Mefenamic Acid Nephropathy

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Dear Sir,

Analgesic nephropathy has most commonly been attributed to the excessive consumption of analgesic compounds commonly containing aspirin, phenacetin and caffeine. Occasional examples of renal papillary necrosis (RPN) with individual analgesics such as aspirin, indomethacin or phenylbutazone have been described but these are uncommon because individual analgesics are rarely addictive [1].

Mefenamic acid has been reported to cause reversible nonoliguric renal failure [2–6], interstitial nephritis [4–6] and oliguric renal failure associated with glomerulo-nephritis and widespread vasculitis [7]. We report two cases of RPN due to the consumption of mefenamic acid.

Case Reports

Case 1 is a 47-year-old male factory worker who had been consuming mefenamic acid (500 mg) regularly for his gouty arthritis since 1975. His consumption of mefenamic acid had been 3 capsules daily from 1975 to 1977, 10 capsules monthly from 1978 to 1984 and 3 capsules monthly over the past year. All in all, he had had consumed about 4,200 capsules of mefenamic acid. He denied the consumption of other analgesics. In 1977 he developed hypertension and was also operated on for left renal calculus. He presented in May 1985 with hematuria. He had no past history of diabetes or tuberculosis. Investigations showed hemoglobin 12.5 g/dl, urea 7.8 mmol/l, creatinine 200 µmol/l and uric acid 580 µmol/l. Urinalysis showed 2+ protein, $5 \cdot 10^6$ leukocytes and $20 \cdot 10^6$ red cells per liter, no epithelial cells or casts and no organisms on culture. However, repeat urinalysis 2 weeks later revealed no abnormalities. The urine ferric chloride test for aspirin was negative. Intravenous urogram (IVU) showed bilateral papillary necrosis.

Case 2 is a 58-year-old female who presented in December 1984 for recurrent episodes of hematuria of 1 month duration. She has been hypertensive for more than 10 years. She has osteoarthritis of both knees for which she had been consuming about 10 capsules of mefenamic acid (500 mg) weekly for the past 2 years, giving a total of about 1,000 capsules. She denied the consumption of other analgesics. She has had no past history of diabetes or tuberculosis. Investigations showed hemoglobin 12.9 g/dl, urea 7.4 mmol/l, creatinine 120 µmol/l and uric acid 424 µmol/l. Urinalysis showed trace of protein, red cells $200 \cdot 10^6$, no leukocytes, epithelial cells or casts and no organisms on culture. The urine ferric chloride test for aspirin was negative. IVU showed bilateral papillary necrosis.

Discussion

Reversible nonoliguric acute renal failure caused by mefenamic acid has been reported [2–6]. Biopsy-proven interstitial nephritis has been documented in 3 of these patients [4–6]. There has been 1 case report of an acute oliguric renal failure associated with glomerulonephritis with widespread vasculitis [7].

We report here 2 cases of RPN due to the consumption of mefenamic acid alone over a prolonged period (11 and 2 years, respectively). Both patients denied consuming other analgesics and the urine ferric chloride test for aspirin was negative.

Animal experiments have shown that mefenamic acid can cause RPN [8]. Mefenamic acid given to rats in a dose of 100 mg/kg/day produced RPN in 67% of animals in 8–20 weeks [8]. The closely related compound N-phenylanthranilic acid has also been shown to produce RPN in rats [9].

Besides indomethacin, phenylbutazone, fenoprofen, antipyrine and ibuprofen [10], mefenamic acid constitutes yet another nonsteroidal anti-inflammatory agent that can cause RPN.

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