Gout: presentation and management in primary care

Edward Roddy
Clinical Senior Lecturer in Rheumatology, Arthritis Research UK Primary Care Centre, Keele University/Honorary Consultant Rheumatologist, Staffordshire Rheumatology Centre, Haywood Hospital, Stoke-on-Trent

Gout is one of the most prevalent inflammatory arthropathies and is largely managed in primary care in the UK. Recent studies from the UK and Germany estimate the prevalence of gout to be 1.4%. It is much more common in men than women and is the most prevalent inflammatory arthropathy in men. The primary risk factor for the development of gout is an elevated serum urate level, or hyperuricaemia. As urate levels rise and body tissues become supersaturated, monosodium urate (MSU) crystals form in and around joints, leading to clinical gout.

Clinical presentation

After a period of asymptomatic hyperuricaemia, which may last for decades, the first presentation of gout is typically an acute attack of excruciating joint pain associated with swelling, erythema and exquisite tenderness. The onset of symptoms is usually very rapid, taking less than 24 hours to reach peak intensity. The most commonly affected joint is the 1st metatarsophalangeal (MTP) joint, which is the site of the first attack of gout in up to 78% of gout sufferers and is involved at some point in the course of disease in up to 89%.
Other commonly affected joints include the mid-foot, ankle, knee, fingers, wrists and elbows (Figure 1). Axial joints such as the shoulders, hips and spine are rarely affected. Even without treatment, acute attacks typically resolve over a period of 1–3 weeks.

A variable period of time then elapses before the next attack of acute gout occurs (the ‘intercritical’ period). Recurrent attacks become more frequent, occur at different joint sites and may become oligo- or polyarticular. Eventually the patient may develop chronic tophaceous gout characterised by chronic joint symptoms and nodular subcutaneous deposits of MSU crystals (tophi) (Figure 2), with superimposed acute attacks. Tophi typically occur at the toes, Achilles tendons, elbows, fingers and, less commonly, the ear.

**Risk factors for the development of gout**

Several risk factors for the development of gout are recognised. Important life-style factors include obesity, excess alcohol consumption (particularly beer) and dietary factors. Various dietary factors have been suggested to predispose to gout, including red meat, seafood, fructose and sugar-sweetened soft drinks, whereas dairy food, coffee and vitamin C are thought to protect against the development of gout. Hypertension, hyperlipidaemia, insulin resistance, the metabolic syndrome and renal disease are recognised independent risk factors for the development of gout. Gout is therefore associated with an excess burden of cardiovascular disease. Both thiazide and loop diuretics also increase the likelihood of developing gout.

**When to arrange diagnostic tests and imaging**

The most important differential diagnoses of acute gout are septic arthritis and other crystal arthropathies such as pseudogout (calcium pyrophosphate dihydrate crystal deposition). Rapid onset of severe joint pain reaching maximal intensity in less than 24 hours is highly characteristic of crystal arthropathies, with gout being the most likely diagnosis if the 1st MTP joint is affected. Acute pseudogout commonly involves the knee, ankle, shoulder or wrist. The onset of septic arthritis tends to be more insidious. Features of infection such as fever are often absent in septic arthritis and may be a presenting feature of crystal arthropathies, so cannot be relied upon to make a diagnosis. Whenever doubt exists as to the cause of an acutely hot, swollen joint, the affected joint should be aspirated to obtain fluid for crystal examination, Gram stain and culture.
Osteoarthritis (OA) is the most common condition to affect the 1st MTP joint and can sometimes be confused with acute gout. OA usually causes chronic symptoms of pain and stiffness without features of inflammation such as soft-tissue swelling, erythema and marked tenderness.

Serum urate levels should be checked to confirm hyperuricaemia and to monitor response to treatment. However, a degree of caution is required in interpreting the results. Serum urate levels tend to decrease during an acute attack of gout and rise again as inflammation settles. Hence, if the serum urate level is found to be normal during a suspected attack of gout it should be repeated once the attack has resolved. Conversely, as most people with hyperuricaemia do not develop gout, concurrent joint symptoms and hyperuricaemia should not be considered to equate with gout unless the clinical presentation is typical or MSU crystals have been identified on aspirated synovial fluid. Renal function should also be assessed.

