Crystal Arthritis – Gout and Pseudogout

Abstract
Crystal arthritis presents often as a monoarticular hot swollen joint. Hot swollen joints are a common presentation with a number of differential diagnoses. The most serious of these is septic arthritis, which should always be considered before making an alternative diagnosis. Hot swollen joints commonly have other underlying diagnoses, including crystal arthritis, reactive arthritis, haemarthrosis and a monoarticular presentation of polyarthritis. Here we review the crystal arthropathies Gout and Pseudogout (now termed Calcium pyrophosphate deposition or CPPD).

Keywords
Crystal arthritis, gout, pseudogout, swollen joint.

Introduction
Gout is a common medical problem and is regularly seen in primary care. It affects 1% men in western countries. Female to male ratio is around 4:1. It only very rarely occurs in premenopausal women. Around 90% gout is due to under excretion of uric acid. Rare causes include inborn errors of metabolism. Gout in a paediatric or adolescent patient should prompt referral for underlying causes.

There are fours stages recognised:

• Asymptomatic Hyperuricaemia – the average length of time between hyperuricaemia and development of gout is 10 years+.
• Acute Gout – This is well recognised. Acute Gout characteristically has a rapid onset over a few hours, often beginning at night. It causes severe pain in the affected joint with a reduced range of movement. The patient may be unable to bear anything touching the joint. There will be swelling, heat and erythema. The most common joint affected initially in gout is the 1st metatarsophalangeal (MTP), known as podagra. This is the first joint affected in 50% of cases. Other joint involvement, in decreasing frequency, include ankles, knees, wrists, fingers, and elbows. An oligo or polyarticular presentation is also possible; the latter may mimic Rheumatoid Arthritis.
• Interval or intercritical Gout – This is the period between acute gout attacks. This can go on for some years before development of tophaceous gout if untreated.
• Chronic tophaceous gout – Chronic severe gout with development of tophi over tendons, ears, fingers etc. Tophi may ulcerate if untreated. The Arthritis is often polyarticular and may show erosion on plain film.

Presentation

• History
Remember, patients with a short history of a hot, swollen and tender joint (or joints) with restriction of movement should be regarded as having septic arthritis until proven otherwise. If clinical suspicion is high, then it is imperative to treat as septic arthritis, even in the absence of fever.

The history and examination should include the joints involved, chronicity, pain, swelling, erythema and systemic symptoms. Risk Factors should be enquired about directly (Table I) including age and sex. The aim is to consider how likely the patient is to be suffering from...
Crystal Arthritis – Gout and Pseudogout

gout. (Gout rarely affects premenopausal women in the absence of marked risk factors such as poor renal function. Oestrogen has a uricosuric and thus protective effect. A hot swollen joint in a young woman should prompt a search for an alternative diagnosis).

Examination

Look for tophi, particularly of the fingers, elbows and ear cartilages (Figures 1, 2, and 3). Assess for signs of sepsis – temperature, tachycardia. Examine the joint – Is there heat, erythema (consider cellulitis), synovitis, effusion? Can the joint be moved? Examine other joints briefly to exclude a polyarticular presentation, as this may change the differential.

Table 1: Risk Factors for Gout.

- Renal insufficiency
- Metabolic syndrome
- Congestive cardiac failure
- Hypertension
- Drugs – diuretics, low dose aspirin, alcohol
- Purines - organ meats, beer, oily fish, meat extracts
- High fructose drinks (Non diet fizzy drinks, orange juice)
- Haematological disorders – myeloproliferative, lymphoproliferative

Investigations (Table 2)

The gold standard for diagnosis is identification of monosodium urate (MSU) crystals by polarized light microscopy; these are needle shaped and negatively birefringent (Figure 5). It is important to be aware that MSU crystals may coexist with other conditions such as Rheumatoid and septic arthritis.

The diagnostic value of serum uric acid (SU) level is limited. A normal SU level does not exclude acute gout. Patients with acute gout may have a high, normal or even low SU level. It has been suggested that as many as 49% of patients may have normal SU levels during bouts of acute gout. Equally, as most patients with hyperuricaemia will never develop acute gout, a raised serum uric acid should not be used in isolation to diagnose gout.

Figure 1: Polyarticular tophaceous gout.

Figure 2: Subtle tophi on the ear lobe.

Figure 3: Polyarticular gout with corresponding erosion on plain X ray of hands.
Crystal Arthritis – Gout and Pseudogout

Treatment

Acute Flare (Figure 4 & 6)

The acute flare must be treated initially. **Never stop, initiate or alter allopurinol during an acute attack.** NSAID’s or colchicine should be used as treatment for acute gout. All NSAID’s are equally effective when given at maximal doses. They should be co-prescribed with a PPI. Higher doses of colchicine are often limited by diarrhoea, in our unit we tend to use 500mcg TDS or BD in older patients. In monoarticular flare such as knee, wrist or ankle intra-articular corticosteroid injection can be used where expertise is available. Where NSAID’s or colchicine is contraindicated or ineffective and intra-articular injection not possible, the addition of oral corticosteroids is helpful.

