Managing gout made easy

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Gout is easy to diagnose and effective treatments are available. Despite this, both patients and doctors often struggle to manage it optimally. In this article, Drs Gibson and McNeil describe three recent cases to outline some simple approaches to managing gout.

John's case

John had suffered from intermittent gout for 10 years. His history was classical with the initial episode located in the first metatarsophalangeal joint. He then experienced increasingly frequent attacks involving his feet, elbows and wrists. John usually took indomethacin during flares and had said that he could not take allopurinol because 'it made things worse'. He refused to take colchicine because in the past, after he had taken colchicine tablets every half hour, he experienced severe diarrhoea within 24 hours. He liked to drink stout beer occasionally and had never received dietary advice to help manage his gout.

On examination, John had tophi involving both olecranon bursae, the dorsum of the left foot and two fingers on his right hand. His serum urate level was 0.59 mmol/L. He did not want to retry allopurinol or colchicine, and was keen to see a surgeon to have the tophi removed.

Matthew's case

Matthew was admitted to hospital with acute severe abdominal pain and was diagnosed with a perforated duodenal ulcer, which was treated surgically. On the fifth postoperative day, he developed acute pain and swelling in his left wrist.

Further investigation revealed that he had a history of gout. Examination of the synovial fluid from his wrist confirmed the diagnosis (urate crystals were present), but excluded sepsis (a Gram stain showed no organisms and a culture was negative). Low dose colchicine 0.5 mg three times daily was started with a gradual resolution of swelling and pain in the wrist over the next week.

After discharge, Matthew's GP prescribed him 300 mg allopurinol daily, after which Matthew developed gout in his hand. Allopurinol was therefore stopped, and colchicine was started again to treat the gout. Allopurinol was restarted when the gout had resolved; however, this reactivated another cycle of allopurinol-induced gout.

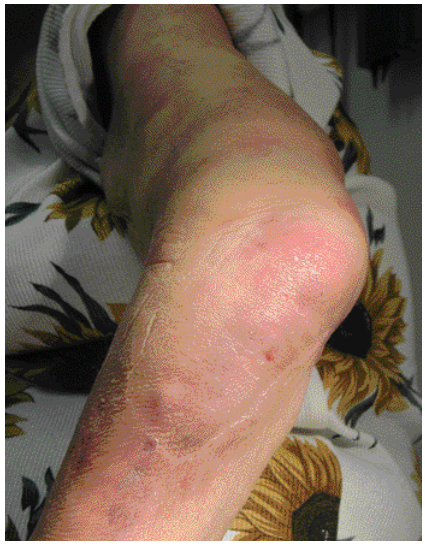

Figure 1. An elbow of a patient with gout showing a tophus with a small discharging wound in the middle of it.

David's case

David was in the intensive care unit requiring management of severe pancreatitis. He had developed pain, swelling and redness over his right first metatarsophalangeal joint, and because of a history of previous attacks of gout, the intensive care unit medical team had made a presumptive diagnosis of gout and had prescribed 0.5 mg colchicine twice daily and 300 mg allopurinol daily.

Within 48 hours, David was intensely distressed having developed polyarticular pain and swelling involving numerous small joints in both his feet, ankles, wrists and left knee. Examination of synovial fluid from his left knee showed numerous urate crystals and a subsequent culture was negative. He was given 50 mg hydrocortisone twice daily and allopurinol was ceased. Over the next 48 hours, the polyarticular gout gradually settled.

Diagnosis of acute gout

Gout is generally a straightforward diagnosis made from a clinical history of recurrent attacks of acute episodic arthritis, with each attack having a rapid onset and a

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Simple rules to follow when prescribing allopurinol

All three cases described in the article illustrate the pitfalls that are often seen in patients who have been prescribed allopurinol. It is almost always the rule rather than the exception that hypouricaemic drugs, such as allopurinol or probenecid, will induce an acute gout flare (as illustrated in Matthew's case). In addition, if these drugs are started during a flare of acute gout they typically exacerbate the patient's condition (as illustrated in David's case).

Occasionally patients develop acute hypersensitivity reactions to allopurinol, such as toxic epidermal necrolysis. These reactions can be life threatening. If a reaction occurs that is thought to be due to allopurinol, this drug should not be readministered to the patient. However, there are reports of successful desensitisation to allopurinol in patients in whom it was considered essential to use this drug again. This should only be undertaken in an appropriate hospital setting. Matthew's case illustrates the application of many of these rules. Once Matthew was reviewed in the rheumatology outpatient clinic, a regimen of 0.5 mg colchicine three times daily was prescribed. He then began 50 mg allopurinol daily and the dose was slowly escalated. Matthew was under instruction to take allopurinol at the same time every day, not to miss a dose and to continue even if the gout recurred.

