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FIGURE 1
Despite the insensitivity of radiographs in diagnosing gout, this X-ray shows the degree of damage which can accumulate over 15 years if gout remains untreated.

There is chronic joint damage in the first metatarso-phalangeal joint with complete destruction of cartilage, peri-articular erosions, tophaceous deposits and soft tissue joint swelling. There is a punched out erosion at the second distal interphalangeal joint

What are the consequences of untreated gout?

What are the treatment options?

How should patients be monitored?

GOUT IS THE MOST COMMON INFLAMMATORY ARTHRITIS WORLDWIDE AFFECTING 2.5% OF THE total UK population.[1] Overall it is four times more common in men than women. Although the incidence of gout starts increasing from the age of 30 years, the peak prevalence and incidence in the UK is in those aged 80-84 years, affecting 15% of men and 6% of women in that age group.[1]

Apart from causing extremely painful acute attacks, untreated gout can result in disabling irreversible peripheral joint damage, see figure 1 above, and chronic usage-related pain. Gout is associated with multiple comorbidities such as nephrolithiasis, chronic renal impairment, metabolic syndrome, depression and heart disease. Gout is also associated with increased mortality.[2,3]

‘Gout is the only curable chronic joint disease’

However, gout is curable. The pathogenic agents that cause gout i.e. urate crystals can be eliminated through a combination of effective patient education and evidence-based targeted urate-lowering therapy (ULT).[4,5]

Unfortunately, recent studies suggest that current gout management is usually suboptimal.[1,6] Although 40% of patients in the UK appear eligible for ULT at first presentation, and 85% are eligible within five years of presentation, only 30% of those with gout receive ULT.[7] Furthermore, variance between practices for prescribing ULT ranges between 0% and 100%, suggesting a wide variation in knowledge and »

evidence-based decision making.[7] Such suboptimal management appears to be caused by a combination of both patient and physician misconceptions and barriers to care.[8]

'Untreated gout can result in disabling irreversible peripheral joint damage and chronic usage related pain'

CAUSES

Gout is caused by the precipitation of monosodium urate crystals in and around a joint. This occurs when the body's uric acid levels are chronically elevated above the saturation point at which crystals form. Urate crystals preferentially form in peripheral, cooler joints and especially in those with osteoarthritis.

Urate crystal deposition occurs slowly in and around multiple peripheral joints and will have been building up for some years without causing any symptoms. However, once there is a very high concentration of crystals it is hypothesised that some of these preformed crystals within articular cartilage spill over (crystal shedding) into the joint space and trigger an acute attack of inflammation.

Although much attention is given to acute attacks, continuing slow build up of crystal deposits that slowly expand within cartilage and subchondral bone may also lead to permanent damage to cartilage and bone resulting in symptoms and signs resembling osteoarthritis.

Elevation of uric acid can either be a result of increased production or reduced excretion of uric acid. Increased production is most commonly caused by obesity but can also result from dietary excess of purine-rich food, e.g. red meat and seafood, fructose which is contained in many fizzy drinks, or beer or spirits.

Uric acid is predominantly renally excreted and the common heritable component of gout is now known to result from relative inefficiency of urate excretion. In addition, chronic kidney disease, metabolic syndrome and drugs that reduce renal function, e.g. thiazide diuretics, β-blockers and ACE inhibitors, will all lead to reduced elimination. In an ageing population and with the obesity epidemic, the prevalence of gout is expected to continue to rise.

PRESENTATION

Acute attacks

Patients with gout may present either acutely or with chronic disease in primary care. Acute attacks are characterised by one or more hot, red, swollen joints that are excruciatingly painful. Acute attacks start abruptly and reach their peak within 12-24 hours. Although any joint can be affected, the most common sites of involvement are feet, knees, hands and elbows. Targeting of the first metatarso-phalangeal joints is very characteristic and is known as podagra (seizing the foot).

Chronic gout

Patients with chronic gout can present with monoarthritis but more commonly with asymmetrical polyarthritis or tophi (see figure 2, opposite).

Joints affected by osteoarthritis are preferentially targeted. Subcutaneous tophi can be evident adjacent to affected joints, but occasionally occur elsewhere such as the pinna of the ear.

'Only 30% of patients with gout receive urate-lowering therapy'

Patients may describe a history of previous acute attacks but some people may present with tophi or chronic joint symptoms. There is still a stigma commonly associated with gout. There is an assumption that it is self-inflicted through poor lifestyle (overindulgence in food and alcohol). Women often assume that it is a man's disease.[8] Hence patients may delay presenting to general practice until gout is well established.

CONFIRMING DIAGNOSIS

Diagnosis can be confirmed in primary care by taking a good history and clinical examination. An acute peripheral monoarthritis which reaches its peak within 24 hours and causes 'the worst pain ever experienced' is characteristic of an acute attack.

A patient may have co-existing risk factors for gout such as osteoarthritis, obesity, hypertension, renal impairment, diuretic and antihypertensive drug use or increased beer or spirit consumption.

During an acute attack clinical examination will reveal an exquisitely tender, swollen joint which may be red and warm. In chronic disease asymmetrical polyarticular arthritis may be seen, with or without tophi.

