Acute kidney injury in a girl with ulcerative colitis and cytomegalovirus-induced focal segmental glomerular sclerosis

Sankar R. Chirumamilla, Chun He, Lorraine C. Racusen, Ann O. Scheimann, Carmen Cuffari
Baltimore, Maryland, USA

Case report

Background: **Mesalamine or 5-aminosalicylic acid (5-ASA) has proven efficacy in treating patients with ulcerative colitis (UC). Although mesalamine is considered safe, it has been associated with acute interstitial nephritis and renal failure.**

Methods: **Herein we present a case of a child with UC who developed acute renal failure on mesalamine therapy.**

Results: **A 15-year-old African-American girl with well-controlled UC presented to the Johns Hopkins Hospital with a four-day history of high fever, malaise, generalized body aches, and productive non-bloody cough. Over the next three days, she developed acute renal failure with fluid retention, and elevated serum creatinine and blood urea nitrogen. A kidney biopsy showed drug induced acute interstitial nephritis and focal segmental glomerulosclerosis with viral inclusion bodies likely secondary to cytomegalovirus.**

Conclusion: **When treating UC patients with a history of underlying renal disease, it is advised to carefully monitor renal function while on mesalamine therapy.**

World J Pediatr 2013;9(1):84-86

Key words: **cytomegalovirus;**
mesalamine;
renal failure;
ulcerative colitis

Author Affiliations: Department of Pediatrics, The Johns Hopkins University School of Medicine, Baltimore, MD, USA (Chirumamilla SR); Department of Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA (He C, Racusen LC); Department of Pediatrics, Division of Pediatric Gastroenterology and Nutrition, The Johns Hopkins University School of Medicine, Baltimore, MD, USA (Scheimann AO, Cuffari C)

Corresponding Author: Carmen Cuffari, MD, Associate Professor of Pediatrics, The Johns Hopkins University School of Medicine, 600N Wolfe St, Brady 320, Baltimore, MD 21287, USA (Email: ccuffari@jhmi.edu)

doi: 10.1007/s12519-011-0302-8

Introduction

Mesalamine has proven efficacy in treating patients with mild to moderate ulcerative colitis (UC).[1] This topical anti-inflammatory agent contains 5-aminosalicylic acid (5-ASA) that has structural similarities to a number of salicylates compounds that are all well known in causing renal toxicity. While the incidence of 5-ASA induced nephrotoxicity is low (<1%), the severity of drug induced renal injury may vary from asymptomatic pyuria to end-stage renal failure requiring renal transplantation.[2,3] The severity of renal toxicity may also have an idiosyncratic component that is difficult to predict and is associated with a delay in clinical onset of up to 12 months.[4-6] Herein we present a case of acute kidney injury (AKI) in an adolescent female with idiopathic hypertension and UC on maintenance (>3 months) delayed release mesalamine therapy.

Case report

A 15-year-old African-American girl with UC on maintenance 6-mercaptopurine (50 mg/day) and delayed release mesalamine (4.8 mg/day) therapy presented to the Johns Hopkins Hospital (JHH) emergency department with a four-day history of high fever, malaise, generalized body aches, and productive non-bloody cough. Although her physical examination was unremarkable, the patient's serum creatinine was at the upper limit of normal (1.0 mg/dL). After appropriate laboratory and radiological evaluation, including a normal complete blood count, negative blood cultures, and normal chest radiographs, she was discharged with a diagnosis of atypical pneumonia and was prescribed azithromycin therapy. Her past medical history included a diagnosis of idiopathic hypertension at age 13 which was well-controlled on amlodipine therapy. She also had a family history of borderline hypertension in her mother and maternal grandmother, but no family history of UC or renal failure. She had no known allergies.

Over the next three days, her cough worsened, and

fever persisted. She returned to the pediatric emergency department where she was found to be tachycardic (104/min), febrile (39.3°C) and hypertensive (131/65 mmHg). A repeat chest radiograph was normal. On this admission, the levels of blood urea nitrogen (39 mg/dL), creatinine (8.0 mg/dL) and C reactive protein (9.3 mg/dL) were all elevated. The level of serum bicarbonate was 13 meq/L and urinalysis showed proteinuria in the nephritic range. Although all bacterial culture results were reportedly negative, the blood was positive for cytomegalovirus (CMV) by polymerase chain reaction. Both IgM and IgG CMV antibody titers were positive. An abdominal ultrasound showed increased renal echogenicity, and helped guide a renal biopsy using a BARDTH biopsy needle. The biopsy specimen showed acute tubular injury, evidence of protein overload consistent with acute tubular necrosis, and focal segmental glomerular sclerosis (FSGS) (Fig. 1). There was also presumed drug induced acute interstitial nephritis with clusters of eosinophils (Fig. 2).

During the first 3 days after admission, she developed oliguria with edema of both hands and feet, and respiratory failure requiring intubation. Both the levels of serum creatinine (18.3 mg/dL) and blood urea nitrogen (166 mg/dL) increased, ultimately requiring hemodialysis. She remained on prednisone, amlodipine, labetalol, clonidine patch and ganciclovir to treat her presumed acute CMV infection. Under this intense treatment regimen she improved in the following 2 weeks in hospital. The levels of serum creatinine and blood urea nitrogen decreased to 1 mg/dL and 17 mg/dL, respectively; the patient was weaned off ventilator support, and dialysis was terminated. At the time of discharge, she was stable and discharged on oral ganciclovir, labetalol, amlodipine, and prednisone therapy. During her 6-month follow-up, the UC remained in remission.

