Crystal deposition diseases

**RAD Magazine, 46, 540, 23-24**

**Dr Mostafa Ellatif**
Specialist registrar in clinical radiology

**Dr Dhiren Shah**
Consultant musculoskeletal radiologist

Department of radiology, Northwick Park Hospital, London

### Introduction

Crystal deposition diseases are a spectrum of arthritides induced by cellular reaction and inflammatory response in and around joints due to microcrystals. The most common of these disorders are gout, calcium pyrophosphate dihydrate and calcium hydroxyapatite deposition disease. The difference in the pathophysiology of these diseases means they are unique in their clinical presentation and radiological appearances. Imaging plays a pivotal role in the diagnosis and subsequent monitoring of treatment response and is a cornerstone of management. Conventional radiography remains the primary modality, but there is an increasing role of ultrasound, CT, MRI and dual energy CT.

### Gout

Gout is the commonest of the crystal arthropathies with an incidence of 0.5% and increasing prevalence with age. The underlying aetiology can broadly be divided into urate overproduction (eg myeloproliferative disorders and defects in purine synthesis) or under-excretion (eg renal failure or use of diuretics). Elevated levels of urate lead to monosodium urate (MSU) crystal formation when levels reach 6.8g/dl. The definitive diagnosis is made by symptomatic joint aspiration with subsequent analysis identifying needle-like negatively birefringent crystals on microscopy.

Clinically, gout presents with recurrent episodes of joint pain, initially with absence of radiological signs. Peak incidence is in males aged 30-60 with a predilection for the first metatarsophalangeal joint (MTPJ). The first MTPJ is the symptomatic joint at presentation in 50% of cases, involvement rising to 90% in patients with untreated gout. Other commonly affected joints are the first interphalangeal and metatarsophalangeal joint (MTPJ). The first MTPJ is the symptomatic joint at presentation in 50% of cases, involvement rising to 90% in patients with untreated gout. Other commonly affected joints are the first interphalangeal and metatarsophalangeal joints. If untreated, these episodes eventually subside but often recur with polyarticular involvement. Peri-articular tophi develop in chronic gout due to amorphous debris containing urate and proteinaceous deposits with surrounding foreign body reaction.

Radiography is typically the first imaging modality used in gout to assess joint destruction and rule out differential diagnoses. Small joints are typically affected more with a predilection for the lower limbs. The overall pattern is usually asymmetric with a monoarthritis, and subsequent oligoarthritis or polyarthritis. The ankle, tarsal and knee usually are affected early in the disease process, with all compartments of the hand, wrist and elbow being other favourable sites.

In early gout, the symptomatic joint is typically normal or demonstrates soft tissue swelling or peri-articular oedema. Once the acute episode has passed, small well-defined erosions may start to develop peripherally at the affected joints with overhanging margins. More classic findings with tophi and increasing erosions become apparent with chronicity. Importantly, there is preservation of the joint space with lack of peri-articular osteopenia. Tophi tend to measure between 5-10mm and faint calcification is seen in 50% of cases. Erosions are eccentric, round, well circumscribed and juxta-articular. Occasionally, extensive erosions can cause a mutilating arthritis, mimicking psoriatic and rheumatoid arthritis.

Crystal deposition may occur at tendon insertions, such as in the calcaneus, olecranon and patella giving the radiological appearance of ‘spiking’. Bilateral olecranon bursitis and swelling at the dorsum of the foot are classic soft tissue manifestations of gout.

The ultrasound features of MSU deposits are the double-contour sign, as well as tophi and erosions. The double-contour line refers to a hyperechoic band over the superficial cartilage and is relatively specific for gout. Tophi are usually identified as hyperechoic aggregates with a surrounding anechoic rim, while erosions demonstrate focal discontinuity of the bony cortex. In the more acute phase, a joint effusion may be identified with evidence of synovitis.

Dual energy CT (DECT) allows differentiation of crystals by their x-ray spectra based on their density and atomic number. Data is acquired at 80kV and 140kV using two x-ray tubes. Using a decomposition algorithm, calcium can be distinguished from MSU with reported specificity between 75-100%. The data is used to produce a colour-coded map, which is fused with a conventional CT, allowing assessment of the affected sites and disease burden.

### Calcium pyrophosphate dihydrate disease (CPPD)

CPPD results in arthritis, synovitis and tenosynovitis secondary to localised inflammatory response to the crystals. The pathophysiology is not fully understood but thought to be due to defects in the metabolism of calcium and phosphate. CPPD is a disease of the elderly population, affecting women and men equally. Chondrocalcinosis is identified radiologically in 5% of the population by the age of 70. Associations with primary hyperparathyroidism, haemochromatosis and hereditary spherocytosis have been described.

The spectrum of clinical presentation of CPPD ranges from incidental (most common), pseudogout, pseudo-osteoarthritis, pseudorheumatoid arthritis, or pseudo-neuropathic arthritis. Pseudogout is a subset of CPPD that mimics gout clinically but is due to calcium pyrophosphate rather than monosodium urate, with aspirated crystals being weakly positive under polarizing light.

