

Omeprazole Induced Acute Interstitial Nephritis in an Adolescent

Damien Noone^{1*}, Chia Wei Teoh¹, Anthony M Dorman² and Atif Awan¹

¹Department of Nephrology and Transplantation, Children's University Hospital, Temple Street, Dublin, Ireland

²Consultant Renal Pathologist, Department of Renal Pathology, Beaumont Hospital, Dublin, Ireland

*Corresponding author: Damien Noone, Department of Paediatric Nephrology and Transplantation, Children's University Hospital, Temple Street, Dublin, Ireland, Tel: 01 8784200; E-mail: dgnoone@gmail.com

Rec date: Mar 31, 2014, Acc date: Apr 22, 2014, Pub date: Apr 25, 2014

Copyright: © 2014 Noone D, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Proton pump inhibitors (PPIs) have emerged as a common cause of drug induced acute interstitial nephritis (AIN) in adults. We present a 15-year-old girl with severe acute kidney injury and biopsy proven AIN attributable to omeprazole. Withdrawal of the drug and steroid therapy affected a recovery of renal function. As the use of PPIs increases in paediatrics, it is important to be aware of this rare but serious side effect.

Keywords: Omeprazole; Proton pump inhibitors; Acute kidney injury; Nephritis; Interstitial

Introduction

Drug induced nephrotoxicity occurs principally as a result of either direct tubular injury or an acute interstitial nephritis (AIN) [1]. The hallmark of AIN is an inflammatory infiltrate and oedema within the renal interstitium. About 75% of cases are drug related with the remainder related to infectious agents, systemic diseases like sarcoidosis or idiopathic like the tubulointerstitial nephritis and uveitis (TINU) syndrome [2]. Penicillins, and the non-steroidal anti-inflammatory drugs (NSAIDs) have long been known to cause AIN [3]. PPIs are increasingly being recognised as the most common cause of medication related AIN in adults, with an estimated 8 events per 100,000 patient years [4]. In another series, 57% of drug induced AIN cases were attributable to PPIs [3].

The use of PPIs for gastro oesophageal reflux disease in paediatrics is increasing [5]. This rare, but severe adverse event needs to be considered early, and the offending agent withdrawn, to prevent permanent renal damage. We report two cases of biopsy proven AIN attributable to Omeprazole in adolescents, one in a native kidney and the other in a renal allograft. Despite the many cases of PPI induced AIN in the adult literature, PPI induced AIN has not been reported in paediatric patients.

Case Report

A 15 year old girl presented with a three day history of vomiting preceded by a three week history of abdominal pain, anorexia and nausea. She had been taking omeprazole 20 mg once daily for three weeks. For the week prior to presentation she had been taking hyoscine butylbromide 10 mg and domperidone 10mg as required. For two days prior to presentation she took mefenamic acid 500mg three times daily. As a young child she had a history of uncomplicated urinary tract infections but no underlying renal tract abnormality was identified.

She was normotensive, clinically euvolaemic with no oedema, rash or arthritis and non-oliguric. On urinalysis there was 3+ proteinuria, trace blood and 2+ glycosuria.

Investigations confirmed severe AKI (urea 22 mmol/L and creatinine 974 μ mol/L) with metabolic acidosis and anaemia (haemoglobin 9.1 g/L). Her initial serum phosphate was 1.87 mmol/L, calcium 2.23 mmol/L, albumin 30 g/L and PTH 7 ng/L. There was no leucocytosis or thrombocytopenia. Urine microscopy revealed 57 white cells (no red cells). A midstream urine culture was negative. Spot quantitative urinary protein/creatinine ratio was 177mg/mmol and urinary β 2-microglobulin was elevated [61.3 mg/L]. Complement studies were normal. ANA, dsDNA and ANCA were negative. Renal ultrasound showed normal sized kidneys with loss of cortico-medullary differentiation.

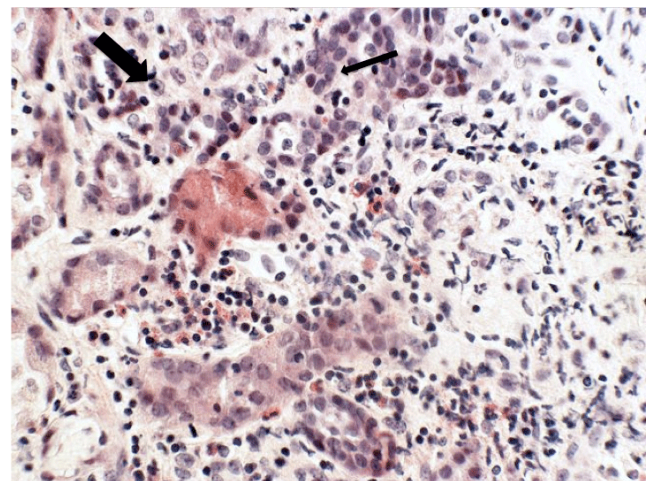


Figure 1: A haematoxylin and eosin stained section (x400) of the cortex which shows interstitial inflammation, lymphocytic tubulitis (thin arrow) and many eosinophils (thick arrow).

Renal biopsy showed diffuse cortical and medullary inflammatory cell (predominantly lymphocytes) infiltration associated with

interstitial oedema (Figure 1). Plasma cells and eosinophils were also present, the latter with focal prominent aggregation. This was associated with multifocal lymphocytic tubulitis and tubule destruction, typical of severe AIN. Glomeruli and blood vessels were normal.