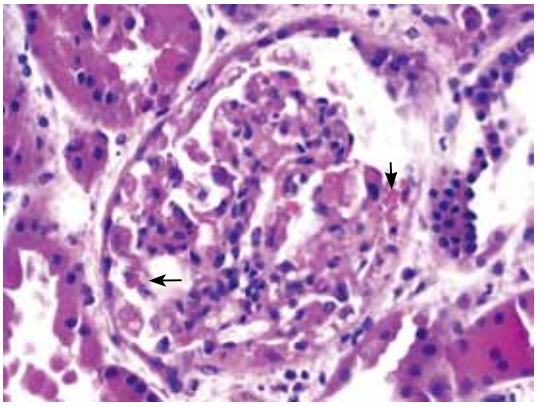

Fig. 1. Photomicrograph of a glomerulus with collapsed capillary loops with prominent podocytes containing numerous protein droplets (arrows) (original magnification × 400).

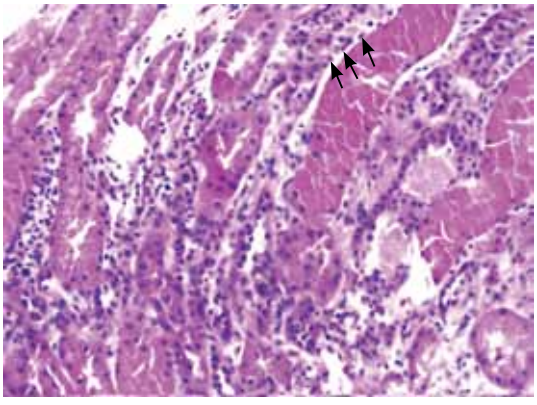

Fig. 2. Photomicrograph of kidney biopsy with interstitial inflammation with cluster of eosinophils (arrows) (original magnification × 400).

Discussion

AKI is characterized by loss of normal fluid and electrolyte function, with increasing serum creatinine and blood urea nitrogen. The most common causes of AKI include acute tubular necrosis, uric acid nephropathy, interstitial nephritis, glomerulonephritis, and vascular lesions. Antibiotics including aminoglycosides and azithromycin have been associated with AKI.[7]

Although the occurrence of interstitial nephritis in patients with inflammatory bowel disease has been mostly associated with sulfasalazine or mesalamine therapy,[2,4,6,8,9] the associated use of azithromycin in our patient cannot be excluded.[7] The precipitous onset of acute renal failure may have also been compounded by CMV-induced FSGS. The underlying pathology behind this adolescent's history of idiopathic hypertension is unclear.

The exact mechanism of mesalamine-induced interstitial nephritis is unclear. This case is most instructive for pediatricians in that clinicians should remain aware of the potential risk of renal injury in patients on salicylate therapy, especially in patients with underlying idiopathic hypertension. Moreover, with the increasing use of anti-metabolite therapy in UC, the risk of CMV infection must be underscored, especially among patients with drug-induced leukopenia. It remains the authors' opinion that all children with UC and suspected renal disease should have serial renal function testing. Moreover, anti-metabolite-induced leukopenia should also be avoided.

Funding: None.

Ethical approval: Written informed consent was obtained from the patient for publication of this case report and accompanying

images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interest: The authors declare that they have no competing interests.

Contributors: Chirumamilla SR, Scheimann AO, and Cuffari C were major contributors in writing the manuscript. He C and Racusen LC performed the histological examination of the renal biopsy and provided valuable comments on histopathology of renal biopsy. Scheimann AO and Cuffari C clinically managed the patient and prepared the final manuscript. All authors read and approved the final manuscript.

References

1 McQuaid Kenneth R. Drugs Used in the Treatment of Gastrointestinal Diseases. In: Katzung BG, eds. Basic & Clinical Pharmacology, 10th ed. New York: McGraw-Hill, 2007: 1009-1041.

2 Agharazii M, Marcotte J, Boucher D, Noël R, Lebel M. Chronic interstitial nephritis due to 5-aminosalicylic acid. Am J Nephrol 1999;19:373-376.

3 Bakris GL, Ritz E; World Kidney Day Steering Committee. The message for World Kidney Day 2009: hypertension and kidney disease: a marriage that should be prevented. J Clin Hypertens (Greenwich) 2009;11:144-147.

4 Haas M, Shetye KR. Acute renal failure in a 53-year-old woman with Crohn's disease treated with 5-aminosalicylic acid. Am J Kidney Dis 2001;38:205-209.

5 Masson EA, Rhodes JM. Mesalazine associated nephrogenic diabetes insipidus presenting as weight loss. Gut 1992;33:563-564.

6 Muller AF, Stevens PE, McIntyre AS, Ellison H, Logan RF. Experience of 5-aminosalicylate nephrotoxicity in the United Kingdom. Aliment Pharmacol Ther 2005;21:1217-1224.

7 Soni N, Harrington JW, Weiss R, Chander P, Vyas S. Recurrent acute interstitial nephritis induced by azithromycin. Pediatr Infect Dis J 2004;23:965-966.

8 Izzedine H, Simon J, Piette AM, Lucsko M, Baumelou A, Charitanski D, et al. Primary chronic interstitial nephritis in Crohn's disease. Gastroenterology 2002;123:1436-1440.

9 Uslu N, Demir H, Saltik-Temizel IN, Topaloğlu R, Gürakan F, Yüce A. Acute tubular injury associated with mesalazine therapy in an adolescent girl with inflammatory bowel disease. Dig Dis Sci 2007;52:2926-2929.

Received February 2, 2011
Accepted after revision September 23, 2011