Update on the diagnosis and management of gout

Allopurinol is the first-line medication for pursuing the target [serum uric acid] reduction

Summary

- Gout is a common clinical problem encountered by both general and specialist clinicians.
- The key principles in gout management include establishing a definitive diagnosis, the swift treatment of acute attacks, and using urate-lowering therapies appropriately to prevent further attacks and joint damage.
- The gold standard diagnostic tool for gout remains the identification by polarised light microscopy of monosodium urate crystals in synovial fluid or in a tophus.
- Emerging diagnostic imaging techniques and novel therapies show promise in the diagnosis and treatment of gout.
- In most cases, using existing therapies judiciously remains the key determinant of success in managing gout.

Gout is a common clinical problem encountered by both general and specialist physicians. Despite its high prevalence and the availability of safe and effective therapies, the optimal approach to its diagnosis and treatment remains uncertain, as a result of which practice varies between clinicians.[1] In this article, we provide an up-to-date review of the diagnosis and management of gout, and outline recent developments in the literature.

The key principles in gout management are:

- establishing a definitive diagnosis;
- the swift treatment of acute attacks; and
- preventing further attacks and joint damage by using urate-lowering therapies appropriately.

Diagnosis

To establish a definitive diagnosis, monosodium urate (MSU) crystals must be demonstrated by polarised light microscopy in synovial fluid or in a tophus. A clinical diagnosis is possible without synovial fluid analysis, but must be considered only provisional. Individual clinical and laboratory features — such as hyperuricaemia, first metatarsal joint involvement, maximal inflammation within 24 hours and local erythema — are of low diagnostic utility, with two exceptions: a prompt response to colchicine (positive predictive value [PPV], 86%) and the presence of tophi (PPV, 91%).[2]

New imaging techniques have recently been explored as diagnostic alternatives to arthrocentesis and synovial fluid analysis. Dual-energy computed tomography (DECT) uses differences in the attenuation of x-rays with different energy characteristics to identify urate deposits, while the double contour sign (DCS) seen in an ultrasound examination indicates deposition of hyperechoic MSU on the surface of the hyaline cartilage. A recent systematic review identified eight studies (case–control or cross-sectional) that compared the use of DECT or DCS with the gold standard for MSU detection, synovial fluid analysis by polarised light microscopy. The pooled sensitivities for DCS and DECT were 0.83 and 0.87, respectively; the pooled specificities were 0.76 and 0.84.[3] Overall, the evidence for the utility of the newer imaging techniques is promising, but their cost and availability and the current lack of standardisation argue against using them in routine clinical practice at this time.

Treatment of acute attacks

Non-steroidal anti-inflammatory drugs (NSAIDs), low-dose colchicine, and glucocorticoids (oral, intramuscular or intra-articular) are all effective therapeutic options for the management of acute gout. In the absence of clear evidence supporting the superiority of a particular agent, the choice should be determined by patient factors such as age, comorbidities, concomitant medications and personal preference. If used, a low-dose colchicine regimen (1 mg immediately, 0.5 mg 1 hour later) is as effective as traditional higher-dose therapy, and is associated with fewer adverse effects.[4] Novel agents, including the anti-interleukin-1 antibody canakinumab, have been investigated, but are not yet part of the standard management of acute gout.[5]

Urate-lowering therapies

Urate-lowering therapy should be initiated in any patient with established gout who is experiencing frequent acute attacks (generally more than two to three per year), or who presents evidence of tophi, gouty arthropathy, stage 2 chronic renal impairment or nephrolithiasis.[6] In these patients, the core strategy for preventing gout flares and subsequent joint destruction and disability is to reduce the patient's serum uric acid (SUA) levels. An SUA concentration of less than 0.36 mmol/L is the minimum target for reducing the frequency of gout attacks. However, a stricter SUA goal (< 0.30 mmol/L) is recommended for patients with tophi, severe disease or joint damage, as it is associated with more rapid tophus reduction and a longer interval before the recurrence of acute attacks after treatment is stopped.[7]

Allopurinol is the first-line medication for reducing SUA levels because of its efficacy, safety, availability and cost.[8] Monthly up-titration of allopurinol should occur until the target SUA level is achieved, with the maximum dose determined by tolerability rather than renal function.[9,10]

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In patients with renal impairment, a lower starting dose and more gradual up-titration are advisable, but a treat-to-target SUA strategy remains vital.[9]

Second-line agents, such as probenecid, febuxostat and benzbromarone, may be used if allopurinol is not tolerated or the patient's response is inadequate despite appropriate dosing. Febuxostat and benzbromarone are available in Australia under individual hospital-based Special Access Schemes. Febuxostat is a non-purine, non-competitive xanthine oxidase inhibitor that is probably as effective as allopurinol in its ability to lower SUA levels and reduce the frequency of gout flares.[11,12] The uricosuric agent benzbromarone was more effective and better tolerated than probenecid in a single trial.[13] Combining a xanthine oxidase inhibitor with a uricosuric agent can be considered when monotherapy fails to achieve the target SUA level.

Pegloticase is an intravenously administered porcine uricase that has been found to be superior to placebo in achieving target SUA levels, but it is associated with adverse events that include frequent acute gout attacks and anaphylaxis.[14] Phase III trials of a further uricosuric agent, lesinurad, have recently been completed.[15] Neither of these new urate lowering agents are currently approved for use in Australia.

Prophylaxis

When urate-lowering therapy is started, prophylaxis should also be routinely initiated to reduce the risk of disease destabilisation and flares. NSAIDs, low-dose colchicine and low-dose glucocorticoids are all options for prophylaxis, alone or in combination. Novel prophylactic therapies, such as the interleukin-1 inhibitor rilonacept, have not yet been demonstrated to have benefit–risk profiles superior to those of already available agents.[16] The optimal duration of prophylaxis is unclear, but it should be continued at least until the target SUA level is reached; the presence of tophi may warrant its prolongation until they have resolved. Urate-lowering therapy itself should be continued for life, and should not be stopped during acute attacks of gout.

In summary, the gold standard diagnostic tool for gout remains the identification of MSU crystals in synovial fluid or a tophus by polarised light microscopy. Emerging new diagnostic imaging techniques and novel therapies show promise, but in most cases the judicious use of existing therapies remains the key determinant of success in managing gout.

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