Medicinal mishap

Interstitial nephritis associated with omeprazole

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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, amoxicillin, 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. 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. 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. 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.

The temporal relationship in this case suggests that omeprazole was the most likely cause of interstitial nephritis, although the possibility that amoxicillin, 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.

References