Progressive Renal Failure despite Discontinuation of Mefenamic Acid

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Dear Sir,

We read the paper by Boletis et al. [1] with interest, we would like to add a similar case and suspect that mefenamic acid may promote the progression to interstitial fibrosis in some cases. A 13-year-old boy was given mefenamic acid (500 mg/day for 1 week and then 750 mg/day) in addition to coumarin in order to control proteinuria (3 g/day) and hypoproteinuria (below 5 g/l). At the age of 5, he was found to have proteinuria. At the age of 8, treatment with dipyridamole and indomethacin was started at another hospital. Proteinuria still continued and he was referred to us. At the age of 11, a renal biopsy was performed and focal segmental glomerulosclerosis was suspected. The above treatment was withdrawn and treatment with glucocorticoid and heparin which followed coumarin and dipyridamole was tried but no response was observed. Before the treatment with mefenamic acid, serum biochemistry revealed a blood urea level of 8.5 mmol/l, serum creatinine 71 μmol/l, serum total protein 4.8 g/l, and 3+ proteinuria without hematuria. During the treatment, urine volume did not decrease compared with that before the treatment and there were no rash or complaints except gastrointestinal upsets which included loose stools, vomiting, and anorexia and resolved spontaneously. Eight months later, an increase in serum creatinine (132 μmol/l) was noticed and mefenamic acid was stopped. However, renal failure progressed gradually (fig. 1).

The nephrotoxicity of mefenamic acid is well known [2,4], and the clinical picture is usually one of nonoliguric renal failure, which is reversed when mefenamic acid is stopped as renal failure due to NSAIDs is generally reversible [5]. Most studies show that NSAID-induced renal failure is due to the diminished renal vasodilatory effect of prostaglandins [5]. However, the mechanism of toxicity in our case seems to be unrelated to inhibition of prostaglandin synthesis since our patient had normal renal function while continuing to take indomethacin, which is a more potent prostaglandin synthetase inhibitor than mefenamic acid.

PSLI

ADτ30ττ3%

J mefenamic acid 750 mg 1

×

Feb.

Apr.

Apr. June

Feb.

June Aug. Oct. Dec.

Fig. 1. Reciprocal of serum creatinine over time. PSL=Prednis-one, ADT = alternate day treatment; Cr = serum creatinine. Arrows denote the time when gastrointestinal upsets were noted.

Renal impairment developed after 8 months of treatment with conventional doses of mefenamic acid. During that time, no rash, colic, or eosinophilia were found.

Renal failure in our case was not as serious as that in previous reports [2–4], since serum creatinine rose from 71 to 131 mol/l and was expected to be reversed with the discontinuation of mefenamic acid. However, the renal failure progressed. This progression may be due to the progression to extensive interstitial fibrosis as reported by Boletis et al. [1].

Renal dysfunction was aggravated (fig. 1), when gastrointestinal upsets were noted retrospectively. This ob-

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servation complements the suggestion of Nicholls et al. [3] and Taha et al. [4]. We should have promptly discontinued the drug when gastrointestinal upsets occurred, although our patient's symptoms resolved spontaneously. Although mefenamic acid has been suggested as being beneficial in the treatment of steroid-resistant focal segmental glomerulosclerosis [6], we should pay much attention to the fact that irreversible renal failure might occur following treatment with mefenamic acid.

References

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