Chronic gout in the diabetic foot

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Article points

1. Gout is a common disease and, in conjunction with diabetes, can put the foot at high risk of ulceration, as well as amputation.
2. Patients should be advised to optimise their diet and lifestyle, as well as being educated about their condition.
3. Comorbidities must be identified and managed, uric acid-lowering therapy should be offered, and the unnecessary use of urate-raising drugs should be reduced.

Key words

- Amputation
- Diabetic foot
- Gout
- Guidelines
- Rheumatology

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Gout is a form of arthritis that causes attacks of painful inflammation in the joints. A gout attack can occur when uric acid levels in the blood become too high and small crystals of uric acid form. These crystals can collect in the joints, which then cause irritation to the joint tissue, leading to the inflammation and pain experienced during a gout attack. Gout can further complicate the already high-risk diabetic foot, contributing to ulceration and possible amputation. The following article presents a case study of a patient with diabetic foot ulcers, complicated by gout, who subsequently underwent major amputation. Published guidelines and management options are also discussed.

Gout is a type of inflammatory arthritis induced by the deposition of monosodium urate crystals in synovial fluid and other tissues, associated with hyperuricemia (Neogi, 2011). It is a common disease both in primary care and hospital practice (Jordan et al, 2007). The prevalence of gout is increasing in many populations, due mainly to lifestyle changes, comorbidities and increased life expectancy. Epidemiological surveys from the UK suggest that gout is becoming more prevalent. Surveys undertaken in general practice diagnostic indices reported gout prevalence per 1000 of 2.6 in 1975, 3.4 in 1987, and 9.5 in 1993.

Subsequent studies conducted in the UK-General Practice Research Database (UK-GPRD) in 1999 and the IMS Disease Analyzer from 2000 to 2005 both found the prevalence of gout to be 1.4% in the UK (Roddy and Doherty, 2010). Gout is more common in men (30–60 years of age) and in older people. Only 3–6% of people with gout have onset of the disease before 25 years of age (Kim et al, 2003).

Gout is controllable and, although not a simple disease, it is well understood and effective treatments are available. However, the delivery and uptake of medical care for gout remains poor in many places (Arthritis Research UK, 2013). A progressive disorder, untreated gout can be debilitating and result in tophi, chronic arthropathy, and recurrent kidney stones. Although joint aspiration is needed for a definitive diagnosis, the majority of patients are diagnosed presumptively based on medical history and presentation with characteristic signs and symptoms. Patients with gout also often have multiple comorbidities, and there is an increasing body of evidence that shows hyperuricemia is associated with hypertension, diabetes, chronic kidney disease, and heart failure.(Bakris et al, 2014).

Elevation of uric acid levels above the saturation point for urate crystal formation usually results from impaired renal uric acid excretion and, although necessary, it is not sufficient to cause gout (Falidas et al, 2011). Hyperuricemia and gout can be attributed to uric acid-elevating drugs, genetic polymorphisms in genes controlling renal urate transport and predisposing dietary factors, such as consumption of red meat, seafood, alcohol, and fructose-containing soft beverages (Lee et al, 2006). Thiazide and loop diuretics are associated with a higher incidence of gout and gout flares (Singh et al, 2011), as are low-dose aspirin (<1 g) and cyclosporine (Neogi, 2011).

Other conditions associated with the disease include insulin resistance, obesity, congestive heart failure, hypertriglyceridemia, hypercholesterolemia, severe psoriasis, lead toxicity, early menopause, and organ transplantation (Underwood, 2006; Neogi, 2011; Singh et al, 2011).

"Untreated gout can be debilitating and result in tophi, chronic arthropathy, and recurrent kidney stones."

People with gout have high rates of metabolic syndrome and type 2 diabetes compared to individuals without gout (Choi et al, 2007). A study of 292 outpatients in New Zealand reported a prevalence rate for gout of 22% in patients with type 2 diabetes. Prevalence rates varied depending on age and sex and were highest (41%) in men with type 2 diabetes over the age of 65 years (Suppiah et al, 2008). Over time, poorly controlled gout may progress to a chronic phase, characterised by polyarticular attacks, painful symptoms between acute flares, and monosodium urate crystal deposition (tophi) in soft tissues or joints (Neogi, 2011). The presence of tophi (*Figure 1*) can cause pain and dysfunction and, in some cases, ulceration (Patel et al, 2010).

