Case Report

Famotidine-induced acute interstitial nephritis

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Introduction

Drug-induced acute interstitial nephritis has been associated with many medications, particularly antibiotics, non-steroidal anti-inflammatory drugs, analgesics, diuretics and anticonvulsive agents [1]. To our knowledge, we observed the first case of acute interstitial nephritis induced by the histamine H2 receptor antagonist famotidine.

Case

A 72-year-old Japanese man presented to a nearby hospital with epigastric pain. He had a history of hypertension treated with nifedipine. Gastroduodenal endoscopy established gastric cancer with pyloric stenosis and ulcer formation. The patient was referred for treatment of gastric cancer on July 31, 1997. His blood pressure was 124/70 mmHg. Physical examination was normal. Laboratory values on admission were as follows: total protein, 6.3 g/dl; albumin, 3.2 g/dl; blood urea nitrogen, 15 mg/dl; and creatinine, 1.2 mg/dl. Proteinuria and microscopic haematuria were absent on urinalysis; microscopic examination of

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the urine showed no casts. The white blood cell count was 6400/μl, with 61% neutrophils, 30% lymphocytes, 7% monocytes, 1% eosinophils and 1% basophils. Serological studies revealed normal levels of serum C-reactive protein (0.52 mg/dl), immunoglobulins (IgG, 1600 mg/dl; IgA, 218 mg/dl; IgM, 238 mg/dl), and complement components (CH50, 39.4 U; C3, 74.2 mg/dl; C4 28.8 mg/dl). Antinuclear antibody, anti-DNA antibody and cryoglobulin were not detected.

Administration of famotidine (40 mg daily) was initiated on August 1. Ten days later, the results of renal function tests were abnormal (BUN, 15 mg/dl; creatinine, 2.6 mg/dl), and abnormalities rapidly worsened (Figure 1). Urinalysis showed no proteinuria or haematuria, but urinary excretion of β2-microglobulin was increased (2074 μg/l). No fever, rash, arthralgia, myalgia or oliguria were noted. Mild eosinophilia was noted (360/μl), and serologic tests revealed an elevated serum concentration of IgE (591 U/ml).

A percutaneous renal biopsy was performed to determine the cause of non-oliguric acute renal failure. On light microscopic examination, the interstitium appeared somewhat oedematous and showed inflammatory cell infiltration (Figure 2). Tubulitis also was apparent. The inflammatory cells included mononuclear cells and eosinophils. No glomeruli showed mesangial, endocapillary or extracapillary proliferation, and vasculitis was not evident. On immunofluorescence examination, no deposition of IgG, IgA, C3, C1q or fibrinogen was observed in the mesangium or in peripheral capillary walls.

Three weeks following initiation of famotidine, the serum creatinine concentration had reached 8.0 mg/dl. All drugs were discontinued, and 4 days later creatinine had decreased to 6.3 mg/dl. Upon recurrence of epigastric pain from the peptic ulcer, famotidine was restarted at a reduced dose (20 mg daily). Six days after restarting famotidine, the serum creatinine concentration had decreased to 3.5 mg/dl, but subsequently rose again. At that point, intravenous famotidine was replaced with oral acid pump inhibitor therapy (lansoprazole 30 mg daily). Five days after this change, serum creatinine peaked at 7.6 mg/dl, and by 4 weeks after stopping famotidine, serum creatinine had decreased to 1.4 mg/dl (Figure 1).

Discussion

In the present case, the absence of any evidence of collagen vascular disease or systemic or local infection, together with renal histopathological findings including interstitial infiltration by eosinophils, argued for a diagnosis of drug-induced acute interstitial nephritis which was confirmed by laboratory improvement following discontinuation of drugs. Additionally, recurrence of non-oliguric acute renal failure upon re-administration of famotidine and recovery of kidney function following its withdrawal established famotidine as the specific cause. Famotidine, cimetidine and ranitidine are selective histamine H2 receptor antagonists widely used in the treatment of peptic ulcer disease. Cimetidine-induced acute interstitial nephritis is well documented [2] and severe ranitidine-induced acute interstitial nephritis has been described [3–5], but to the best of our knowledge no report of famotidine-induced acute interstitial nephritis has been published. Drug-induced acute interstitial nephritis may be
caused through cellular or humoral immune mechanisms, or both. It has been suggested that delayed hypersensitivity is involved in the genesis of cimetidine-induced acute renal failure [6]. In the present case, interstitial infiltration of mononuclear cells and eosinophils in the renal biopsy specimen, peripheral eosinophilia and elevation of serum IgE suggest an immunological hypersensitivity reaction to the offending drug.

Recovery from drug-induced acute interstitial nephritis upon prompt withdrawal of the responsible agent is the rule. Some reports of acute interstitial nephritis induced by other histamine H₂ receptor antagonists have suggested that steroid administration may improve renal lesions, hasten recovery and permit continuation of histamine H₂ receptor antagonists [3–4,7–10]. In the present case, however, we did not attempt steroid therapy because of the peptic ulcer accompanying his gastric cancer.

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References


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