Acute Interstitial Nephritis Induced by Ethambutol

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Dear Sir,

Drug-induced acute interstitial nephritis is recognized with increasing frequency with antibiotics, diuretics and nonsteroidal anti-inflammatory agents being the more commonly implicated drugs [1]. We report here an unusual case of acute renal failure secondary to ethambutol-induced acute interstitial nephritis.

A 58-year-old woman was admitted with asthenia, anorexia, weight loss and episodes of macroscopic hematuria. Blood pressure was 170/102 mm Hg, hemoglobin 13.8 g/dl with a normal white blood cell count and an erythrocyte sedimentation rate of 90 mm/h; BUN 44 mg/dl (15.7 mmol/l), plasma creatinine 2 mg/dl (177 µmol/l), total serum protein 6.9 g/dl (69 g/l) and albumin 3.4 g/dl (34 g/l). Urinalysis protein was 2.5 g/24 h, 15–20 erythrocytes pmf and 20–25 leukocytes pmf. Urine cultures were negative; Mycobacterium tuberculosis bacilli were identified (Löwenstein) in the urine. She was immediately started on antituberculous treatment: Rifampin 10 mg/kg/day, isoniazid 5 mg/kg/day and ethambutol 15 mg/kg/day. The patient was readmitted to hospital 5 weeks later with fever and generalized cutaneous papuloerythematous lesions as well as oral vesicles. Blood pressure was 150/80 mm Hg; laboratory data at that time revealed a hemoglobin level of 11.3 g/dl with a white blood cell count of $8.3 \times 10^9/l$ (eosinophils $0.9 \times 10^9/l$), BUN 118 mg/dl (42.1 mmol/l), plasma creatinine 4.6 mg/dl (407 µmol/l), total serum protein 6.6 g/dl (66 g/l), albumin 3.2 g/dl (32 g/l). Serum Ig and C values were within normal ranges. The urinary volume was 1.5 liters/day with a urinary protein excretion of 3.5 g/24 h, microhematuria and abundant white blood cells. Fractional excretion of sodium 3.1%. An open kidney biopsy was done showing advanced glomerular sclerosis and a intense interstitial mononuclear cell infiltrate with a discrete degree of interstitial fibrosis. Direct immunofluorescence studies showed no Ig and/or C deposits in the kidney tissue. Treatment with rifampin and isoniazid was stopped, and treatment with prednisone (45 mg/day) was initiated. Three weeks later, and due to the persistence of clinical manifestations as well as renal insufficiency, the administration of ethambutol was suspended. After 2 weeks, the cutaneous lesions disappeared and improvement of renal function was noted with BUN 50 mg/dl (17.8 mmol/l) and creatinine 2.1 mg/dl (186 µmol/l). The patient was

PRED PZM RFP

INH ETB

125

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30 1

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i-∞H

■ y ← r

30

ω 25 0

10

Time, weeks

Fig. 1. Graphical representation of the evolution of acute renal failure and drugs administration.

PRED = Prednisone; PZM = pir-azinamide; RFP = rifampin; INH = isoniazid; ETB = ethambutol;

Biopsy = renal biopsy; PCT = plasma creatinine.

reintroduced to rifampin as well as isoniazid; pirazinamide (25 mg/ kg/dl) was also added.

Improvement continued and urine cultures in Löwenstein medium remained sterile.

It is difficult to elucidate, after the administration of number of different classes of drugs, the agent responsible for an adverse reaction. Nephrotoxicity during treatment with antituberculous drugs has been amply reported, with rifampin being the most frequently implicated agent [2].

Ethambutol may cause neurotoxicity (ocular neuritis), but allergic reactions are extremely rare [3]. To our knowledge, only 2 cases of tubulointerstitial nephritis due to ethambutol

administration have been previously described [4]. As in our case, renal failure occurred after a

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month of treatment, remitted after withdrawal of the drug and further confirmed when the remaining drugs (isoni-azid and rifampin) were reintroduced several months later with no further clinical manifestations. It is our opinion that nephrotoxicity can be excluded as the mechanism responsible for the renal damage because the dose administered (15 mg/kg/day) was below that usually used in the treatment of tuberculous patients [5]. On the other hand, the presence of cutaneous manifestations and eosinophilia strongly suggest a hypersensitivity reaction.

Although most of the acute renal failures occurring in patients treated with antituberculous drugs must be attributed to rifampin administration, we believe ethambutol should also be considered as being possibly an agent with the potential to induce an acute interstitial nephritis.

References

Nephropathies. New York, Churchill Livingstone, 1983, pp 151–185.

Grünfeld JP, Kleinknecht D, Droz D: Acute interstitial nephritis; in Schrier RW, Gottschalk CW (eds): Diseases of the Kidney. Boston, Little Brown, 1988, pp 1461–1487.

Alexander M: Allergic reaction to specific drugs: other antibacterial drugs; in de Week AL, Bundgaard H (eds): Allergic Reactions to Drugs. New York, Springer, 1983, pp 521–557.

Collier J, Joekes AM, Philalithis PE, Thompson FD: Two cases of ethambutol nephrotoxicity. Br Med J 1976;ii:1105–1106.

Iseman MD, Globe M: Treatment of tuberculosis. *Adv Intern Med* 1988;33:235–266.