There is little in the medical literature relating to gout in the diabetic foot, yet clinicians specialising within this field will be all too familiar with the presence of gouty tophi within some diabetic foot ulcers, further complicating the management of an already complex condition.

Case study

Mrs X was a 91-year-old woman who had attended a local multidisciplinary diabetic foot clinic periodically for recurrent episodes of diabetic foot ulceration. She had a known history of gout, peripheral vascular disease, insulin-treated type 2 diabetes, atrial fibrillation, chronic renal impairment (stage 4), idiopathic thrombocytopenia, and ischaemic heart disease. On 3 October 2009, she was admitted to hospital with "cellulitis and general decline in health", having been discharged from the hospital diabetic foot clinic with intact feet in July 2009. The foot clinic discharge letter to the GP noted "gouty tophi evident under the skin of some smaller toes".

The community nurse had noted a new haematoma on the sole of the left foot a week earlier on 28 September, which subsequently erupted. The patient was septic on admission and X-ray confirmed osteomyelitis in the left foot. Podiatry review on the ward 5 October noted "ulcer very malodorous … with evidence of extensive gouty tophi …" She was treated with intravenous antibiotics for the infection and referred to the vascular surgeons. She subsequently underwent surgical debridement on 9 October followed by above knee amputation on 16 October. She went on to develop pneumonia and a *Clostridium difficile* infection and died in hospital on 6 December. The family of Mrs X submitted a written complaint to the hospital as they felt her untreated gout had caused her death.

Mrs X's medical notes were reviewed as part of the complaint investigation. When Mrs X had initially been assessed in the diabetic foot clinic in 2002, it was noted that her medical history included gout and that she was being treated with allopurinol 100 mg. Tophi were noted in her foot ulcers, which subsequently healed and she was discharged. Attempts at improving her diabetes control were documented, along with vascular assessment.

On reviewing her records it was noted that at some point the allopurinol had been stopped by the GP, but the reasons for doing this were unknown. Despite the presence of tophi being noted in later assessments in the foot clinic, no action was taken to specifically address the management of the gout.

A written response to the complaint was sent to the family by the hospital, who were also offered the opportunity for a face-to-face meeting with members of the diabetes team – this offer was declined. No further action was taken by the family.

Mrs X's case was subsequently discussed at a diabetes multidisciplinary team meeting, where the team felt that treating the gout was unlikely to have had significant benefits given her very poor health, multiple comorbidities, and already extensive polypharmacy. However, the diabetes team felt that the patient's care had not been optimal, and that as "non-specialists" in the management of gout, further guidance should be sought and local guidelines developed.

Discussion

In 2007, the British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology published a guideline for the management of gout (Jordan et al, 2007) – the aim being to develop concise, patient-focused, evidence-based recommendations for the management of gout for doctors and allied health professionals. The guideline discusses

Figure 1. Severe chronic gout in toe of patient with diabetes. Tophi visible under skin and in wound base lateral aspect of nail.

recommendations for the management of acute gout; diet, lifestyle modification and non-pharmacological modalities of therapy; and the management of recurrent and chronic gout.

NICE has produced a range of Clinical Knowledge Summaries (CKS) for various conditions (NICE, 2008). The CKS for gout includes up-to-date evidence, goals and outcome measures, background information, diagnosis, management, prescribing information, and references.

The following recommendations relate to the management of chronic gout in the diabetic foot. Further guidance on the management of acute gout can be found in the guidelines mentioned above.

Diagnosis

The diagnosis of chronic gout should be based on the clinical history and examination. Septic arthritis and other differential diagnoses should be considered. The presence of tophi will signify chronic gout as they usually take around 10 years to develop. Tophi most commonly occur on fingers and toes. Serum uric acid or plasma urate can confirm hyperuricemia, but the presence of hyperuricemia alone does not equate to a diagnosis of gout. It should also be noted that plasma urate levels fall during an acute attack. Where possible, tophi should be removed from wounds and sent to microbiology for microscopy and culture in a plain pot (no formalin) – this will distinguish between other calcifications that occur in wounds that might not be uric acid crystals/tophi.

An X-ray of an affected joint may be considered to look for chondrocalcinosis (calcification of cartilage within joints) and subcortical cysts, which can be associated with gout.

Management

The clinician again should refer to the full BSR guidelines (Jordan et al, 2007) and the CKS for a comprehensive management approach, but the following summary may be helpful for clinical practice (*Figure 2*).