This was presumed secondary to omeprazole which was withdrawn and she was treated with intravenous methylprednisolone 600 mg/m² for three doses followed by prednisolone for a 6 week period (Figure 2). At 3 months, her urinary protein/creatinine ratio had normalised and her creatinine was 94 µmol/L. Her anaemia resolved without specific therapy. At one year her serum creatinine is 65 µmol/L.

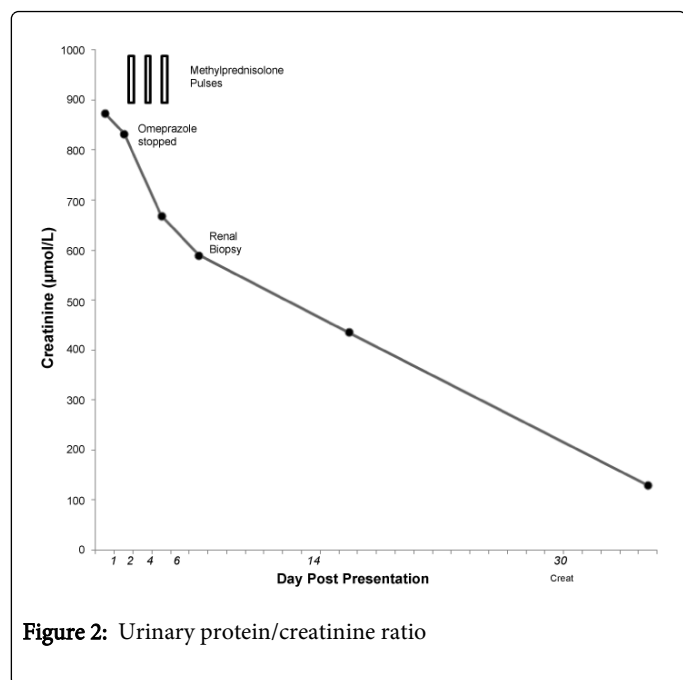


Figure 2: Urinary protein/creatinine ratio

Discussion

Although common in the adult population, this is the first report of PPI induced AIN in the paediatric population to our knowledge. Whether it is rarer in paediatrics or under recognised is not clear.

Medications induce a cell-mediated immune response either after deposition in the interstitium or following integration with a normal component of the tubular basement membrane and behaving as a hapten. Antibody mediated immunity has no role in drug induced AIN and immunofluorescence studies of biopsies are typically negative. The initial lesion is inflammatory, consisting primarily of CD4 positive T lymphocytes. Cytokines induce expansion of the extracellular matrix with fibroblasts, inflammatory cells and eosinophils [2,6].

AIN is unrelated to the dose or duration of treatment of the medication and with regard to PPIs, all members of the class are implicated [4]. Patients with AIN typically present with nonspecific

symptoms like malaise, anorexia, nausea and vomiting as well as AKI and proximal renal tubulopathy as in our patient [7].

Although she had taken hyoscine butylbromide and domperidone, these drugs are not known to cause AIN. Mefenamic acid is associated with AIN but we feel it is very unlikely to have caused such a rise in creatinine and tubulopathy in just two days. NSAID related AIN is usually a more delayed presentation and diagnosed in patients taking the drug for a mean of 6 months [2]. In all patients with drug induced AIN, the mean time from commencing the drug and renal impairment is 10 days [3]. In all patients with drug induced AIN, the mean time from commencing the drug and renal impairment is 10 days [8]. In one large series the median creatinine at presentation was 670 µmol/L, and time to biopsy three and a half weeks, reflecting the common delay in diagnosis of AIN [9].

Steroids are used to treat AIN and may shorten the duration of renal failure but may not affect long-term outcomes [3]. A case report of a patient with Pantoprazole induced AIN suggests that steroids may eradicate the inflammatory infiltrates [7]. In general, a full recovery of renal function is expected upon withdrawal of the offending drug [3,4]. It is important for paediatricians to be aware of this rare but reversible side effect of PPIs, especially as their use in children increases.

References

1. Racusen LC, Solez K (1986) Nephrotoxic tubular and interstitial lesions: morphology and classification. *Toxicol Pathol* 14: 45-57.
2. Praga M, González E (2010) Acute interstitial nephritis. *Kidney Int* 77: 956-961.
3. Torpey N, Barker T, Ross C (2004) Drug-induced tubulo-interstitial nephritis secondary to proton pump inhibitors: experience from a single UK renal unit. *Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association* 19:1441-1446.
4. Sierra F, Suarez M, Rey M, Vela MF (2007) Systematic review: Proton pump inhibitor-associated acute interstitial nephritis. *Aliment Pharmacol Ther* 26: 545-553.
5. Tighe MP, Afzal NA, Bevan A, Beattie RM (2009) Current pharmacological management of gastro-esophageal reflux in children: an evidence-based systematic review. *Paediatr Drugs* 11: 185-202.
6. Ten RM, Torres VE, Milliner DS, Schwab TR, Holley KE, et al. (1988) Acute interstitial nephritis: immunologic and clinical aspects. *Mayo Clin Proc* 63: 921-930.
7. Kim MJ, Heim M, Mayr M (2010) Effect of corticosteroids during ongoing drug exposure in pantoprazole-induced interstitial nephritis. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association* 25:1716-1719.
8. Rossert J (2001) Drug-induced acute interstitial nephritis. *Kidney Int* 60: 804-817.
9. Clarkson MR, Giblin L, O'Connell FP, O'Kelly P, Walshe JJ, et al. (2004) Acute interstitial nephritis: clinical features and response to corticosteroid therapy. *Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association* 19: 2778-2783.