An approach to gout: tailoring strategies to difficult situations

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Gout is usually easy to recognise and simple to manage, yet errors in diagnosis and treatment remain common. In this article, Dr McGill describes his approach to difficult management situations.

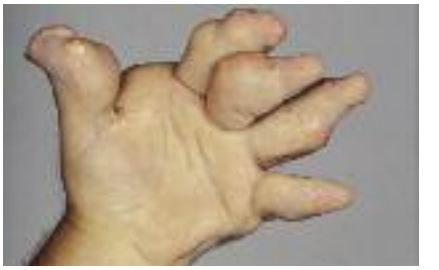

Figure. Severe tophaceous gout.

What is gout?

Gout is a painful metabolic disorder caused by the presence of urate crystals in a joint. Crystal formation requires hyperuricaemia and the correct balance of promotors and inhibitors affecting crystallisation at the site of deposition, and occurs over weeks to months with no immediate clinical effect.

An attack of acute gout is caused by interaction between urate crystals and the inflammatory system – joint pain develops abruptly and is accompanied by redness and swelling. After an attack, the crystals remain in the joint. Tophi usually appear after many years but may appear earlier in the distal interphalangeal joints of postmenopausal women, and irreversible joint damage becomes apparent at about this stage (Figure).

Basic principles of management

The aims of treatment for gout are:

- to settle acute attacks by suppressing the inflammatory response to the urate crystals, and
- to rid the body of the crystals (in those who require prophylactic therapy).

The saturation level of uric acid is about 0.42 mmol/L in plasma and synovial fluid. However, to obtain reasonable rates of crystal dissolution, the level should be maintained below 0.36 mmol/L – even then, the crystals usually take years to dissolve, and patients can continue to suffer attacks in the meantime.

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Diet and lifestyle changes

Dietary modification and lifestyle changes are difficult to achieve but can often reduce the uric acid level by about 15%, and occasionally more. Obesity and excessive alcohol intake are the most important correctable factors. An obese man who drinks heavily and has a uric acid level of 0.45 mmol/L may be able to reduce it below the saturation level with lifestyle and dietary changes alone. On the other hand, a slim person who has two alcoholic drinks each week and a uric acid level of 0.53 mmol/L has no chance of achieving sufficient reduction by dietary means, and pushing for lifestyle changes would be inappropriate in this case.

Treatment for acute gout

Acute gout in patients who are otherwise well will usually be best treated with nonsteroidal anti-inflammatory drugs (NSAIDs), including COX-2 specific inhibitors. Alternative treatments are available for attacks that respond poorly or situations in which NSAID therapy is inappropriate (such as in a patient with peptic ulceration or taking warfarin) – these options include:

- intra-articular corticosteroid, administered after aspiration of the joint to allow crystal identification and to exclude infection
- systemic corticosteroid therapy – either intramuscular injection of tetracosactrin (Synacthen Depot, 1 mg, a synthetic preparation of ACTH) or oral prednisone (Panafcort, Sone, 20 to 40 mg daily in divided doses initially and reducing to zero in 10 to 14 days)
- low dose colchicine (Colgout, 0.5 mg twice daily), a helpful adjunct to prevent recurrence when the effect of the corticosteroid (either injection or short oral course) wears off, and
- high dose colchicine (rarely).

Prophylactic therapy

Although about 90% of patients with gout have impaired renal clearance of uric acid (rather than overproduction), the majority can achieve normouricaemia by inhibiting uric acid production with allopurinol (Allohexal, Allopurinol-BC, Allorin, Capurate, Progout, Zyloprim). A uricosuric drug such as sulfinpyrazone

Table. Indications for long term hypouricaemic therapy*

- Presence of tophi
- Gouty erosions on x-ray
- Persistent joint symptoms between attacks
- A history of uric acid renal calculi
- Failure of acute attacks to settle promptly

* In cases where the diagnosis is confirmed by examination of either synovial fluid or tophus.

(Anturan) or probenecid (Pro-Cid), which increase renal clearance, can also achieve normouricaemia.

Good reasons to begin long term hypouricaemic therapy are listed in the Table. However, if the diagnosis is in doubt, it is better to wait for a further attack to allow joint aspiration and synovial fluid examination to clarify the situation before starting therapy. A poor response to therapy may be due to misdiagnosis: calcium pyrophosphate arthropathy (pseudogout) and an osteoarthritic great toe or bunion can mimic gout in the presence of hyperuricaemia. Conversely, the serum uric acid may be normal in an acute attack.

