Irreversible Renal Failure following Mefenamic Acid

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Dear Sir,

Mefenamic acid has been implicated in a number of reports on acute reversible renal failure [1–10]. Where renal biopsy has been undertaken, interstitial nephritis has been found in some cases [2, 4–7, 9, 10], and on cessation of the drug, an improvement in renal function has been observed. We report a case of irreversible acute renal failure due to interstitial nephritis progressing to interstitial fibrosis following the consumption of mefenamic acid.

Case Report

A 61-year-old male was admitted to hospital for treatment of a prolapsed intervertebral disc, L4/5. Treatment consisted of bed rest and skin traction, and analgesic treatment which included aspirin and mefenamic acid. Approximately 4 weeks later, he was transferred to this hospital for myelography. For 4 days prior to transfer, he had been unwell with diarrhoea and nausea, and had noted a diminution in his urine output.

On arrival he was noted to be ill, slightly dehydrated and oliguric. Blood pressure was 120/80, and there was no evidence of a vasculitis. Serum biochemistry revealed a blood urea of 63.2 mmol/l, serum creatinine 1,573 μ mol/l and urinalysis +++ protein, but no casts. The serum creatinine 4 weeks previously had been within the normal range, and there was no history of analgesic abuse.

Mefenamic acid treatment was withdrawn, and in view of his condition, he underwent emergency haemodialysis. A subsequent renal ultrasound examination revealed two normal-sized kidneys; a renal biopsy was performed, which revealed a dense inflammatory cell infiltrate in the interstitium with fibrosis. There was superimposed tubulorrhectic tubular necrosis with an active tubulitis (fig. 1). The infiltrate involved both the cortex and the medulla, but was heavier in the medulla. The glomeruli displayed mesangial expansion and proliferation. In view of the biopsy findings, prednisolone (60 mg/day) was commenced. The patient remained oliguric and dialysis-dependent and 1 week later sustained an anterior myocardial infarction.

Fig. 1. There is interstitial expansion with a brisk inflammatory infiltrate, early fibrosis and an active tubulitis. The glomerulus displays a mild degree of mesangial expansion and proliferation. HE $\times$ 170.

Fig. 2. The interstitium is diffusely expanded with interstitial fibrosis and minimal cellular infiltrate. Atrophic tubular profiles are identified. The glomerulus displays mild residual mesangial proliferation. HE $\times$ 170.

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He made an uncomplicated recovery from this, but remained oliguric, and in view of this, a second renal biopsy was undertaken 4 weeks later. This revealed that the cellular element of the interstitial nephritis had largely disappeared, but the interstitial fibrosis was diffuse and established with atrophic tubular profiles. There was mild residual mesangial hypercellularity in the glomeruli (fig. 2). In view of the biopsy findings, the steroid treatment was gradually withdrawn, and the patient commenced continuous ambulatory peritoneal dialysis.

Discussion

The nephrotoxicity of mefenamic acid is well recognised, and the clinical picture is usually one of non-oliguric reversible renal failure [1–10]. However, papillary necrosis [1,11] and glomerulonephritis with systemic vasculitis [12] have been documented. In the majority of cases, evidence of renal biopsy indicates an interstitial nephritis; however, in all cases reported, cessation of drug therapy, and in some cases treatment with prednisolone, have resulted in either partial or complete restoration of renal function.

The interstitial changes in the initial biopsy were predominantly cellular, but also included an element of fibrosis. Despite both prednisolone and discontinuation of mefenamic acid, the second biopsy revealed progression to established interstitial fibrosis with tubular atrophy, and the patient remains dialysis-dependent. The treatment reduced the inflammatory cell infiltrate as expected, but did not prevent the progressive fibrosis that occurred, and it is interesting to note that recognisable fibrosis was present in the first biopsy, after some 4 weeks of mefenamic acid therapy. The progression of acute interstitial nephritis to irreversible end-stage renal failure following mefenamic acid treatment has not previously been documented, but resembles one case previously reported, where histological progression to interstitial fibrosis was found to occur following treatment with diclofenac and flurbiprofen [9]. The patient was treated with both aspirin and mefenamic acid, and a summative effect of these two non-steroidal anti-inflammatory drugs cannot be ruled out. Histological features which may predict the progressive interstitial fibrosis are difficult to identify. In contrast to the cases reported by Nicholls et al. [7], where patients regained adequate renal function, the tubular changes are more severe and of a destructive nature.

This case report reiterates the nephrotoxic potential of mefenamic acid, and illustrates the rapid progression of interstitial nephritis to irreversible end-stage renal failure despite treatment with prednisolone and withdrawal of the drug.

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