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LETTERS TO THE EDITOR
EDİTÖRE MEKTUP
Acute tubulointerstitial nephritis due to 5-aminosalicylic acid in a patient with ulcerative colitis and chronic renal failure

Ülseratif kolit ve kronik böbrek yetmezliği tanılı bir olguda 5-aminosalisilik aside bağlı gelişen akut tübülointerstisyel nefrit

To the Editor

A 56-year-old male patient was admitted to our department with a two-week episode of bloody mucous diarrhea occurring 7 to 10 times per day and associated with crampy lower abdominal pain. His past medical history included an elevated blood pressure for the last five years; he had taken antihypertensive therapy (amlodipine 10 mg/day) during this period. In addition, he had been diagnosed as chronic renal failure (CRF) two years ago, and further investigations resulted in a diagnosis of hypertensive nephropathy in the Nephrology Department. He had a serum creatinine level of 2.1 mg/dl in June 2002 and of 2.2 mg/dl in July 2003. His blood pressure had remained in normal limits during the last two years. At admission, his physical examination was unremarkable, with a weight of 63 kg, blood pressure of 135/80 mmHg and pulse rate of 72/min. The laboratory findings were as follows: hemoglobin: 11.2 g/dl, hematocrit: 34%, white blood cell count: 9200/mm^3, platelet: 489x10^3/mm^3, erythrocyte sedimentation rate: 87 mm/h, C-reactive protein: 8 mg/dl, urea: 48 mg/dl, creatinine: 2.1 mg/dl, and creatinine clearance: 35 ml/min. Liver function tests, electrolytes, and urinalysis were normal. Stool culture was negative. Rectosigmoidoscopy was performed which showed mucosal inflammation, friability, excess mucus and ulcerations. Colonoscopy revealed pancolitis.

With the findings above, he was hospitalized with a diagnosis of active ulcerative colitis. Intravenous prednisolone at a dose of 40 mg/day and oral 5-aminosalicylic acid (ASA) (Salofalk) at a dose of 3x500 mg/day were started. On the 6th day of the therapy, while the symptoms settled, the laboratory data revealed a serum creatinine level of 4.2 mg/dl and 1.5 g/day proteinuria. Urinalysis was normal except proteinuria. Rheumatoid factor, antinuclear antibodies, and serology for hepatitis B and C were all negative. C3 and C4 were in normal ranges. Renal ultrasonography showed normal kidneys with no obstruction. 5-ASA was stopped immediately while prednisolone was continued.

Two days after the withdrawal of 5-ASA, the serum creatinine level was 6.3 mg/dl with a creatinine clearance of 12 ml/min. No metabolic acidosis or hyperkalemia was detected, and urine output was almost 1500 ml/day. On the same day, renal biopsy was performed. On light microscopic examination, biopsy samples consisted of cortex containing a total of 14 glomeruli, with none showing glomerular pathological findings. The cortical interstitium showed a mild degree of patchy interstitial mixed type inflammatory cell infiltration, predominantly mononuclear cell (lymphocytic) infiltration (Figure 1). There were a few eosinophils. Mild interstitial edema, tubulitis and some tubular degenerative changes were also observed. Interlobular arteries showed mild intimal arteritis compatible with aging process. The diagnosis was acute tubulointerstitial nephritis (TIN) and was compatible with drug-induced changes. No renal

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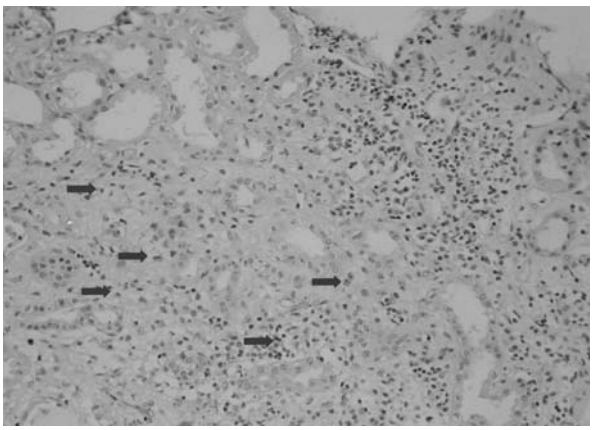

Figure 1. Predominantly mononuclear cell infiltrates and with eosinophils (arrows), edema and mild interstitial fibrotic changes (hematoxylin-eosin; original magnification x 200)

replacement therapy was performed and the creatinine level dropped to baseline (2.2 mg/dl) 11 days after withdrawal of 5-ASA.

Common adverse effects related to 5-ASA include skin reactions, headache, nausea, dyspepsia, pancreatitis and TIN (1, 2). In cases with TIN, withdrawal of 5-ASA leads to restoration of renal function in 85% of cases; however, a trial of high-dose steroid is recommended in patients whose renal function does not respond to drug withdrawal (3). Patients with persisting renal impairment are at risk of end stage renal failure and dialysis dependence (4). Thus, it is recommended that patients under 5-ASA therapy who had a normal baseline creatinine level should be monitored monthly for the first three months, tri-monthly for the next nine months, and annually after five years of treatment (3). However, there is no guideline for monitoring renal functions in patients with creatinine levels over the normal values and using 5-ASA (5). It is well known that patients with CRF are more susceptible of being affected by nephrotoxic agents or prerenal azotemia. In addition, patients with inflammatory bowel disease are usually dehydrated during the acute episode due to diarrhea. Thus, we suggest that renal functions should be monitored closely in patients with high baseline creatinine levels who are under 5-ASA therapy.

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