A short course of prednisolone at 20-40mg for 5-7 days can be used. If using prednisolone as prophylaxis at the initiation of urate lowering therapy this should be a lower dose of 5-10mg continued for 4-8 weeks.

Urate lowering therapy (Table 3)

Urate lowering therapy should be offered if a second attack, or further attacks occur within 1 year. It should also be offered to all patients with tophi, renal insufficiency, continued diuretic use and those with uric acid stones and gout. Allopurinol continues to be first the first line option for urate lowering therapy. It works as a purine analog inhibitor of xanthine oxidase. Initial dose is 100mg/day. This can be titrated up to a maximum of 900mg/day, though the most common dosage is 300mg. Dose can be titrated up in 50-100mg increments every few weeks.

Treatment should be ‘to target’ aiming for a serum uric acid (SUA) level <300 µmol/L (BSR guidance). The saturation point of Monosodium uric acid (MSU) is 360µmol/L and the target should be below this to prevent crystal formation and to aid resolution of established tophi. Dose adjustment is required in renal impairment: < 30ml/min = 100mg max/day (may need to be considerably lower, suggest renal specialist input), 30-60 ml/min = 200mg max/day.

Febuxostat is a newer non-purine selective inhibitor of xanthine oxidase, approved by NICE in 2008. It can be used as second line drug choice in patients either intolerant of allopurinol or in whom allopurinol has been ineffective at maximal tolerated dose. It can be prescribed in primary care. It is not licensed in renal impairment with GFR<30 ml/ min. It requires no dose adjustment in mild to moderate renal or hepatic failure (i.e. GFR > 30 ml/min). Starting dose is

---

**Table 2: Baseline Investigations in suspected gout.**

<table>
<thead>
<tr>
<th>Test</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC</td>
<td>Glucose</td>
</tr>
<tr>
<td>Urea &amp; Electrolytes incl eGFR</td>
<td>Serum Urate</td>
</tr>
<tr>
<td>CRP</td>
<td>Blood Pressure</td>
</tr>
<tr>
<td>If fluid aspirated send for MC&amp;S, cell count and crystals</td>
<td>(identification of Monosodium Urate (MSU))</td>
</tr>
</tbody>
</table>

---

Figure 4: Classical gout of 1st metatarsophalangeal joint.

Figure 5: Prolaizing light microscopy showing urate crystals.

Figure 6: Acute gout with metacarpophalangeal synovitis and tenosynovitis.

---
Crystal Arthritis – Gout and Pseudogout

80mg o.d. and can be increased to 120mg/day if serum urate > 360 micromol/L when rechecked after 4 weeks.

There are further alternatives such as benzbromarone or sulphinpyrazone but these are not widely available and are often poorly tolerated by patients. They are not recommended to be introduced by a non-specialist.

Other modifications (Table 4)

Rationalise diuretic use where possible. It is worth considering adjusting other medications where possible in preference for uricosuric agents. Examples of drugs with uricosuric properties include Losartan (angiotensin II blocker) and fenofibrate (hypolipidaemic). These effects are particular to the drug and are not class effects. Treat comorbidities such as hypertension and diabetes. Assess cardiovascular risk factors. Lifestyle modifications include restricting alcohol consumption to recommended levels or below. Avoid high purine foods and other dietary precipitants e.g. shellfish, offal, game, sardines, beer, stout (listed in risk factors). Gradual weight loss is helpful. ‘Crash dieting’ should be avoided (risk of precipitating gout flare). For those patients interested in other beneficial dietary choices, vitamin C and cherries lower SUA.

Calcium Pyrophosphate dehydrate (CPPD) crystal arthritis or ‘Pseudogout’ introduction and terminology

CPPD is also common. It is slightly more common in men than women 1.5:1. Frequency increases with age and is relatively rare below age 50 except in secondary cases. Radiological evidence of chondrocalcinosis is seen in 15% of 65–75 year olds and >40% of 85+ years.8

CPPD comprises 3 separate forms:

1. Chondrocalcinosis – This is a radiographic finding of cartilage calcification (Figure 7) which may be completely asymptomatic.
2. Acute CPPD arthritis – Known as pseudogout because of its presentation similarities to Gout.
3. Chronic CPPD – This may be inflammatory and can mimic Rheumatoid Arthritis or osteoarthritis.

Acute CPPD or Pseudogout is a clinical syndrome in which calcium pyrophosphate dehydrate (CPPD) crystals deposit in joints and soft tissue, resulting in inflammation and tissue damage. The clinical presentation resembles gout in its acute attacks of crystal synovitis, thus the term pseudogout. Unlike gout there is currently no specific treatment to eliminate calcium pyrophosphate (CPP) crystals.

