Calcium Pyrophosphate Deposition - including Pseudogout

Pseudogout is an inflammation of joints caused by the deposition of calcium pyrophosphate (CPP) crystals in articular and periarticular tissues. It is but one manifestation of calcium pyrophosphate dihydrate crystal deposition (CPPD) disease. The recommendations of the 2011 European League Against Rheumatism (EULAR) are that CPPD should be an umbrella term and that the following terminology should be used for the clinical entities it encompasses: [1]

- Asymptomatic CPPD: CPPD with no overt clinical consequences. Isolated cartilage calcification, or chondrocalcinosis (CC) - identified by imaging or histology - or osteoarthritis (OA) with CC can occur.
- OA with CPPD: this term is used where there is CPPD in a joint with OA changes sufficient to cause symptoms.
- Acute CPP crystal arthritis: self-limiting acute-onset arthritis caused by CPPD (also known as ‘pseudogout’).
- Chronic CPP crystal inflammatory arthritis: this is a chronic inflammatory condition associated with CPPD.

Epidemiology [1, 2]

- CPPD is common in the elderly. Half of adults develop radiographic changes typical of CPPD by the age of 80.
- One English study reported a prevalence of CC of 7-10% in people over the age of 60. This study also reported an equal gender distribution. [3]
- American statistics suggest an annual incidence of acute CPP crystal arthritis of 1.3 per 100,000. [4]
- Most cases of CC are non-familial but mutations in the ANK human gene (ANKH) have been demonstrated in some families. [5]

May be precipitated by:

- Dehydration
- Intercurrent illness
- Hyperparathyroidism
- Long-term use of steroids
- Hypothyroidism
- Any cause of arthritis
- Haemochromatosis
- Wilson's disease
- Acromegaly
- Dialysis
- Surgery or trauma
- Hypomagnesaemia

Presentation [1]

It is often asymptomatic, with only radiographic changes of CC.

CPPD may cause an acute or chronic arthritis.
Acute CPP crystal arthritis

- Causes an acute monoarticular or oligoarticular arthritis. It most often affects the knees but often also wrists, shoulders, ankles, hands and feet. Almost any joint may be affected.
- Presentation is similar (but usually milder) to acute gout, with acute joint pain and swelling.
- Affected joints are acutely inflamed with swelling, effusion, warmth, tenderness and pain on movement. Attacks may be associated with fever and raised white cell count.

Chronic CPP crystal arthritis

- Destructive changes like OA (but more severe). It may progress to cause a destructive arthropathy producing a neuropathic joint.
- Most often, it affects knees, wrists, shoulders and hips.

Differential diagnosis

- Acute gout
- Septic arthritis
- OA
- Rheumatoid arthritis

Investigations\(^{[1]}\)

- Joint X-rays: linear opacification of articular cartilage - CC.
- Ultrasound may also be a useful diagnostic tool.
- Dual-energy CT and diffraction-enhanced synchrotron imaging are being evaluated as potential avenues for improved visualisation of CPP deposits.\(^{[6]}\)
- Aspiration of the joint fluid: raised white cell count which is predominantly neutrophils. Glucose levels usually are normal.
  Intracellular and extracellular weakly positive birefringent crystals (intracellular crystals are pathognomonic for acute pseudogout). The joint fluid often looks purulent and septic arthritis must be excluded.
- Exclusion of other causes of acute arthritis.
- Evaluation of possible underlying cause as listed above.

Management\(^{[7]}\)

Unlike gout, there are no specific treatments for the elimination of CPP crystals from the body. Apart from therapy for any underlying cause, treatment is therefore symptomatic. Care should be tailored to individual patients and should take account of any comorbidities and existing medication regimes. Non-steroidal anti-inflammatory drugs (NSAIDs), for example, may not be ideal for the group most commonly developing symptomatic CPPD disease - ie the elderly.

The body of evidence supporting the use of various treatments is not as well established in CPPD-related conditions as that for gout. It is acknowledged, therefore, that the management regimes have often been developed as a result of the custom and practice over the years rather than supported by large-scale clinical trials.

The most widely used treatments for acute crystal arthritis are as follows:

- Ice, cool packs, temporary rest.
- Aspiration of the joint.
- NSAIDs.
- Intra-articular steroid injections.
- Systemic steroids.
- Colchicine - an alternative if NSAIDs or steroids are contra-indicated.

One study has reported successful use of acute CPP-related synovitis with anakinra, an interleukin-1\(\beta\) blocking agent.\(^{[8]}\)

Treatment of OA with CPPD should be managed according to the general guidelines for treating OA. See separate Osteoarthritis article.

Treatment of chronic crystal arthropathy is largely based on evidence from the treatment of gout and OA and consists of NSAIDs with proton pump inhibitor (PPI) cover. Other treatments tried include low-dose colchicine, low-dose methotrexate, hydroxychloroquine, oral steroids and intra-articular radiocolloid.

Prognosis\(^{[2]}\)

- Acute attacks usually resolve within ten days.\(^{[9]}\)
- Some patients develop progressive joint damage with functional limitation.
- Prognosis will also be dependent on any underlying cause.

Further reading & references

1. EULAR recommendations for calcium pyrophosphate deposition - Part I: terminology and diagnosis; European League Against Rheumatism (2011)
4. Rothschild BM, et al; Gout and Pseudogout, Medscape, Sep 2015
7. EULAR recommendations for calcium pyrophosphate deposition - Part II Management; European League Against Rheumatism (2011)

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