Radiographs play a limited role in the diagnosis of gout. In early disease they are usually normal. Later in the course of disease, asymmetrical soft-tissue swelling, joint damage and typical ‘punched-out’ erosions may be seen.

In view of the association of gout with traditional cardiovascular risk factors, the metabolic syndrome and cardiovascular disease, presentation with gout should be regarded as a red flag for cardiovascular risk. Blood pressure, lipids and glucose should be checked and managed appropriately if abnormal.

Management

Treatment of gout is usually considered in two separate phases. The aim of treatment of acute gout is to provide rapid relief from joint pain and inflammation, whereas long-term management aims to lower serum urate levels sufficiently to dissolve existing MSU crystals and prevent formation of new crystals, thereby preventing further acute attacks and irreversible joint damage.

Management of acute gout

The initial drug of choice for acute gout is a non-steroidal anti-inflammatory drug (NSAID) or colchicine. A rapid-acting NSAID, for example diclofenac or naproxen, should be used in full dose, although recent concerns about cardiovascular side-effects of diclofenac have led to GPs in some regions being discouraged from prescribing it. The cardiovascular risk associated with using a short course of diclofenac to treat acute gout is unknown. There is no evidence that any particular NSAID is more effective than any other. Although, historically, indometacin has often been regarded as the NSAID of choice for acute gout, it is best avoided in view of frequent gastrointestinal and renal toxicity. In patients at risk of gastrointestinal complications, co-prescription of an NSAID and proton-pump inhibitor (PPI) or use of the cyclooxygenase-2 (COX-2) selective agent etoricoxib can be considered.

Colchicine is a naturally occurring alkaloid derived from autumn crocus. For acute gout it should be given orally in doses of 0.5 mg 2–4 times daily. Until very recently, the British National Formulary (BNF) recommended the use of colchicine in higher doses, for example 1 mg immediately followed by 0.5 mg every 2–4 hours until pain abates or gastrointestinal side-effects occur. Gastrointestinal symptoms such as diarrhoea and vomiting occur very frequently with such high-dose regimes. Low-dose colchicine, as advocated above, is as effective as high-dose regimes but has fewer gastrointestinal side-effects. Recent editions of the BNF have changed the recommended dose schedule accordingly.

The most effective treatment for acute gout is joint aspiration and injection of intra-articular corticosteroid. Joint aspiration reduces intra-articular hypertension and often brings about immediate relief of symptoms, as well as having the advantage of allowing the diagnosis to be confirmed by identification of MSU crystals in aspirated fluid.

When NSAIDs or colchicine are poorly tolerated or contraindicated, intramuscular or oral corticosteroids, for example prednisolone 20 mg daily, are an appropriate treatment. They are particularly useful when monoarticular attacks occur at sites not readily amenable to joint aspiration/injection, such as the 1st MTP joint or midfoot, or when attacks are oligo- or polyarticular.

Finally, local application of ice-packs to an affected joint can also help to reduce pain and inflammation.
**Long-term management**

The aim of long-term management is to lower serum urate levels below the physiological saturation threshold of urate in body tissues and hence both prevent formation of new MSU crystals and bring about dissolution of existing crystals. The European League Against Rheumatism (EULAR) management recommendations advocate lowering serum urate below 360 μmol/l (6 mg/dl), which has been shown to prevent acute attacks, reduce crystal load and shrink tophi. However, the British Society for Rheumatology (BSR)/British Health Professionals in Rheumatology (BHPR) guidelines recommend a more stringent target of below 300 μmol/l (5 mg/dl), based on the observation that the rate at which tophi reduce in size is directly related to the level to which serum urate is lowered. A sensible compromise between these two recommendations is that a serum urate level of below 360 μmol/l should be the most conservative target for all patients but that lower levels are desirable whenever possible.

Urate-lowering can be achieved by a combination of pharmacological and non-pharmacological measures. Where appropriate, patients should be advised to lose weight and restrict their intake of alcohol (particularly beer) and purine-rich foods such as red meat and seafood. Diuretics should also be stopped where possible, although this may not be feasible if the indication for treatment is cardiac/renal failure rather than hypertension. Patient education is a fundamental part of management and patients should be provided with written information such as the Arthritis Research UK ‘Gout’ booklet.

