LESSON OF THE MONTH

Missed opportunity following diagnosis of gout

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Case report

A self employed decorator developed his first attack of gout, affecting his first metatarsophalangeal (MTP) joint, at age 40. Risk factors were regular beer drinking and a family history of gout in his father; he had no history of urolithiasis, was not obese, and his blood pressure was normal. His general practitioner diagnosed classic podagra, confirmed an increased serum uric acid concentration of 540 $\mu\text{mol/l}$ (normal range in males 100–400 $\mu\text{mol/l}$), and advised reduction of beer intake. Despite elimination of beer drinking, the patient suffered increasingly frequent attacks of podagra and was therefore started on allopurinol 300 mg daily. This reduced his attack frequency and brought his serum uric acid concentration into the normal range. However, over subsequent years he continued to experience attacks (up to six per year) affecting both midtarsal and ankle joints, in addition to first MTP joints. His serum urate concentration was checked on several occasions and found to be normal; his allopurinol dose was therefore not altered.

At age 55 the patient was admitted to hospital with an uncomplicated acute anterolateral myocardial infarction. He had never smoked. He was given thrombolytic therapy and analgesics. On day 3, however, he developed acute florid synovitis with overlying erythema of his left knee. Aspiration yielded 80 ml of turbid fluid; monosodium urate crystals were identified by compensated polarised microscopy; gram stain and culture were negative. His gout attack quickly settled following intra-articular injection of steroid and he was rapidly mobilised. At clinic review six weeks later, his serum urate concentration was 350 $\mu\text{mol/l}$ and a spot urinary uric acid:creatinine ratio supported undersecretor status (that is, it was <0.5); serum concentrations of urea and creatinine, haemoglobin and random glucose concentrations and urine analysis were all normal. His dose of allopurinol was increased to 400 mg in the first instance and he was reviewed six weekly with repeat serum urate estimations. Investigation of fasting lipids and lipoproteins (three months after discharge) revealed markedly increased triglyceride concentrations (6.1 mmol/l), mildly increased cholesterol (6.6 mmol/l) and low HDL-cholesterol. This improved with dietary advice and subsequently by addition of bezafibrate (an isobutyric acid derivative). On a greater allopurinol dose (500 mg daily), his serum urate concentration was maintained less than 250 $\mu\text{mol/l}$. The frequency of acute

attacks gradually diminished and over the past year he has had only one minor episode.

Discussion

RISK FACTORS AND ASSOCIATIONS

At the time of initial diagnosis of gout, both risk factors and disease associations merit consideration and appropriate screening.¹ This man had the common form of 'primary' gout presenting around middle age and relating to renal undersecretion, rather than primary overproduction, of uric acid. There was no chronic use of diuretic drugs or renal impairment to suggest 'secondary' gout. Principal correctable risk factors in men with primary gout are obesity and excess alcohol (especially beer) intake.² Hypertension, hypertriglyceridaemia (especially type IV lipoproteinaemia), and ischaemic heart disease are important disease associations^{2–4} (though hyperuricaemia itself is not an independent risk factor for atherosclerosis). In this non-obese patient, excessive beer intake was correctly identified and addressed. His practitioner checked his blood pressure, but omitted to screen for uric acid overproduction ($<15\%$ of primary gout), renal impairment, or an abnormal lipoprotein profile (present in about 30–75% of men with primary gout^{2–4}). The opportunity was therefore missed for early detection and primary prevention of a major (in this patient the only) correctable risk factor for cardiovascular disease.

TREATMENT OF GOUT

Primary gout is potentially 'curable'. In a patient such as this, the management aim is to abolish attacks and prevent development of chronic tophaceous gout. Modification of lifestyle alone (correction of obesity or alcohol excess) may accomplish this, but addition of hypouricaemic drug treatment is often required. Allopurinol and uricosuric drugs are equally effective in primary undersecretors with normal renal function, though compliance varies. Despite 'normalisation' of serum urate with allopurinol and lifestyle modification, this patient not only continued to suffer acute attacks but recruited new sites of involvement. His treatment was therefore inadequate and his tissue uric acid concentration insufficiently reduced to encourage dissolution of urate crystals and prevention of further crystal formation. The therapeutic aim is to reduce serum urate not just to within normal concentration ranges, but into the mid-lower half of the normal range^{5 6} — well below the

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concentration at which serum urate saturates the extracellular fluid in peripheral tissues. It was only when this was accomplished, by appropriate titration of allopurinol against serum uric acid concentrations, that this patient's gout was effectively controlled. Whilst, in some patients, attacks may be diminished by suboptimal reductions in uric acid, progression of bony tophi may continue,⁷ further advocating the need for more aggressive therapeutic aims. Treatment is effectively life long, but may be modified according to successful alterations in risk factors.⁵

The lesson

In primary gout:

- Lipid (+/-lipoprotein) profiles should be included in the screen for risk factors and disease associations at presentation.
- Correctable risk factors (obesity, alcohol excess) should be identified and addressed.
- Effective treatment usually requires maintenance of serum uric acid concentrations in the lower half of the normal range.

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