

Associate Professor McDonald has received research funding from Air Liquide Health Care and from Boehringer Ingelheim. She has received honoraria for speaking at meetings sponsored by Boehringer Ingelheim, GlaxoSmithKline and the National Prescribing Service. Associate Professor McDonald has received travel sponsorship from GlaxoSmithKline and AstraZeneca and has served on an advisory panel for GlaxoSmithKline.

Self-test questions

The following statements are either true or false (answers on page 83)

1. Anticholinergic bronchodilators are ineffective in chronic obstructive airways disease.
2. Lung volume reduction surgery reduces mortality in patients with widespread emphysema.

Medicinal mishap

Interstitial nephritis associated with omeprazole

Prepared by Chin Soon Ng, Senior Registrar, Department of Clinical Pharmacology, Medical Specialties, Princess Alexandra Hospital, Woolloongabba, Qld

Case

A 62-year-old man presented with acute renal failure. On examination, there were no allergic features such as rash, fever or eosinophilia. Urine examination was normal. Previous renal function was normal. His creatinine peaked at 470 micromol/L. Investigations included tests for anti-neutrophil cytoplasmic and antinuclear antibodies, antibodies against extractable nuclear antigens, double-stranded DNA, complement, hepatitis serology, serum paraprotein concentration and renal ultrasound, all of which were normal. Renal biopsy showed florid interstitial nephritis.

A few weeks earlier, he was diagnosed with *Helicobacter* gastritis and treated with triple therapy (omeprazole, amoxycillin, clarithromycin) followed by omeprazole 40 mg daily. He had previously been taking pantoprazole for dyspepsia. Other medical history included a knee injury six months earlier. This had been treated with diclofenac, which was associated with the development of a rash and was substituted with rofecoxib. The exact duration of treatment with rofecoxib was unclear.

Omeprazole was changed to ranitidine and the man was treated with tapering doses of prednisolone, commencing at 75 mg daily. On examination three years later, his creatinine had improved to 123 micromol/L.

Comment

Acute interstitial nephritis is due to a hypersensitivity reaction and is typically associated with reversible acute renal failure. Drugs account for 71% of cases of acute interstitial nephritis.¹ Medicines commonly implicated include non-steroidal anti-inflammatory drugs (NSAIDs), penicillins, cephalosporins, sulfonamides and proton pump inhibitors. Drug-induced interstitial nephritis is not dose dependent and can recur with

rechallenge. The classic triad for interstitial nephritis of fever, rash and eosinophilia occurs in less than 10% of cases.² Urine examination including microscopy may show haematuria, proteinuria, white cells, casts and eosinophiluria, but may be unremarkable.

Interstitial nephritis may occur with all of the proton pump inhibitors, although most reports to the Australian Adverse Drug Reactions Advisory Committee (ADRAC) have been with omeprazole.³ To date (14 May 2007) ADRAC have 82 reports associated with proton pump inhibitors. Of these cases, 50 were associated with omeprazole, 12 with esomeprazole, 6 with pantoprazole and 14 with rabeprazole. The duration of proton pump inhibitor treatment before presentation is usually between two weeks and nine months.⁴

The temporal relationship in this case suggests that omeprazole was the most likely cause of interstitial nephritis, although the possibility that amoxycillin, pantoprazole or the NSAID were implicated cannot be excluded.

Recommendation

Maintain a high index of suspicion for interstitial nephritis in patients who develop acute renal failure while on a proton pump inhibitor. The diagnosis can only be confirmed on renal biopsy. Management involves drug withdrawal and supportive treatment. The efficacy of corticosteroids has not been demonstrated in controlled trials.⁴

References

1. Baker RJ, Pusey CD. The changing profile of acute tubulointerstitial nephritis. *Nephrol Dial Transplant* 2004;19:8-11.
2. Myers RP, McLaughlin K, Hollomby DJ. Acute interstitial nephritis due to omeprazole. *Am J Gastroenterol* 2001;96:3428-31.
3. Interstitial nephritis with the proton pump inhibitors. *Aust Adv Drug React Bull* 2003;22:7.
4. Torpey N, Barker T, Ross C. Drug-induced tubulo-interstitial nephritis secondary to proton pump inhibitors: experience from a single UK renal unit. *Nephrol Dial Transplant* 2004;19:1441-6.