Urate-lowering therapies (ULTs) are the mainstay of long-term pharmacological management. The most commonly used ULT in the UK is allopurinol, an inhibitor of xanthine oxidase. The indications for ULT are recurrent attacks of gout (three attacks occurring in a 12-month period), tophi, radiographic joint damage and, less commonly, renal urate stones and urate nephropathy. Allopurinol is usually started at a dose of 100 mg daily and escalated in 100 mg increments until target serum urate levels are reached. Hence, serum urate levels should be checked to guide dose escalation approximately 4 weeks after each dose increase. The most common dose in the UK is 300 mg daily, but in many patients this does not achieve target serum urate levels and they may require higher doses. The maximum dose of allopurinol in the UK is 900 mg daily. However, the maximum permitted dose of allopurinol is lower in the presence of impaired renal function, determined by the degree of impairment. In severe renal failure, allopurinol should be commenced at the lower dose of 50 mg daily and increased in 50 mg increments. ULT is usually considered to be lifelong. Serum urate levels should be checked annually once target levels have been achieved.

Allopurinol is usually well-tolerated but can be complicated by a rash, deranged liver function or bone marrow suppression. Rarely, a potentially life-threatening hypersensitivity reaction can occur, characterised by fever, malaise, severe rash and multi-organ failure. This occurs most commonly in patients with renal failure. The most common complication of allopurinol, and indeed all ULTs, is the precipitation of an acute attack of gout. Urate-lowering leads to partial dissolution and shrinkage of MSU crystals, which are more easily shed from articular cartilage into the joint space, leading to acute inflammation. Hence, such acute attacks of gout should be seen as a sign of successful urate-lowering rather than a ‘side-effect’ of ULT.

**BOX 1. Strategies to reduce the likelihood and impact of gout flare following initiation of urate-lowering therapy (ULT).**

- Advise the patient that an attack of gout may occur following initiation of ULT and reassure them that this is a sign that ULT is working.
- ULT should not be stopped if an acute attack of gout occurs.
- If started during an attack of gout, ULT can exacerbate that attack and hence it is customary to wait for 1–2 weeks after an acute attack has resolved before commencing ULT.
- ULT should be started in low dose (e.g. allopurinol 100 mg daily) and escalated gradually, titrated to serum urate levels and renal function.
- NSAID or low-dose colchicine should be co-prescribed with ULT to prevent ULT-induced gout flare and continued until the target serum urate level has been achieved.
A number of strategies exist to reduce the likelihood and impact of a ULT-induced gout flare (Box 1). First, patients should be advised when starting ULT that an acute attack of gout may occur following initiation of ULT and be reassured that this is a sign of successful urate-lowering. The attack should be treated in the same way as any other acute attack and ULT should not be discontinued. Secondly, if commenced during an attack of gout ULT can exacerbate that attack and hence it is customary to wait for 1–2 weeks after an acute attack has resolved before commencing ULT. This approach also allows the patient to be educated about the need for ULT and rationally consider the management options once the pain of acute gout has settled. Thirdly, as outlined above for allopurinol, ULT should be commenced in low doses and escalated gradually until target serum urate levels are achieved. Gradual dose escalation leads to smaller sequential reduction in serum urate levels, more measured MSU crystal dissolution and hence less shedding of crystals into the joint space. Finally, prophylaxis against ULT-induced acute attacks can be provided by the co-prescription of an NSAID (with a PPI if indicated) or colchicine 0.5 mg 1–2 times daily until target serum urate levels have been achieved.

Most gout can be managed successfully in primary care. However, referral to a rheumatologist should be made to consider alternative ULT when allopurinol is not tolerated. Several options for ULT are available in this situation. Febuxostat, a novel xanthine oxidase inhibitor, was approved in 2008 by the National Institute for Health and Clinical Excellence (NICE) for the treatment of people who have both chronic hyperuricaemia and symptomatic gout and are intolerant of allopurinol. Target serum urate levels appear to be achieved more frequently with febuxostat 80 mg and 120 mg than allopurinol at a fixed dose of 300 mg daily, although febuxostat has not been compared to titrated doses of allopurinol recommended as best practice above. Febuxostat appears to be well tolerated although, as with all ULTs, initiation frequently precipitates an acute

---

**Key messages**

- Serum urate levels are frequently normal during an attack of acute gout. A normal serum urate level obtained during an attack should be repeated once the attack has resolved.