Pseudo-osteoarthritis mimics osteoarthritis clinically and radiologically. Patients will demonstrate the typical features of joint space loss, subchondral sclerosis and cysts with or
without chondrocalcinosis. Osteophytosis is often absent. Distinguishing features in such cases may be an atypical distribution, such as predominantly patellofemoral or metacarpophalangeal joint involvement. CPPD will also be more progressive than osteoarthritis causing formation of intra-articular osseous bodies. CPPD favours radiocarpal, metacarpophalangeal and non-weight bearing joints in comparison to osteoarthritis.

Pseudorheumatoid arthritis mimics rheumatoid arthritis clinically with chronic history of morning stiffness and restricted range of motion in a symmetrical distribution. Chondrocalcinosis may be the only distinguishing feature in such cases. In pseudoneuropathic CPPD there are radiological findings of joint destruction and subluxation in the absence of a neurological abnormality.

The definitive diagnosis is made based on the aspirated crystals as well as imaging findings of chondrocalcinosis. If only one of the two is identified then the diagnosis is presumed. CPPD crystals are deposited in fibrocartilage and hyaline cartilage. Fibrocartilage deposition is most common in knee menisci and the triangular fibrocartilage of the wrist. Radiologically this is identified as irregular or linear calcification within the cartilage. Synovial calcification is often seen in conjunction, typically in knee, metacarpal or metatarso-phalangeal joints. Tendon calcification also occurs in the Achilles, triceps, quadriceps and supraspinatus tendons – often thin and linear.

Hyaline, fibrocartilage and tendinous calcification can be reliably identified sonographically as hyperechoic foci (linear or amorphous) with the affected structures in more chronic cases. Acutely, similar to gout, a degree of hyperaemia and synovitis may be identified.

**Calcium hydroxyapatite deposition disease (HADD)**

Deposition of calcium hydroxyapatite crystals in joints, periarticular soft tissues, tendons and bursa are responsible for HADD. The underlying aetiology is not yet understood, with no gender predilection and most patients between the ages of 40-70. Aspirated crystals are needle-like on microscopy and stain purple with Wright’s stain.

Patients are often asymptomatic with only 34-45% of patients presenting with symptoms. Clinically, HADD is usually monoarticular and tends to affect the shoulder joint, but can be polyarticular. Patients present with severe pain and tenderness with restricted range of motion, mimicking gout, septic arthritis or CPPD. It may occur in isolation or in association with connective tissue disease, renal osteodystrophy, trauma, or iatrogenic secondary to steroid injections. HADD can cause bursitis, tendonitis or acute arthritis.

Radiographic appearances depend on the chronicity of the disease. Cloud-like and poorly defined calcific deposits are seen, which become denser and more linear with chronicity. HADD most commonly affects the shoulders with capsular, tendinous and bursal tissue calcification. Appearances are bilateral in 50% of cases and affect the supraspinatus tendon, but all rotator cuff tendons may be involved. Bony erosions may be present at the insertion sites of tendons and ligaments, which may have associated bone marrow oedema on MRI. Elbow involvement is also common and can affect the collateral ligaments and triceps tendon at its olecranon insertion, where it is occasionally associated with rupture.

Axial skeleton involvement has been described, affecting the longus colli muscle in the neck as well as the interspinous bursae. In the hips, gluteal tendinous insertion...
involvement, extending to the greater trochanter and surrounding bursae, is frequently identified.\textsuperscript{21} Quadriceps, patellar and Achilles tendon involvement is often seen.

Crystal deposition can occur within the synovium or cartilage involving the shoulder, knee, hip and small joints of the hands/feet. Destructive HADD arthropathy of the shoulder is termed Milwaukee shoulder syndrome with features of joint space loss, subchondral sclerosis, joint disorganisation and deformity.\textsuperscript{7} There is often an associated joint effusion with superior migration of the humeral head due to disruption of the rotator cuff.

Ultrasound in HADD is primarily used to identify the deposits, which will be hyperechoic with posterior acoustic shadowing. Doppler activity around a deposit and presence of an effusion suggest inflammation and may correlate with pain.\textsuperscript{22}

**Conclusion**

Crystal deposition diseases are a common cause of inflammatory arthropathy, especially with an increasing ageing population. The three most common crystal arthropathies are gout, CPPD and HADD. Conventional radiography remains the mainstay of diagnosis. Ultrasound is playing an increasingly important role in early diagnosis and percutaneous intervention. Dual energy CT use in crystal deposition disease is in its infancy but has great potential in aiding with diagnosis and assessing disease burden. The discussed multimodality imaging features of the different conditions allow their differentiation. Clinicians, reporting radiographers and radiologists should be aware of these features to ensure patients are diagnosed promptly and treated appropriately to prevent debilitating chronic disease.

**References**