

## Calcium Pyrophosphate Deposition: Sonographic Features in a Familial Case

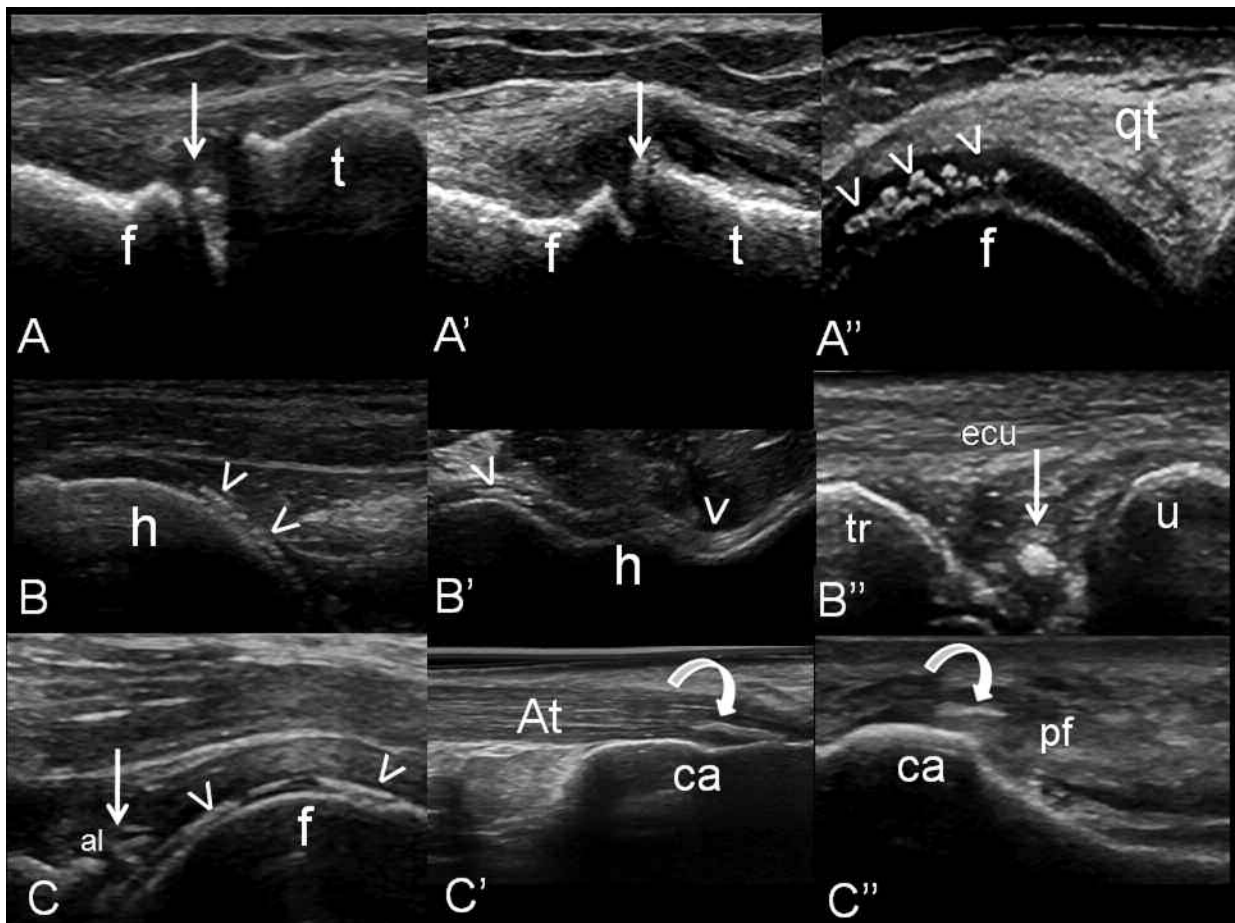
To the Editor:

Calcium pyrophosphate deposition (CPPD) disease is a metabolic arthropathy caused by the deposition of calcium pyrophosphate (CPP) crystals in and around joints, especially in hyaline and fibrous cartilage. CPPD disease is generally categorized into sporadic, familial, and secondary (metabolic) forms. Prevalence increases with age; indeed, radiographic evidence of CPPD is found in up to 40% of elderly subjects. The sporadic form is the most common. Secondary CPPD disease is an infrequent condition related to a variety of metabolic causes including hyperparathyroidism, hypomagnesemia, hypophosphatasia, and hemochromatosis. Familial CPPD disease is characterized by distinctive clinical and radiographic features, but its prevalence is unknown<sup>1,2,3,4</sup>.

