

# Acute interstitial nephritis caused by two different proton pump inhibitors

## Introduction

Acute interstitial nephritis is an important cause of acute kidney injury and drugs account for about 85% of cases. Since 1992 it has been established that proton pump inhibitors can cause acute interstitial nephritis.

This case report describes a 47-year-old woman who presented with acute kidney injury secondary to proton pump inhibitor (omeprazole) induced acute interstitial

nephritis, with a further episode of acute interstitial nephritis when rechallenged with a different proton pump inhibitor (pantoprazole). Previous case studies have shown that reintroduction of the same proton pump inhibitor caused recurrent worsening of renal function.

This is the first report of acute interstitial nephritis occurring secondary to two different proton pump inhibitors in the same individual. This strengthens the hypothesis that proton pump inhibitor-induced acute interstitial nephritis is a class effect and should raise caution when clinicians consider initiating another proton pump inhibitor in a patient who has previously been diagnosed with proton pump inhibitor-induced acute interstitial nephritis.

## Discussion

Proton pump inhibitors are one of the most commonly prescribed drug classes and, in 2003, the Food and Drug Administration

approved the sale of proton pump inhibitors 'over the counter'. The increased availability of these medications has led to improved awareness and documentation of the side-effect profile. While proton pump inhibitor-induced acute interstitial nephritis is a rare idiosyncratic reaction, the prevalence of proton pump inhibitor prescribing makes it an increasing problem (Sierra et al, 2007).

Proton pump inhibitor-induced acute interstitial nephritis has been well described in many series and four case reports have shown that the renal function deteriorates on reintroduction of the same proton pump inhibitor (Christensen et al, 1993; Badov et al, 1997; Landray et al, 1998; Ra and Tobe, 2004). This article presents the first case of proton pump inhibitor-induced acute interstitial nephritis caused by two different proton pump inhibitors. This is important because it demonstrates that proton pump inhibitor-induced acute interstitial nephritis is a class effect, despite

**Dr Frederick JA Torlot** is Foundation Year 2 Doctor in the Department of Gastroenterology and Hepatology

**Dr Duncan J Whitehead** is Consultant Acute Physician and Nephrologist in the Department of Acute Internal Medicine and Nephrology, Musgrove Park Hospital, Taunton and Somerset NHS Foundation Trust, Taunton TA1 5DA

Correspondence to: Dr FJA Torlot (f.torlot@gmail.com)

## CASE REPORT

A 47-year-old woman was referred to the medical assessment unit with a 5-month history of general malaise, dry cough and anorexia. She had been found to have an elevated serum creatinine level by her GP and referred to the acute medical take. Her past medical history included type 2 diabetes mellitus, Barrett's oesophagus, gastro-oesophageal reflux disease, musculoskeletal back pain and hypertension. Her medications on admission included naproxen, omeprazole and paracetamol. Clinical examination was unremarkable and she was euvolaemic. Her serum creatinine level was 202 µmol/litre at presentation; 5 months previously her serum creatinine concentration had been 50 µmol/litre. Urine dipstick showed a trace of blood and protein. Ultrasonography of the kidney, ureters and bladder indicated normal sized kidneys and no evidence of an obstructed renal system.

A drug-induced acute interstitial nephritis was suspected as the cause of her acute kidney injury. Naproxen and omeprazole were

both stopped. She had a renal biopsy 4 days later, which showed acute interstitial nephritis with eosinophilic nephritis and granulomatous infiltration, features suggestive of a drug-mediated aetiology. The culprit drug was suspected to be omeprazole, which she had been taking regularly for the previous 7 years, so this was stopped. Naproxen had not been taken in the previous 3–4 months and before that infrequently.

Oral prednisolone 60 mg and ranitidine were started. Her gastro-oesophageal reflux symptoms significantly worsened, necessitating prednisolone to be rapidly weaned and stopped over 2 weeks and she was prescribed domperidone. During this period her renal function improved rapidly; her creatinine level fell to 99 µmol/litre 28 days after commencing the prednisolone.

Despite the medication changes her reflux symptoms had a major impact on her sleep and sense of wellbeing. After consulting colleagues in the gastroenterology and nephrology

departments and a review of the literature regarding proton pump inhibitor-induced acute interstitial nephritis, it was agreed that the patient should be tried on pantoprazole. The potential for a relapse of the acute interstitial nephritis was explained to the patient. She proceeded with weekly blood tests to monitor her serum creatinine level and over 14 days this had risen to 125 µmol/litre, although her reflux symptoms had markedly improved. She was otherwise systemically well at that time, and the clinical diagnosis of recurrent proton pump inhibitor-induced acute interstitial nephritis was made and her pantoprazole was immediately stopped. Subsequently her serum creatinine concentration fell over 3 months to 86 µmol/litre, which is now her baseline level (Figure 1).

She was started on famotidine in place of ranitidine as a result of poor symptom control some months later. The gastroenterology team have deemed her Barrett's oesophagus as low risk and she will remain under their surveillance.