In general, patients with chronic tophaceous gout should be treated with a xanthine oxidase inhibitor to normalise serum uric acid levels, prevent acute attacks of gout, protect the kidneys and reduce the amount of tophi within the tissues and joints. Allopurinol and febuxostat are the two drugs available – febuxostat should only be used for patients who are intolerant of allopurinol, or for whom allopurinol is contraindicated (NICE, 2008). In some parts of the UK, febuxostat has to be initiated by a specialist. Allopurinol is effective, but it is slow to work – tophi can take months or even years to fully resolve. Tophi can act as a focus for infection, so it is particularly important to try and eradicate them from ulcers in the diabetic foot. Tophi are usually regarded as a clear indication to consider urate-lowering therapy.

Generally, allopurinol therapy should be started low (e.g. 100 mg once daily, and increased weekly by 100 mg per day until serum urate is below 300 µmol/L). The dose can be titrated up to a maximum of 900 mg daily – doses over 300 mg given in divided doses. Febuxostat (80 mg) is to be taken once daily, but can be increased to 120 mg once a day in severe cases – caution is required in patients with estimated glomerular filtration rate (eGFR) of less than 30 mL/minute/1.73m^2.

Starting treatment can be complicated by the paradoxical increased risk of an acute flare, so cover with NSAIDs or colchicine is recommended. The treatment is further complicated in patients with reduced renal function where NSAIDs are relatively contraindicated.

The GP should be encouraged to initiate and titrate allopurinol levels in line with serum urate results. It should be suggested that a specialist referral to a rheumatology service be considered for cases where there is clinical concern and in complicated cases (e.g. the comorbid patient, or where there is a lack of confidence in the original diagnosis).

In terms of lifestyle advice for the individual with gout, recommendations can be found in *Box 1*.