A joint aspiration can be done to confirm the presence of urate crystals on microscopy if you feel you have the skill and confidence to do this. A raised serum uric acid (SUA) can confirm the diagnosis; however, this can be normal in the acute phase.

Radiographs are rarely helpful in showing any characteristic features for gout, but joint ultrasound may demonstrate deposits in cartilage, the synovium and peri-articular sites.

MANAGEMENT OPTIONS

Acute attacks

Acute attacks are recognised to be one of the most painful experiences known and should be managed promptly. All patients should be offered analgesia for the duration of the attack, commenced as early as possible after the first symptoms appear, and advised to place an ice pack over the affected joint.[9]

Low-dose oral colchicine or NSAIDs are recommended first-line treatments.[10] Colchicine has no direct analgesic benefit but one of its many actions is to reduce interaction between crystals and innate immune (inflammasome) response.

It only works effectively if started within 12-24 hours of symptom onset. It can be started at 0.5 mg twice daily and increased if tolerated to three times daily and then to a maximum of 4 times daily. It should be used at 0.5 mg daily in renal impairment. Such dosing should minimise the risk of side effects particularly diarrhoea which is common at higher doses.[11]

An optional 1 mg loading dose followed by 0.5 mg one hour later for the first day (subsequent days 0.5 mg twice to four times daily) can be used.

Colchicine interacts with cytochrome P450 3A4 inhibitors (ciclosporin, ketoconazole, ritonavir, clarithromycin, erythromycin, verapamil extended release (ER), and diltiazem ER)[12] so should be used with caution in patients taking these drugs.

Those taking a statin should stop this temporarily while on colchicine.

NSAIDs should be used at maximal doses in combination with a PPI, but should be used with caution in people with renal impairment or cardiovascular disease.[10] The evidence suggests all NSAIDs are equally effective.[13-16]

'The lower the serum uric acid the faster the rate of crystal dissolution and the sooner the patient is cured'

Cox-2 inhibitors can also be used as an alternative,[17] again with a PPI, but their use is also limited by renal impairment or cardiovascular disease.

Steroids, either orally[18,19] or given as an intramuscular[20] or intra-articular injection,[21] can be used second line where there is a contraindication to NSAIDs or colchicine or inability to tolerate these drugs.

There is no evidence to guide optimal dosage, however one trial found that in patients with an acute attack oral prednisolone 35 mg daily was equivalent in efficacy to oral naproxen 500 mg bd.[19]

Chronic disease

The aim of long-term treatment is to cure gout by reducing the SUA to well below the saturation threshold around 360 μmol/L or 6 mg/dl. This prevents any further crystal formation and gradually dissolves away existing crystals, after which no further attacks occur and further risk of urate crystal joint damage is removed.

The British Society for Rheumatology recommends aiming for a target of below 300 μmol/L[10] but the lower the SUA the faster the rate of crystal dissolution and the sooner the patient is cured.

Full patient information about gout, its risk factors, outcomes and available treatment strategies, and an agreed management plan individualised to the patient's requirements are paramount in achieving this target and maintaining adherence to treatment.[4] Patient information leaflets, for example the one produced by Arthritis Research UK, see Useful information box, p19, can be used to support this process.

Lifestyle modification should be tailored to the patient and it is important to try to reduce the negative perception of gout as a self-inflicted condition. Where appropriate patients should be encouraged to lose weight; reduce intake of high-purine foods such as red meat, offal and seafood,[22] beers, spirits and fructose-rich drinks;[23] stop any retinol supplements[24] and increase intake of cherry and dairy products.[22,25]

For the treatment of hypertension losartan and calcium channel blockers, which are uricosuric and lower SUA, can be used in preference to beta blockers, diuretics, ACE inhibitors and non-losartan angiotensin II receptor blockers, which all increase SUA through reduced renal excretion.[26]

Even when there are modifiable risk factors almost all patients also require, and wish to receive, ULT to cure their gout.[3] ULT can be commenced once the acute attack has settled and the patient can focus on a full discussion of treatment. The recommended first-line therapy is allopurinol, a xanthine oxidase inhibitor.[10] The usual starting dose is 100 mg which should be slowly increased by 100 mg every month to a maximum dose of 900 mg to reduce the SUA to below the target of 300 μmol/L. This requires serial »



FIGURE 2
Chronic tophaceous gout

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key points

SELECTED BY
Dr Peter Saul
GP, Wrexham and Associate GP Dean for North Wales

Gout affects 2.5% of the total UK population and is four times more common in men than women. The peak prevalence and incidence in the UK is in those aged 80-84 years. Untreated gout can result in disabling irreversible peripheral joint damage and chronic usage-related pain. However, gout is curable. The pathogenic agents that cause gout i.e.urate crystals can be eliminated through a combination of effective patient education and evidence-based, targeted urate-lowering therapy (ULT).

Gout is caused by the precipitation of monosodium urate crystals in and around a joint. The crystals preferentially form in peripheral, cooler joints and especially in those with osteoarthritis. It is hypothesised that some of these preformed crystals within articular cartilage spill over into the joint space and trigger an acute attack of inflammation.