To achieve good compliance, it is important to explain the need for lifelong therapy and the possibility of continuing attacks over the initial months or even years. Cessation of hypouricaemic therapy will almost always result in recurrent hyperuricaemia followed by recurrent gout over the next couple of years.

Difficult management situations

Acute flares when starting therapy

Flares of acute gout are common in the first weeks of hypouricaemic therapy, and can largely be prevented with low dose colchicine (0.5 mg twice daily or, in sensitive patients, 0.5 mg daily) or continuing NSAID (generally less safe than colchicine). Alternatively, the patient can be warned about flares and asked to commence an NSAID at the first sign.

Acute flares are less likely if the fall in uric acid is gradual, so hypouricaemic therapy should be introduced at a low dose (e.g. 100 mg of allopurinol daily for two weeks followed by a gradual increase until the uric acid level has fallen below 0.36 mmol/L, provided that the dose remains in the safe range). Occasionally, patients find that flares make starting hypouricaemic therapy very difficult – even with a small dose – in these cases, the gout is usually a longstanding problem. Strategies that may help include:

- continuing colchicine (usually 0.5 mg twice daily but a higher dose can be used, if tolerated) plus an NSAID and, occasionally, prednisone (about 10 mg daily)
- using a very small initial dose of hypouricaemic therapy (e.g. 50 mg of allopurinol daily, with slow increases every two to four weeks)
- settling any attack without stopping the hypouricaemic therapy.

Gout in patients with renal failure

Gout in the presence of renal failure is difficult to manage – achieving the ideal uric acid level may not be possible and the risk of drug toxicity is increased. Uricosuric therapy should not be used in those with a history of renal calculi or low urine flow (less than 1.4 L/day), or who overproduce uric acid (over 3.6 mmol/day on a low purine diet or more than 4.8 mmol/day on a normal diet).

Uricosuric therapy is ineffective in the presence of marked renal insufficiency (i.e.

a glomerular filtration rate of less than 30 mL/min). Allopurinol and its active metabolite, oxypurinol, are excreted by the kidney, so the maximal safe dose of allopurinol is reduced in renal insufficiency.

Allergy to allopurinol

Allergy to allopurinol usually presents as an unpleasant skin rash, but it can be life threatening. Consider allopurinol desensitisation only if uricosuric therapy is ineffective or contraindicated and the gout is so severe that prophylactic low dose colchicine is insufficient. In a patient with short life expectancy, low dose colchicine will usually control acute attacks and, although it does not prevent progression of tophi or joint damage, may be the best option for the patient with allopurinol allergy who has other serious disease.

Treatment for coexisting disease

Drug interactions involving hypouricaemic therapies that are worth noting include:

- azathioprine and allopurinol – potentially lethal
- allopurinol and ampicillin/amoxycillin – the risk of rash is about 20%
- probenecid and methotrexate – reduced methotrexate excretion results in potential for increased toxicity
- probenecid and aspirin – the uricosuric effect of probenecid is inhibited by moderate dose aspirin but can be avoided by using low dose aspirin (150 mg daily) or by taking aspirin six hours before or after probenecid.

Severe tophaceous gout

Patients with severe tophaceous gout may benefit from a combined medical and surgical approach. Before removing tophaceous deposits, it is important to reduce the uric acid level below saturation. If a single hypouricaemic drug proves insufficient, sulfinpyrazone and allopurinol in combination is likely to be more effective.

Poor compliance

Other than renal failure, poor compliance is the most common reason for failure of hypouricaemic therapy. The usual clue is marked variability of uric acid levels on treatment, but if doubt persists a brief stay in hospital with supervised drug administration can clarify the problem. Education, not an increase in the drug therapy, is the appropriate response.

Summary

The treatment of acute gout can present problems in some cases (such as in patients with renal failure or peptic ulceration or taking warfarin), but the major obstacle is usually maintaining long term control. Converting correct management decisions to long term success will depend on good compliance – providing the patient with a clear, simple explanation of the pathogenesis of the disease and the rationale behind therapy is the key first step. MT