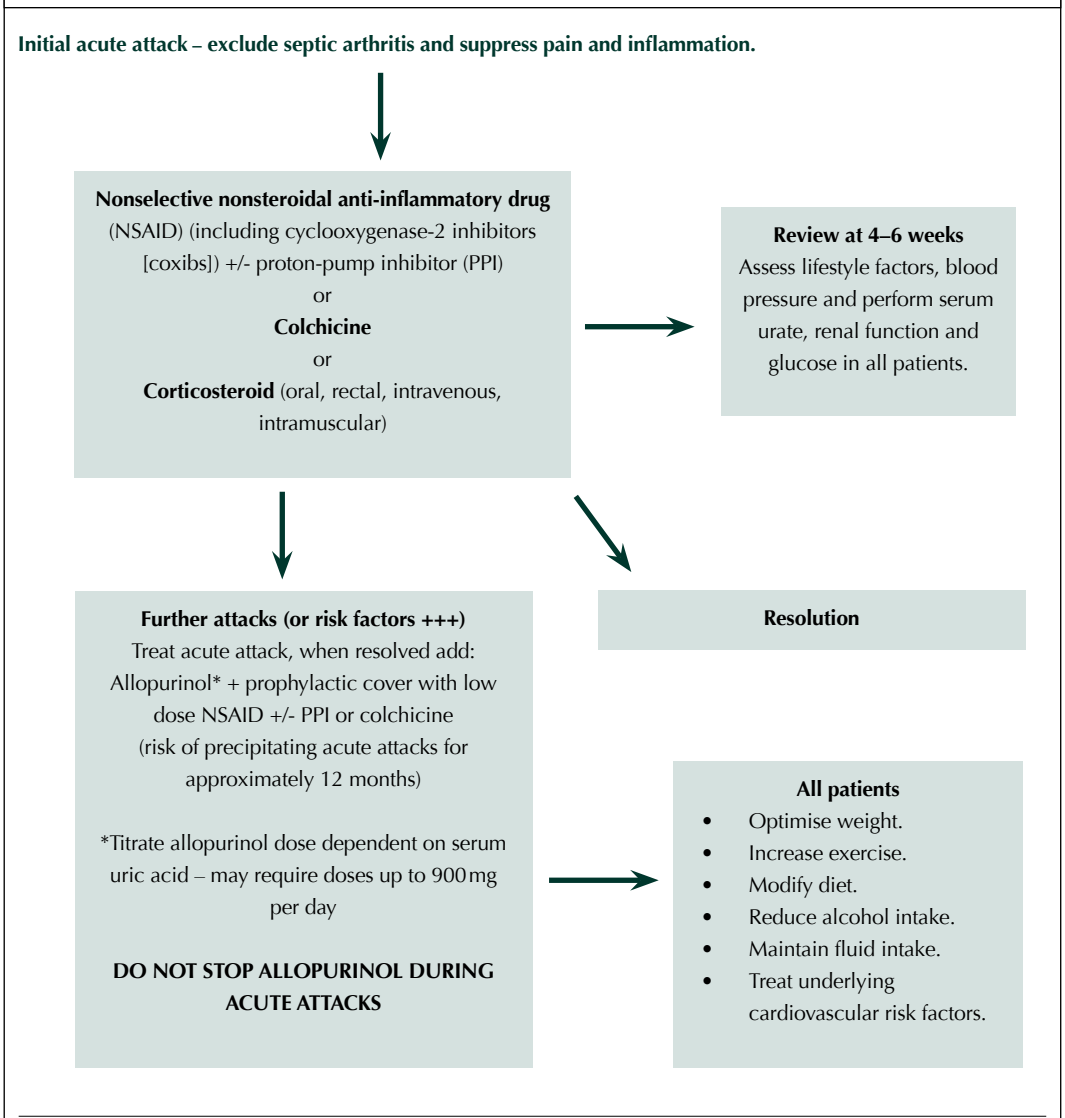
Key messages for clinicians

Clinicians should consider the following key messages when treating individuals with diabetic foot ulcers who have gout:

- The importance of initiating urate-lowering therapy – usually with allopurinol – starting at 100 mg/day and increasing the dose slowly until the target urate level (300 µmol/L) is reached, and monitoring thereafter regularly.

"The diagnosis of chronic gout should be based on the clinical history and examination."

Figure 2. Gout management pathway (adapted from British Society for Rheumatology and British Health Professionals in Rheumatology Guideline for the Management of Gout).



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- Uric acid-lowering therapy should be offered to patients with tophi.
- The importance of patient education with respect to the aims of treating gout and also optimising diet and lifestyle must be stressed.
- Episodes of acute gout must be treated promptly and effectively.
- Comorbidities must be tackled to improve cardiovascular risk.
- The unnecessary use of urate-raising drugs, such as thiazides and loop diuretics, must be reduced.

Conclusion

Gout is a common disease and combined with diabetes can put the foot at high risk of ulceration and subsequent amputation. Management of gout should be considered a high priority in patients with diabetes, particularly where tophi are evident within the foot.

Box 1. Lifestyle advice.

Advise people with gout to:

- Aim for an ideal body weight, but avoid crash dieting and high protein/low carbohydrate diets.
- Eat sensibly – restrict red meat consumption and avoid high-protein intake. Avoid excessive consumption of foods rich in purines (e.g. liver, kidneys, seafood).
- Drink alcohol sensibly – avoid binge drinking and restrict alcohol consumption to 21 units per week for men and 14 units per week for women, with at least two alcohol-free days a week.
- Avoid dehydration by drinking water (up to 2 L per day unless medically contraindicated).
- Drink skimmed milk or consume low-fat dairy products (up to two servings daily).
- Limit consumption of sugary drinks and snacks.
- Take regular exercise, but avoid intense muscular exercise and joint trauma.
- Stop smoking.
- Consider taking vitamin C supplements.

The clinician should also provide written information (e.g. www.scpod.org/foot-health/common-foot-problems/gout), and direct the patient to the support available from the Gout Society (www.ukgoutsociety.org).

Podiatrists are ideally placed to identify gout within the diabetic foot, and should liaise with the patient's GP to diagnose and manage the condition. Referral to a specialist rheumatology clinic should be considered for complex patients who do not respond to first-line therapy with allopurinol.

Since the 2007 BSR guidelines were published, NICE has recommended febuxostat as an option for the management of chronic hyperuricaemia in gout, but only for people who are intolerant of allopurinol or for whom allopurinol is contraindicated (NICE, 2008). Once the course of allopurinol or febuxostat is initiated, treatment is usually lifelong, especially in people at higher risk (i.e. those with renal impairment, gouty tophi, uric acid stones, or those taking long-term diuretics; or those who have recurrent attacks of gout when trying to stop urate-lowering treatment).

A recent study published this year has highlighted the increasing prevalence of gout (Kuo et al, 2014), but reports that the use of urate lowering therapies remains low. Podiatrists are in a unique position to raise awareness and ensure treatment is initiated. ■

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