Simple rules to follow when prescribing allopurinol are summarised below.

- Allopurinol should not be started during an acute episode of gout. There is usually no urgency to start inducing a negative uric acid balance and there is a risk of making the acute attack more severe.[2] It is best to wait until the acute flare has resolved. Very occasionally in patients with severe tophaceous gout, the inflammation is ongoing, therefore treatment with allopurinol in combination with high dose anti-inflammatory agents should be commenced, for example 25 mg prednisolone daily, with close monitoring of the patient's status.
- If possible, coprescribe an anti-inflammatory (e.g. colchicine, corticosteroids or COX inhibitors) when starting allopurinol and when escalating the dose.
- Start allopurinol at a low dose (50 to 100 mg daily) and gradually escalate over one month intervals to achieve the target serum urate level of approximately 0.3 mmol/L.
- Emphasise to patients that allopurinol must be taken regularly, preferably at the same time every day and that days should not be skipped.
- Do not stop allopurinol, even if patients experience an episode of acute gout. Treat the acute attack by starting or increasing the dose of the anti-inflammatory and continue with the same dose of allopurinol.

gradual resolution. John's case illustrates this scenario.

Septic arthritis is the major differential diagnosis to exclude, especially when a single large weight-bearing joint is involved. In these cases, a Gram stain and culture of the synovial fluid and a microscopic examination for the presence of urate crystals should be performed. Matthew and David's cases illustrate this scenario.

Hyperuricaemia is not diagnostic for gout, as up to 25% of patients with proven acute gout have a normal serum uric acid level at the time of the attack, and unrelated hyperuricaemia can be present in patients with alternative causes for joint pain and/or swelling.

Management of acute gout

The goal of management of acute gout is the prompt and safe termination of the acute arthritic event. Despite gout being a common illness, there are few randomised controlled trials examining the optimal management of gout. Recently EULAR (the European League Against Rheumatism) published guidelines for the management of gout based on the available evidence.[1]

The following advice is based on the existing evidence and on the authors' clinical experience. The available pharmacological agents include cyclo-oxygenase (COX) inhibitors (either nonselective inhibitors, e.g. the classical NSAIDs, or the newer COX-2 selective inhibitors), low dose colchicine (Colgout, Lengout) or corticosteroids, the latter given either orally or intra-articularly. The choice of therapy is limited by ensuring the safe treatment of patients with gout.

Nonselective COX inhibitors are generally safe in young patients who do not have a history of peptic ulceration, anticoagulant therapy, or renal or cardiac disease. COX-2 selective inhibitors offer greater safety if the risk of gastrointestinal ulceration is high, but there is no reduction in concern with respect to renal or cardiovascular side effects. Furthermore, the recent withdrawal of lumiracoxib (Prexige) due to severe hepatotoxicity warrants caution when using new COX inhibitors.

Low dose colchicine (maximum dose is 1.5 mg daily) is effective although slower to act. High dose colchicine should not be prescribed because it invariably produces gastrointestinal upset, which may be severe and tends to result in patients, such as John, saying that they will never use it again. Low dose colchicine is often well tolerated and is useful particularly in patients who are unable to tolerate COX inhibitors.

In the authors' experience, if there is no major contraindication, 15 to 20 mg prednisolone (Panafcortelone, Predsolone, Solone) daily, often in combination with low dose colchicine, offers rapid efficacy and is reasonably safe in patients in whom COX inhibitors are contraindicated. Intra-articular corticosteroid therapy is a safe approach in patients who have large joints

Key dietary advice for patients with gout

- Achieve and maintain a healthy body weight as obesity is a risk factor for gout.
- Drink two to three litres of fluid per day to enhance urinary urate excretion.
- Avoid purine-rich foods, such as shellfish, sardines, herring, offal and yeast supplements.
- Limit meat intake to 150 g per day.
- Ensure intake of three serves of low-fat dairy foods per day.
- Limit alcohol intake to two standard drinks per week. Beer should be avoided completely.
- Eat plenty of fruit and vegetables. 'Acidic' foods such as oranges and tomatoes do not cause gout.

