradually progressing bilateral knee and heel pain of 1.5 months' duration. Patient consent was obtained. His medical history was significant for RA, which was diagnosed 7 years earlier. The patient fulfilled the 2010 ACR/EULAR criteria for RA. The patient was on methotrexate, antimalarial, and NSAIDs for RA. He had shown a good response to treatment in the previous years, but had been off treatment since 2 months. Physical examination confirmed arthritis in both knees, plantar fasciitis, and Achilles tendinitis, in addition to symmetrical polyarthritis of the second and third proximal interphalangeal joints (PIPs) and metacarpophalangeal joints (MCPs) in both hands, wrists, and elbows. Initial workup showed thrombocytosis, elevated erythrocyte sedimentation rate (95 mm/h), elevated level of C-reactive protein, positive rheumatoid factor, positive anticyclic citrullinated peptide, normal uric acid level, and normal liver and kidney functions. Plain radiographs showed juxta-articular cysts at PIPs, subchondral cysts at the second and third MCPs, multiple cysts at the carpal bones, narrowing of both radiocarpal joint space with subchondral cysts, multiple cysts and erosions at the ulnar styloid processes, and narrowing of the medial side of both tibiofemoral joint space with subchondral cysts. Subsequent workup showed normal parathyroid

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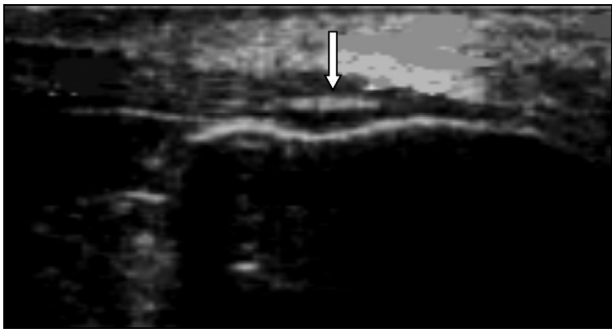
hormone, normal calcium and phosphorous levels, and normal magnesium and alkaline phosphatase.

Ultrasonographic examination of the joints, Achilles tendon, and plantar fascia revealed knee calcification [several thin hyperechoic spots (punctate pattern)] at the fibrous cartilage, Achilles tendon calcification (hyperechoic deposits within the fibrillar tendon structure not in continuity with the bone profile) of pattern I (multiple thin linear bands) (Fig. 1), and plantar fascia calcification (hyperechoic deposits in the superficial region of the insertional tract of the fascia, not in continuity with the bone profile) of pattern I (multiple thin linear bands) (Fig. 2) – which are characteristic of CPPD – and supraspinatus calcification (hyperechoic appearance) (Fig. 3) – which is characteristic of hydroxyapatite deposition.

Macrosopic examination of synovial fluid showed that synovial fluid viscosity was normal, aspect was clear, and its color was yellow. Microscopic examination of synovial fluid was performed for identification of crystals and showed both CPPD (weakly positive birefringent rhomboidal crystals) using polarized light microscopy and hydroxyapatite crystals (nonbirefringent), which were identified with routine light microscopy and staining of the fluid with alizarin red S.

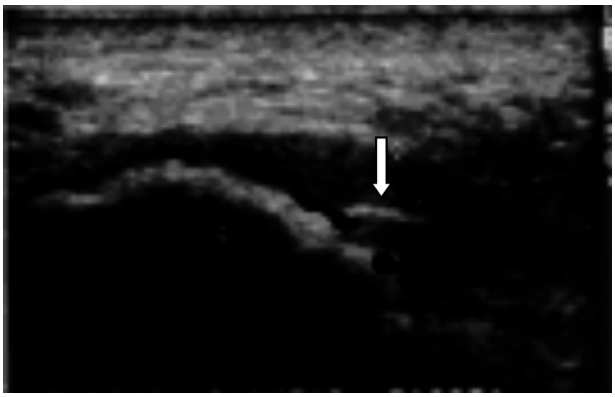
Aspiration of the knee joint followed by an intra-articular steroid injection was performed, and low-dose oral colchicine (0.6 mg twice a day) was added to the previous treatment.

Figure 1



Longitudinal scan of Achilles tendon showing Achilles tendon calcification (arrow)

Figure 2



Longitudinal scan of plantar fascia showing plantar calcification (arrow)

Discussion

RA is a chronic inflammatory disease determined by an inflammation of the synovial membrane leading to destruction of cartilage and bone [3].