Recognised risk factors for CPPD are increasing age, osteoarthritis, previous joint trauma or damage and metabolic conditions including primary hyperparathyroidism, haemochromatosis, hypothyroidism and hypomagnesaemia.9

Presentation

CPPD occurs almost exclusively in articular tissues i.e. it only very rarely presents as tendinitis or bursitis. The

Table 3: Principles of urate lowering therapy.

| Wait 1-2 weeks after flare has settled |
| Continue gout prophylaxis for at least one month (though some guidelines recommend up to six months) |
| Initiate allopurinol at 100mg, increasing up to max 900mg to ‘treat to target’ (common dose 300mg) |
| Aim for Serum Uric Acid (SUA) <300 µmol/L |

Table 4: Additional therapies in the management of gout.

| Other treatments |
| Rationalise diuretic medication |
| Treat comorbidities |
| Address alcohol consumption and diet |
| Optimise weight |

TOP TIPS/PITFALLS IN PATIENT WITH SUSPECTED GOUT

Patients may have a high temperature (up to 39 ºc) and feel systemically unwell - Note septic arthritis should always be considered.

Overlying erythema can extend beyond the involved joint and resemble cellulitis.

Look for tophi overlying joints and also ear cartilage.

Polyarticular gout may cause marked diffuse swelling e.g. over hand, wrist into forearm.

Look for and manage comorbidities/risk factors aggressively.

Too often gout therapy fails simply due to the allopurinol dose being too low (see treatment).

Gout attacks can be precipitated by dehydration and acute illness – hospitalized or unwell patients are at risk.
Crystal Arthritis – Gout and Pseudogout

knee is the most common site for CPPD followed by the wrist or shoulder. Most commonly it presents with a mono or oligoarticular distribution (90%) though 10% will be polyarticular. Diagnosis can be difficult in polyarticular presentations and often requires specialist evaluation.

**Investigation**

Secondary causes should be considered therefore Ca +/- PTH, thyroid function, ferritin and Mg measurement may be helpful. Correcting contributing pathology is felt to benefit disease outcome.

Aspiration often reveals frankly haemorrhagic effusion. Identification of CPP crystals is by polarized light microscopy. Crystals are classically positively birefringent, rhomboid crystals which are often intracellular. They are often fewer in number than gout crystals and so can be more difficult to identify.

Acute CPPD crystal arthritis and septic arthritis may coexist, so when infection is suspected microbiological investigation of synovial fluid should be performed even if CPP crystals and/or chondrocalcinosis on radiograph are identified.

**Treatment** (Table 5)

NSAID’s or colchicine can be used until acute symptoms subside. Proton pump inhibitors should be co-prescribed. A low dose colchicine regimen is recommended A low dose colchicine regimen is recommended (no loading dose) upto 500mcg 3 times daily. In our unit we use up to 80mg of either triamcinolone (Kenalog) or methylprednisolone (Depomedrone) for intra-articular injection of knees or shoulders in acute flare, and 20-40mg for a wrist injection.

Acute CPPD crystal arthritis and septic arthritis may coexist, so when infection is suspected microbiological investigation of synovial fluid should be performed even if CPP crystals and/or chondrocalcinosis on radiograph are identified.

**Table 5:**

<table>
<thead>
<tr>
<th>TREATMENTS FOR CALCIUM PYROPHOSPHATE DEHYDRATE (CPPD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asymptomatic Chondrocalcinosis</strong> – This requires no treatment</td>
</tr>
<tr>
<td><strong>Acute CPPD flare</strong> – Relative rest, Joint cooling</td>
</tr>
<tr>
<td>NSAID’s or colchicine (low dose)</td>
</tr>
<tr>
<td>Intra-articular long acting corticosteroid if expertise available</td>
</tr>
<tr>
<td><strong>Chronic with OA</strong> – Treatment as for OA (more inflammatory presentations require further assessment)</td>
</tr>
</tbody>
</table>

**TOP TIPS/PITFALLS IN PATIENTS WITH CALCIUM PYROPHOSPHATE DEHYDRATE (CPPD)**

Presentation with features suggesting crystal inflammation involving the knee, wrist or shoulder of a patient over age 65 years is likely to be acute CPP crystal arthritis.

Most commonly affects knee > wrist > shoulder.

Don’t treat asymptomatic chondrocalcinosis.

CPPD often coexists with osteoarthritis.

Acute CPPD can present with very high CRP and or fever though septic arthritis must always be considered.

Intra-articular corticosteroid (e.g. Triamcinolone or methylprednisolone) is particularly helpful in mono/oligoarticular flare.

**Declaration of competing Interests:** Nothing to declare.
Crystal Arthritis – Gout and Pseudogout

References


Further reading

2. www.ukgoutsociety.org – Excellent patient information sheets including comprehensive dietary advice.