Diagnosis requires detection of CPP crystals in synovial fluid<sup>1</sup>; however, an increasing body of evidence indicates a role for ultrasound (US) as a bedside procedure to improve diagnostic accuracy and clinical decision making in routine rheumatological practice. US possesses some ideal features for assessing crystalline arthropathies. Its high spatial resolution

enables depiction of minimal deposits at multiple anatomical sites<sup>5,6,7,8,9,10</sup>; in gout and CPPD disease it has revealed subclinical pathological findings at previously unaffected sites<sup>8,9</sup>.

We describe a case in which sonographic findings of massive crystal deposition even at clinically uninvolved sites prompted further investigation, leading to a diagnosis of familial CPPD disease. A 58-year-old man presented to our outpatient clinic with acute right knee synovitis and an 11-month history of recurrent monoarthritis of both knees. The attacks were self-limiting and resolved in less than a week. Pain onset was rapid, with significant joint swelling and functional impairment associated with fever and a flu-like malaise. Clinical examination revealed marked swelling of the right knee with a positive bulge sign; no signs or symptoms of inflammation were seen in other joints or tendons. He had elevated erythrocyte sedimentation rate (89 mm/h, normal range 0–20) and C-reactive protein (3.3 mg/dl, normal range 0–0.8). US examination of the right knee documented signs of joint inflammation (i.e., marked suprapatellar pouch enlargement due to abnormal amounts of intraarticular synovial fluid), large, rounded hyperechoic deposits in the menisci, and confluent deposits, associated with partial shadowing, embedded in the femoral hyaline cartilage (Figure 1, A-A'').



**Figure 1.** A-A'': Sonographic findings indicate calcium pyrophosphate (CPP) crystal deposits in the fibrous (arrows) and hyaline (arrowheads) cartilage of the right knee. A. Lateral meniscus, longitudinal scan. A'. Medial meniscus, longitudinal scan. A''. Hyaline cartilage of the lateral femoral condyle, longitudinal scan with knee in maximum flexion. f: femur; t: tibia; qt: quadriceps tendon. B-B'': Sonographic findings indicate CPP crystal deposits in fibrous (arrows) and hyaline (arrowheads) cartilage at clinically uninvolved sites (upper limbs). B. Shoulder, posterior scan. B'. Elbow, anterior transverse scan. B''. Wrist, triangular ligament, longitudinal scan. h: humerus; tr: triquetrum bone; u: ulna; ecu: extensor carpi ulnaris tendon. C-C'': Sonographic findings indicate CPP crystal deposits in fibrous (arrows) and hyaline (arrowheads) cartilage and tendon (curved arrows) at clinically uninvolved sites (lower limbs). C. Hip, anterior longitudinal scan. C'. Achilles tendon, longitudinal scan. C''. Plantar fascia, longitudinal scan. f: femur; ca: calcaneus; al: acetabular labrum; At: Achilles tendon; pf: plantar fascia.

Analysis of synovial fluid demonstrated intracellular monocyclic crystals showing no birefringence by compensated polarized light microscopy. A diagnosis of CPPD disease was made according to international criteria<sup>1</sup>. A triamcinolone acetonide injection (40 mg) and oral colchicine 1 mg/day led to symptom resolution without recurrences.

The degree of knee cartilage involvement prompted a multisite and multitissue US assessment, which disclosed signs of crystal deposition in shoulder, elbow, hip, and ankle cartilage and tendons (Figure 1, B-B" and C-C"), all sites that had never been clinically involved. The crystal size and the widespread distribution suggested an underlying metabolic disease or a familial form. The patient tested negative for hyperparathyroidism, hemochromatosis, hypophosphatasia, hypomagnesemia, hypothyroidism, familial hypercalciuria, acromegaly, diabetes mellitus, and Wilson disease, thus excluding a metabolic disorder involving recognized risk factors for CPPD. The radiographic evidence of meniscal calcifications in his mother and 62-year-old brother led to a clinical diagnosis of familial CPPD disease.

Conventional radiography is widely available and radiographic evidence of CPPD and possible secondary osteoarthritis is familiar to rheumatologists. However, US provides rapid bedside multisite and radiation-free assessment of patients with suspicious CPPD with a high degree of accuracy, especially in the hands of a trained sonographer. It can also disclose subclinical and radiographically invisible signs of disease in crystal-related arthropathies<sup>8,9,10</sup>. Although sonographic findings are not yet included in the international diagnostic criteria for CPPD disease, our case demonstrates that unexpected sonographic detection of CPP crystals at multiple anatomical sites and tissues warrants further investigation and can lead to a diagnosis of nonsporadic, familial CPPD disease despite a negative clinical history and physical examination.

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