- Most hyperuricaemic individuals do not develop gout. Joint symptoms in the presence of hyperuricaemia should not be attributed to gout unless typical of gout or confirmed by monosodium urate crystal identification.

- Gout should be seen as a red flag for associated cardiovascular risk factors and co-morbidity: blood pressure, lipids and glucose should be checked and treated if abnormal.

- The first-line treatment for acute gout is with an NSAID or colchicine. NSAIDs should be fast-acting and used at full dose – indometacin is best avoided. Colchicine is well-tolerated and effective in low doses, e.g. 0.5 mg 2–4 times daily.

- Where appropriate, patients should be advised to lose weight and restrict their intake of alcohol (particularly beer) and purine-rich foods such as red meat and seafood.

- The indications for urate-lowering therapy, most commonly with allopurinol, are recurrent attacks of gout (e.g. three attacks occurring in a 12-month period), tophi and radiographic joint damage.

- Allopurinol is usually started at a dose of 50–100 mg daily and escalated in 50–100 mg increments until the target serum urate level of <360 μmol/l is reached.

- Many patients require a higher dose than the ‘standard’ dose of 300 mg daily, guided by renal function, to achieve target serum urate levels.

- Allopurinol should not be stopped if an acute attack occurs following initiation. Strategies to reduce the impact and likelihood of an attack after starting allopurinol can be found in Box 1.
attack of gout. It undergoes hepatic metabolism and does not require dose reduction in patients with renal impairment. Its use in patients with severe renal failure, ischaemic heart disease and congestive cardiac failure is not currently recommended. Other options for ULT in patients intolerant of allopurinol include uricosuric drugs such as sulfinpyrazone, probenecid and benz bromarone, or oral desensitisation to allopurinol.

**Conclusion**

Gout is the most prevalent inflammatory arthropathy in men and in most cases can be managed successfully and safely in primary care. Presentation with gout should be viewed as a cardiovascular red flag and should lead to screening for cardiovascular risk factors. First-line treatment of acute gout should be with an NSAID or low-dose colchicine. Optimal long-term management of gout combines pharmacological and non-pharmacological therapies with the aim of reducing serum urate levels below 360 μmol/l in order to facilitate crystal dissolution and bring about ‘cure’.

**Useful resources and further reading**


**Continuing professional development (CPD) task**

Various aspects of gout management are suitable for clinical audit in primary care. Two examples are:

- audit of serum urate levels in gout patients on ULT, compared to the target of <360 μmol/l
- audit of how many gout patients have had an annual cardiovascular disease risk assessment.
FORTHCOMING AUTUMN 2011

Osteoarthritis – more than just ‘wear and tear’

There has been a sea change in the way that we think about osteoarthritis. Recent years have seen significant advances in evidence-based management and the basic biology of this, the most common rheumatic disease. In recognition of this, the next issues of Hands On and Topical Reviews will be linked around the theme of OA, providing a comprehensive overview of this important topic. Don’t miss them!
Would you prefer to receive our reports in electronic format?

If you enjoy Hands On, Synovium or Topical Reviews but would prefer to view them electronically you can now opt to receive a free email notification as soon as new issues are published.

In addition, Topical Reviews will change to electronic-only distribution after the Summer 2012 issue, so to keep receiving Topical Reviews after this time you must sign up to our email notification list. To do this please go to www.arthritisresearchuk.org/medical-professional-info and follow the link on the right-hand side.

Once you have entered your details you will, at the time of the next issues, receive an email containing links direct to the latest Hands On, Synovium and Topical Reviews, plus a link to the full on-line archive of back issues.

Postal distribution of Hands On and Synovium

If you are a GP please note that, from Autumn 2011 onwards, our postal distribution of Hands On and Synovium to GPs will take place as inserts with the RCGP’s British Journal of General Practice (please look out for Arthritis Research UK’s logo on the cover sheet of their October/November issue). Other, non-GP, audiences will continue to receive these items via our usual mailing house.

If you are a GP and you do not receive the Autumn 2011 issues by post when you previously have done so, we would like to know – please sign up to our postal mailing list or email notification list to keep receiving your copies (see the link above).