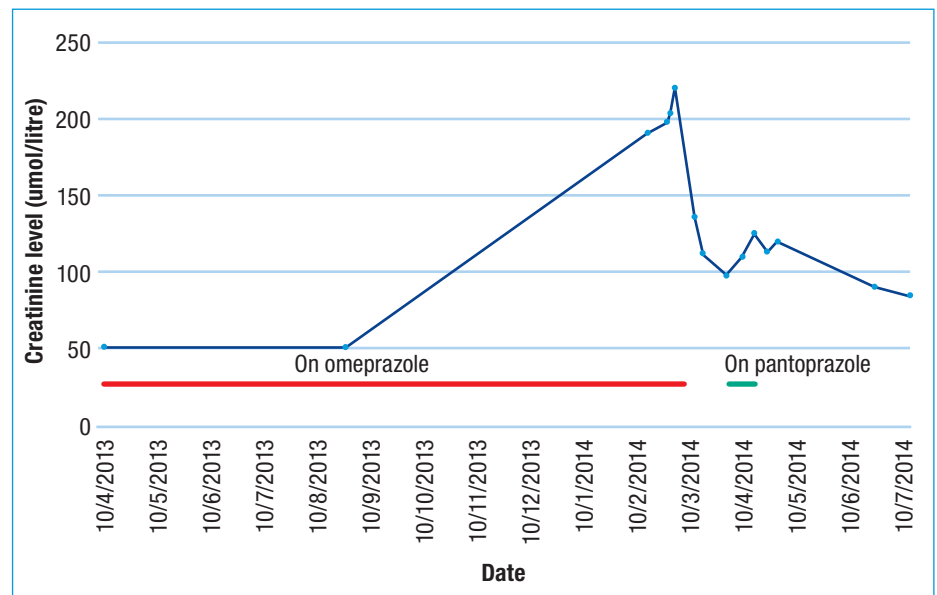
## LEARNING POINTS

- Drug-induced acute interstitial nephritis is an important and easily overlooked cause of acute kidney injury.
- Acute interstitial nephritis is a rare but important side effect of proton pump inhibitor therapy.
- Reintroduction of a different proton pump inhibitor to an individual who has already developed proton pump inhibitor-induced acute interstitial nephritis is likely to cause disease recurrence.

differences in molecular structure between these drugs, and it should caution physicians who are considering reintroducing a different proton pump inhibitor to a patient who has had previously demonstrated proton pump inhibitor-induced acute interstitial nephritis. [BJHM](#)

Badov D, Perry G, Lambert J, Dowling J (1997) Acute interstitial nephritis secondary to omeprazole. *Nephrol Dial Transplant* **12**: 2414–16 (doi: 10.1093/ndt/12.11.2414)

Figure 1. Creatinine levels with proton pump inhibitor exposure.



Christensen PB, Albertsen KE, Jensen P (1993) Renal failure after omeprazole. *Lancet* **341**: 55 (doi: 10.1016/0140-6736(93)92531-W)

Landray MJ, Ringrose T, Ferner RE, Arnold IR (1998) Pyrexia, anaemia and acute renal failure secondary to omeprazole. *Postgrad Med J* **74**(873): 416–18 (doi: 10.1136/pgmj.74.873.416)

Ra A, Tobe SW (2004) Acute interstitial nephritis due to pantoprazole. *Ann Pharmacother* **38**: 41–5 (doi: 10.1345/aph.1D085)

Sierra F, Suarez M, Rey M, Vela MF (2007) Systematic review: proton pump inhibitor-associated acute interstitial nephritis. *Aliment Pharmacol Ther* **26**: 545–53 (doi: 10.1111/j.1365-2036.2007.03407.x)

## Images in Medicine

## Dark necrotic mucosa in sinonasal mucormycosis

**A** 75-year-old man presented with a 2-week history of right-sided orbito-facial pain, epistaxis and nasal obstruction. Nasal endoscopic examination showed a black necrotic nasal mucosa. Pathological examination revealed the diagnosis of mucormycosis. The patient underwent wide endoscopic debridement and received a high dose of liposomal amphotericin B.

Sinonasal mucormycosis is an uncommon devastating fungal infection. The best treatments for mucormycosis are early diagnosis, correction of underlying diseases, proper surgical debridement and aggressive

antifungal agent therapy. Sinonasal mucormycosis should be considered in patients with predisposing factors and manifesting sinonasal findings of necrotic and devitalized tissue. [BJHM](#)

Figure 1. Black necrotic crusts with the fungal spores present at the right middle turbinate, septum and lateral nasal wall.

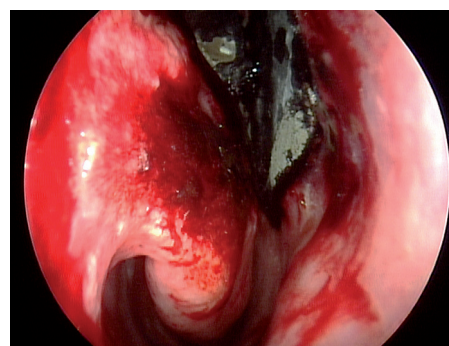
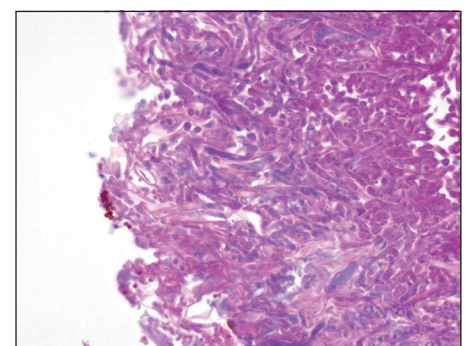


Figure 2. Pathological examination revealed the wide non-septate hyphae with obtuse angled branches. (Periodic acid-Schiff stain, × 400).



**Dr Ju Wan Kang** is Clinical Assistant Professor

**Dr Jeong Hong Kim** is Associate Professor in the Department of Otorhinolaryngology, Jeju National University School of Medicine, Jeju 690-756, South Korea

Correspondence to: Dr JH Kim (jeonghongkimmd@gmail.com)