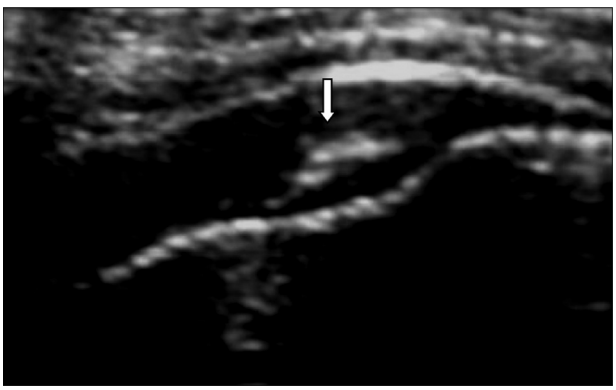
CPPD disease is confirmed as equally common in RA by synovial fluid and macroscopic skeletal examination [4].

The clinical features that should alert one to the likelihood of CPPD arthropathy include the following: an unusually severe or destructive arthropathy, a history of other joint involvement or of a previous joint operation, clinical evidence or a history of a disorder known to be associated with CPPD, and a family history of joint disease. There may also be evidence of chondrocalcinosis or other distinctive radiological signs of CPPD [5].

Doherty *et al.* [6] reported that when RA and CPPD coexist, atypical radiographic features reflecting a hypertrophic reparative response may occur.

Our patient was an elderly man who had had RA since 7 years and developed bilateral knee and heel pain of 1.5 months' duration with gradual onset and progressive course. Physical examination revealed polyarticular

Figure 3



Transverse scan of the right supraspinatus muscle showing supraspinatus calcification (arrow) characteristic of hydroxyapatite deposition

involvement of the knees, second and third PIPs, and MCPs of both hands, wrists, and elbows, in addition to bilateral plantar fasciitis and Achilles tendinitis. Radiography revealed features of RA in both hands and features of severe osteoarthritis in both knees with no signs of chondrocalcinosis. US of the joints, Achilles tendon, and plantar fascia revealed knee, Achilles tendon, and plantar fascia calcifications – characteristic of CPPD – and supraspinatus calcification – characteristic of hydroxyapatite deposition.

Ultrasonography (US) is an emerging technique that could be used for detection of the CPPD deposits (hyperechoic deposits), particularly those that are too small to be visible on plain radiographs [7].

In our case, plain radiography did not show any calcifications either in Achillles tendon or in the plantar fascia; however, the calcific structure of the deposits was observed by US. This could be due to low density of the thin linear calcific deposits [8].

Some studies confirm the usefulness of US in revealing signs of CPPD deposits in periarticular structures (elbow enthesis and Achilles tendon) that show no calcification on plain radiographs [8,9]. The calcific deposits of HA CPPD may look like CPPD deposits, but their shapes differ from CPPD deposits as they are homogeneous, rounded, and hyperechoic [8].

Diagnosis of CPDD can be confirmed by the demonstration of rhomboid or rod-shaped, weakly positive birefringent CPPD crystals in synovial fluid or articular tissues and the presence of characteristic intra-articular calcified deposits in the synovium, articular cartilage, or menisci [5].

Deposition of HA crystals in different sites results in calcifications, and the rotator cuff is one of the most frequent sites of localization of HA deposits [10,11]. Although the deposition of apatite in the soft tissues of RA is known to occur rarely, Dossick *et al.* [12] reported the first known case of intraosseous apatite deposition in a 63-year-old woman with a 12-year history of RA.

Hydroxyapatite can be detected in synovial fluid, but because these crystals are generally nonbirefringent, it is impossible to detect them by polarized microscopy. A useful and rapid method for detecting hydroxyapatite and other calcium-containing crystals is the staining of fluid with alizarin red S stain and looking for clumps of crystals under routine light microscopy. These crystals also have been identified using electron microscopy [13].

CPDD is associated with age, trauma, osteoarthritis, and some metabolic diseases such as hyperparathyroidism, hypomagnesemia, gout, hemochromatosis, hypothyroidism, and hypophosphatasia [14]. Our patient was old and had RA in addition to knee osteoarthritis, but had no evidence of metabolic disorders. Thus, the tissue injury caused by arthritis can induce crystal formation as reported by Sun and Hanley [15].

Conclusion

CPPD and HA crystals could be detected in patients with RA. US is a useful indirect sign for the presence of CPPD and HA crystal deposition diseases, with the importance of searching for calcification both in articular and periarticular tissues. US could allow early management of these cases to prevent future attacks in RA patients that could lead to exacerbation of joint symptoms that may be missed as activity of the rheumatoid disease. Diet control and colchicine treatment may be more effective if started early before exacerbation.

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Conflicts of interest

There are no conflicts of interest.

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