Acute Tubular Necrosis following Co-Trimoxazole Therapy

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Dear Sir,

We report survival of a patient following a drug reaction to co-trimoxazole. The patient suffered acute tubular necrosis and bone marrow, liver and dermal involvement, including scrotal infarction. Although multisystem involvement [1] and interstitial nephritis are known, there has been only one previous report suggesting acute tubular necrosis [2].

Case Report

A fit 78-year-old man was admitted with a clinical diagnosis of epididymo-orchitis and acute retention of urine. This was confirmed on examination and he also had benign prostatic hypertrophy. There was no significant past history apart from the occasional use of different non-steroidal anti-inflammatory drugs for 'backache'.

A urinary catheter was inserted and he was commenced on flucloxacillin (500 mg/8 h) and co-trimoxazole (2 tablets/12 h). Initial investigations revealed normal electrolytes, blood urea 8 mmol/l (48 mg/dl) and serum creatinine 130 µmol/l (1.47 mg/dl). The haemoglobin was 155 g/l (15.5 g/dl), white cell count $10.6 \times 10^9/l$ (10,600/mm³) and platelet count $164 \times 10^9/l$ (164,000/mm³). Urine microscopy and culture, and blood cultures were negative.

Two days after admission he was noticed to have generalised erythema of the skin, particularly in the groins and inner aspect of the thighs and also extensive purple black discolouration of the scrotum. He was thought to be developing Fournier's gangrene of the scrotum. Co-trimoxazole and flucloxacillin were discontinued, and he was commenced on piperacillin and metronidazole. On the third day after admission it was noted that his urine output had fallen to 187 ml/24 h. Investigations showed a blood urea of 29.3 mmol/l (176 mg/dl), serum creatinine 507 µmol/l (5.74 mg/dl), serum Na⁺ 123 mmol/l (123 mEq/l) and K⁺ 4.5 mmol/l (4.5 mEq/l). There had been no impairment of haemodynamic status since admission, and he had received over 2 litres of fluid the previous 24 h.

Renal ultrasound showed the right and left kidneys to measure 12.6 cm and 12.1 cm in length, respectively. There was no evidence of

Fig. 1. Renal biopsy showing acute tubular necrosis. HE.

obstructive uropathy. It was felt that the deterioration in renal function was drug-induced, and a renal biopsy was performed. This showed acute tubular necrosis (fig. 1). Fixation in absolute alcohol demonstrated no crystals.

The skin rash extended without involving mucous membranes and the appearance was consistent with erythema multiforme. A skin biopsy was performed and did not show any evidence of

vasculitis, the appearances being compatible with a drug eruption. The discolouration of the scrotal skin proceeded to infarction and ulceration, but was confined to a well-demarcated area. In addition to the renal and skin involvement, there was hepatic dysfunction and thrombocytopenia (serum bilirubin 82 $\mu\text{mol/l}$ (4.79 mg/dl), serum aspartate transaminase 49 IU/l, alkaline phosphate 318 IU/l, serum albumin 25 g/l (2.5 g/dl) and platelets $52 \times 10^9/\text{l}$ ($52,000/\text{mm}^3$). Maximum urea and creatinine were 42 mmol/l (252 mg/dl) and 771 $\mu\text{mol/l}$ (8.72 mg/dl), respectively.

He was peritoneally dialysed and renal function gradually improved. The skin rash, liver function tests and platelet count returned to normal over 7–10 days. During dialysis his haemoglobin dropped to 80 g/l (8 g/dl). Serum ferritin, vitamin B₁₂ and folate levels were normal. The anaemia resolved and the scrotal ulcer healed within 2 months.

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Discussion

Acute reactions to co-trimoxazole with multi-system involvement have been previously reported [1]. Although our patient had only 4 doses of co-trimoxazole, the temporal relationship of events and the lack of any other causative factor leads us to believe that a hypersensitivity reaction to 1 moiety of co-trimoxazole was responsible, although an effect of flucloxacillin cannot be ruled out. Scrotal lesions following co-trimoxazole therapy and similar to that seen in our patient have been reported previously [3].

Side effects following co-trimoxazole therapy have been reported in 0.4–8.7% of drug recipients [2]. The majority of side effects are due to blood dyscrasias and skin reactions [4]. Renal toxicity is rare and has been reported mainly in those with underlying renal disease or renal transplants [2].

Acute interstitial nephritis following co-trimoxazole therapy has been frequently reported and there have been reports of favourable outcome following high-dose steroid therapy [5]. There is only one previous report of acute tubular necrosis [2] and the association of acute tubular necrosis with multi-organ involvement has not been reported before.

Early renal biopsy in patients with drug-induced acute renal failure may be useful to clarify the mechanism of renal failure and to suggest treatment modifications, not least to avoid unnecessary steroid therapy.

Morbidity and mortality due to side effects of co-trimoxazole are greater in the elderly patient. Deaths per million prescriptions are 15 times higher in patients aged 65 or over than in those under 40 years of age [4]. Co-trimoxazole should be used cautiously in the elderly and only be prescribed if a safer, acceptable alternative antibiotic is unlikely to be effective.

References

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