Practice points

- Gout is diagnosed from a clinical history of the condition. It is confirmed by finding uric acid crystals in joint fluids, not by high serum uric acid levels.
- Septic arthritis can mimic gout and should be excluded if suspected by joint fluid culture and Gram stain.
- Starting treatment with allopurinol during an acute attack of gout is likely to make it worse.
- Allopurinol should be started at a low dose and gradually escalated to achieve a serum uric acid level of approximately 0.3 mmol/L.
- If possible, give the patient an anti-inflammatory agent until the dose of allopurinol is stabilised.
- If a patient has an attack of gout during escalation of allopurinol therapy, do not stop the allopurinol but add additional anti-inflammatory agents.

involved, have had septic arthritis excluded and cannot use COX inhibitors or oral prednisolone. Matthew's case illustrates the dilemma in which COX inhibitors and corticosteroids were considered too risky because of his peptic ulcer and postoperative state, therefore low dose colchicine was prescribed, sacrificing prompt relief for a safer approach.

Long term management

Gout is due to a chronic imbalance between uric acid production and excretion. It usually takes years for urate crystals to precipitate (due to the production of more uric acid than is excreted, creating a positive uric acid balance) in and around the joints to cause the first attack of gout. In most patients, the problem is a low excretion of uric acid relative to production.

The effective long term management of gout involves creating a negative uric acid balance. This is usually achieved with allopurinol (Allohexal, Allosig, Progout, Zyloprim), an inhibitor of uric acid production, or probenecid (Pro-Cid), which increases uric acid excretion. Both of these treatments should be combined with dietary modifications to reduce purine intake. It will generally take years of a sustained negative uric acid balance to rid the body of excessive urate deposition. The patient will continue to be at risk of acute gout attacks during this period, although the risk will decrease over time.

Hyperuricaemia is an indirect sign of a positive uric acid balance. The aim of hypouricaemic therapy is to establish a negative uric acid balance so that excretion exceeds production. A serum urate level of approximately 0.30 mmol/L should be targeted. This is substantially below the level at which monosodium urate is saturating in extracellular fluids, but such a level is needed to 'desaturate' the body of the excessive urate that has accumulated over many years.

John's case is typical of a less than optimal management scenario, which is frequently encountered. John would have had a positive uric acid balance for years before his first episode of gout, a homeostatic imbalance that continued for a further 10 years with no effective treatment given to him. He received no advice about dietary modifications and attempts to use allopurinol have been unsuccessful, probably because of the lack of patient education and failure to institute an appropriate escalating dosage regimen (see box on page 62). Even though John has had gout for 10 years, his views of treatment are short term; he thinks that his gout will be effectively managed by using indomethacin (Arthrexin, Indocid) for acute attacks and undergoing surgery for removal of the tophi.

Surgical removal of tophi is occasionally indicated if there is sepsis or ulceration, and even less often indicated for diagnostic purposes or to minimise damage to other structures. Unfortunately, there is a high rate of reported complications, including delayed wound healing, and unless the underlying hyperuricaemia is addressed, the tophi will invariably recur.[3]

Our approach to manage John's gout was to:

- provide an explanation about the long term nature and underlying cause of gout
- provide information about dietary factors that can contribute to gout (see box on this page)
- explain how drugs, such as allopurinol, typically induce acute gout when first commenced or when the dose is escalated

continued

- institute allopurinol, starting at 50 mg daily (half of a 100 mg tablet), gradually escalating at one month intervals to 100 mg then 200 mg daily, etc, to achieve a serum urate level of approximately 0.3 mmol/L
- prescribe a preventative anti-inflammatory (e.g. low dose colchicine 0.5 mg twice daily) continuously until a stable dose of allopurinol is achieved and gout flares become infrequent (this often takes six to 12 months). Alternative preventative anti-inflammatory approaches that would be considered for John include prednisolone 5 to 10 mg daily (using the higher dose for a week around the time of allopurinol dosage escalations) or a COX inhibitor (e.g. indomethacin 25 mg twice daily).

Summary

Effective patient education and explanation is time well spent in the overall management plan for gout. Patients need to appreciate the long term nature of how their gout has occurred and the time it will take to restore their uric acid balance. Following some simple rules when prescribing hypouricaemic drugs, such as allopurinol, will avoid problems and improve patient compliance. Practice points for managing patients with gout are listed in the box on page 63. MT

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DECLARATION OF INTEREST: None.

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