Naproxen-Associated Fatal Acute Renal Failure in Multiple Myeloma

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Dear Sir,

Nonsteroidal antiinflammatory agents (NSAIDs) including naproxen have become a common and accepted measure for treating fever associated with malignancy including myeloma fever [1,2]. Naproxen as well as other NSAIDs are rarely associated with renal abnormalities such as acute renal failure, sodium retention with edema, hyponatremia, hyperkalemia, nephrotic syndrome and acute interstitial nephritis [3]. Until January 1987, in over 10 years of postmarketing experience with naproxen in the USA and over 1.6 billion patient days' exposure, only 19 cases of naproxen-associated renal failure have been reported (Syntex Laboratories). Recently Wu et al. [4] described 2 patients with low back and hip pain who developed acute renal failure after 1 week of treatment with the drug. Later, multiple myeloma was diagnosed in these patients. The authors conclude that multiple myeloma should be added to the list of precipitating factors for developing renal failure in patients who are treated with NSAIDs. Other factors include volume depletion, diuretic therapy, heart failure, liver disease and underlying renal failure.

We present herein a 62-year-old woman with light chain multiple myeloma, osteolytic lesions and hypercalcemia diagnosed in 1983. Between 1983 and 1984 she received irradiation to the involved bones and chemotherapy according to the M-2 protocol [5]. In March 1985, she suffered from a febrile disease treated by intravenous gentamycin. This was followed by transient acute renal failure of which the patient soon recovered completely.

Since then until August 1988 her renal function tests and urinalysis were normal: serum creatinine 1.0 mg/dl and blood urea nitrogen 32 mg/dl. In August 1988 the patient was admitted to the hospital for a prolonged fever of 38–40°C. The fever was attributed to the myeloma since comprehensive investigation did not reveal infection, and a therapeutic trial with broad spectrum antibiotics did not result in defervescence. Treatment with naproxen, 1,000 mg/day, was started followed by immediate return of body temperature to normal levels and marked improvement in the patient's general feeling. Ten days after the initiation of treatment with naproxen, the patient developed asynchronized multiple myoclonic jerks in her face and limbs. Her body temperature was normal; laboratory results revealed signs of acute renal failure: blood urea nitrogen was 265

mg/dl with hyperkalemia and hypercalcemia. One hour after arrival at the emergency room the patient developed severe pulmonary insufficiency and died a short time later.

Postmortem examination revealed pronounced precipitation of large hyaline casts around proximal and distal tubular cells. A few scattered small interstitial foci of nonatypical plasma cells were seen. The glomeruli were normal. Immunoperoxidase staining of paraffin-embedded sections identified the casts as λ -light chains. Congo red staining for amyloid protein was negative. Bone marrow showed massive replacement by atypical plasma cells which stained monoclonally for λ -light chains.

In view of the previous reports [4], and the time relationship between naproxen administration and develop-

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449

Garella S, Matarese RA: Renal effects of prostaglandins and clinical adverse effects of nonsteroidal anti-inflammatory agents. *Medicine* 1984;63:165–181.

Wu MJ, Kumar KS, Kulkarni G, et al: Multiple Myeloma in naproxen-induced acute renal failure. *N Engl J Med* 1987; 317:170–171.

Case DC, Lee BJ, Clarkson BD: Improved survival times in multiple myeloma treated with Melphalan, Prednisone, Cyclo-phosphamide, Vincristine and Bcnu: M-2 Protocol. *Am J Med* 1977;63:897–903.

In the event of renal failure, we feel that our report represents 3 another case of naproxen-associated acute renal failure in multiple myeloma. It demonstrates that naproxen should not be given to myeloma patient even when urinalysis and renal function are normal. Previous reports did not include histopathological kidney studies. The 5 histological finding in our case suggest that a subclinical myeloma kidney could predispose this organ by an unknown mechanism to damage by naproxen.

References

Chang JC, Gross HM: Neoplastic fever responds to the treatment of an adequate dose of Naproxen. *J Clin Oncol* 1985; 3:552–558.

Azeemuddin SK, Vega RA, Kim TH, et al: The effect of naproxen on fever in children with malignancies. *Cancer* 1987; 59:1966–1968.