Uric acid is predominantly renally excreted and the common heritable component of gout is now known to result from relative inefficiency of urate excretion. In addition, chronic kidney disease, metabolic syndrome and drugs that reduce renal function (e.g. thiazide diuretics, β-blockers and ACE inhibitors) will all lead to reduced elimination.

Patients with chronic gout can present with monoarthritis but more commonly present with asymmetrical polyarthritis or tophi. Joints affected by osteoarthritis are preferentially targeted, the most common sites of involvement are feet, knees, hands and elbows. A raised serum uric acid (SUA) can confirm the diagnosis, however, this can be normal in the acute phase and radiographs are rarely helpful.

Low-dose oral colchicine or NSAIDs are recommended first-line treatments. NSAIDs should be used at maximal doses in combination with a PPI. Colchicine only works effectively if started within 12-24 hours of symptom onset. It interacts with cytochrome P450 3A4 inhibitors and statins should be stopped temporarily.

The aim of long-term treatment is to cure gout by reducing the SUA to well below the saturation threshold. The recommended first-line therapy is allopurinol. The usual starting dose is 100 mg which should be slowly increased by 100 mg every month to a maximum dose of 900 mg. Serial SUA should be checked every 4-6 weeks. After the target has been reached SUA can be measured at three months and then yearly to ensure SUA is maintained below target.

SUA measurements every 4-6 weeks.

A recent study found that the median dose of allopurinol required to achieve cure was 400 mg which is higher than the commonly used fixed dose prescription of 300 mg.[4] Slow upward titration should reduce the risk of developing acute attacks which can occur when commencing ULT.

If patients are not informed about the risk of continuing acute attacks until all the crystals have been eliminated this can reduce adherence to treatment.

Prophylaxis to reduce attack frequency may be considered with either low-dose colchicine or an oral NSAID (plus PPI) for the first few months of treatment. However, one study found that when given a choice, patients preferred to manage acute attacks as required rather than take two drugs simultaneously.[4] The active metabolite (oxypurinol) is excreted via the kidney so lower doses (initially 50 mg daily) should be used in people with marked renal impairment, and because of competition with warfarin for protein binding, slow up-titration with regular checks of the INR is required with occasional requirement to lower the warfarin dose.

‘Patients preferred to manage acute attacks as required rather than take two drugs simultaneously’

The majority of patients, around eight or nine out of ten, tolerate allopurinol without upsets. A very rare side effect of allopurinol is drug hypersensitivity or DRESS (Drug Reaction or Rash with Eosinophilia and Systemic Symptoms). This usually occurs early in treatment in patients with renal impairment commenced straightaway on 300 mg, which is another reason to up-titrate slowly.

Alternative evidence-based options to allopurinol are currently only available through hospital-initiated prescriptions, but once initiated could be maintained in general practice.

Febuxostat (80-120 mg daily) is an alternative xanthine oxidase inhibitor, which is recommended if patients are unable to tolerate allopurinol. It mainly undergoes hepatic metabolism so no dose reduction is required in patients with renal impairment. However, it is only available in two efficient doses and even the lower dose (80 mg) may provoke acute attacks, so prophylaxis with colchicine or an NSAID is recommended.

‘Reducing elevated serum uric acid may reduce cardiovascular risk and CKD progression’

Other alternatives are uricosurics such as benzbromarone (50-200 mg daily), probenecid (250-500 mg bd) and sulfinpyrazone (200-800 mg daily). The uricosurics, although cheap, are currently difficult to obtain because of reduced supply. In the case of benzbromarone concerns have been raised over hepatotoxicity, particularly in Asia, although the reported risk in European populations is low. Nonetheless, monitoring of liver function is recommended where this drug is used.

ULT can be initiated at first presentation to reduce the long-term complications associated with gout.

MONITORING AND FOLLOW-UP

After initiation of ULT patients should be monitored every 4-6 weeks with regular SUA measurements until the SUA is well below the target of 300 μmol/L.

After the target has been reached SUA can be measured at three months and then annually to ensure SUA is maintained below target. Patients may continue to have acute attacks for up to one or two years after successful maintenance of the target SUA, but as long as SUA is maintained below target, attacks should cease, any subcutaneous tophi will resolve (though sometimes leaving small fibrous/scar tissue soft swellings) and quality of life is improved.

Apart from eliminating gout there is growing evidence that reducing elevated SUA may reduce the risk of

cardiovascular events and progression of chronic kidney disease, though currently ULT is not indicated for that purpose (although it is in Japan). Therefore ULT may have other health benefits in addition to eliminating urate crystals.

CONCLUSION

Gout is the only curable chronic joint disease. Cure can be achieved through effective patient education and by using ULT to treat to a target SUA

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Useful information

Arthritis Research UK
Patient information leaflets can be obtained from
www.arthritisresearchuk.org/arthritis-information/conditions/gout.aspx

Arthritis Care
www.arthritiscare.org.uk/LivingwithArthritis/gout-nation-2014

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