Case report

Nephrotic syndrome and renal impairment associated with fenclofenac

L. SELLARS,¹ R. WILKINSON,¹ A. R. MORLEY¹ AND R. H. SALTER²

From the ¹Freeman Hospital, Newcastle upon Tyne and the ²Cumberland Infirmary, Carlisle, Cumbria

SUMMARY We report a case of nephrotic syndrome and renal impairment following treatment with fenclofenac. Biopsy showed an interstitial nephritis with minor glomerular changes. Resolution occurred on withdrawal of the drug and treatment with prednisolone.

A 57-year-old man presented with a 4-week history of swelling of the legs. On examination there was oedema of the lower limbs and sacrum. The jugular venous pressure was not elevated, the blood pressure was 220/110 mmHg, and the fundi showed arteriovenous nicking and a few dot haemorrhages. The previous history was negative apart from a painful right hip, for which he had received ibuprofen for approximately 12 months, but this had been replaced by fenclofenac 6 weeks before he developed oedema. He was not taking any other drugs.

On admission plasma creatinine was $422 \mu\text{mol l}^{-1}$, serum albumin 20 g l^{-1} , and urinary protein $10.1 \text{ g } 24 \text{ h}^{-1}$. Differential protein clearance (IgG: transferrin) was 0.59. Urine microscopy showed red cells, white cells, and granular casts. Culture of a midstream specimen of urine was sterile. Haemoglobin concentration was 13.4 g dl^{-1} , white cell count $7.7 \times 10^9/\text{l}$, 82% neutrophils, 18% lymphocytes. Serum C3 was 1.10 g l^{-1} (normal $0.70\text{--}1.80 \text{ g l}^{-1}$), C4 0.43 g l^{-1} (normal $0.14\text{--}0.70 \text{ g l}^{-1}$), IgG 7.50 g l^{-1} (normal $9.50\text{--}16.50$), IgM 2.25 g l^{-1} (normal $0.65\text{--}2.00$), and IgA 2.60 g l^{-1} (normal $0.90\text{--}4.50$). Tests for rheumatoid factor and antinuclear factor were negative. Random blood glucose was 12.8 mmol l^{-1} , and an oral glucose tolerance test confirmed mild diabetes mellitus. Chest x-ray revealed a right pleural effusion, and intravenous urogram was normal.

Renal biopsy was performed, and under light microscopy some glomeruli showed moderate mesangial increase. The basement membranes appeared nor-

mal or showed early wrinkling. There was mild interstitial oedema, and the proximal tubules showed marked dilatation, osmotic vacuolation, and hyaline droplet change. There was an interstitial infiltrate of lymphocytes, plasma cells, and occasional eosinophils. Immunofluorescence microscopy showed trace amounts of IgA in the mesangium and of fibrin and C3 in peripheral capillary loops. Electron microscopy showed no evidence of glomerular immune deposits, but there was basement membrane wrinkling, a little mesangial cell interposition, and moderate foot process fusion.

On this evidence a diagnosis was made of tubulointerstitial nephritis, probably due to fenclofenac. The fenclofenac had been discontinued at presentation, and resolution of oedema was achieved with frusemide and mefruside. After 2 weeks there was no improvement in proteinuria, serum albumin, or plasma creatinine, so treatment with prednisolone 40 mg daily was started. The course taken by serum albumin, creatinine, and proteinuria, together with the daily dose of prednisolone, is shown in Fig. 1.

Discussion

The nephrotic syndrome with impairment of renal function has been previously reported in a patient taking fenclofenac; biopsy revealed mild focal proliferative glomerulonephritis.¹ In our patient the main histological abnormality was interstitial nephritis, the glomeruli showing only slight changes; the quantity and the non-selectivity of the proteinuria indicated a glomerular origin. It is likely that an adverse reaction to fenclofenac was responsible for

Accepted for publication 16 September 1983.

Correspondence to Dr L. Sellars, Department of Medicine and Nephrology, Freeman Hospital, Newcastle upon Tyne NE7 7DN.

Fig. 1 Course taken by plasma creatinine (●), serum albumin (○) and proteinuria, together with the daily dose of prednisolone.

these changes. There have been several reports of nephrotic syndrome and renal failure in patients treated with the phenylalkanoic acid derivatives naproxen and fenoprofen; biopsies showed interstitial nephritis with minimal glomerular changes and a favourable response usually followed drug withdrawal, with or without steroid treatment.^{2,3} The pathogenesis is not clear, but the demonstration in the case of fenoprofen that the interstitial infiltrate was composed almost entirely of T lymphocytes has led to the suggestion that a drug-induced T-cell reaction may be responsible for both the interstitial nep-

hritis and the minimal change glomerular lesion.³ Fenclufenac is also a phenylalkanoic acid derivative, and the mechanism of renal damage may be similar.

References

- 1 Hamilton D V, Pryor J S, Cardoe N. Fenclufenac-induced nephrotic syndrome. *Br Med J* 1979; **ii**: 391.
- 2 Brezin J H, Katz S M, Schwartz A B, Chinitz J L. Reversible renal failure and nephrotic syndrome associated with nonsteroidal anti-inflammatory drugs. *N Engl J Med* 1979; **301**: 1271-3.
- 3 Finkelstein A, Fraley D S, Stachura I, Feldman H A, Gandy D R, Bourke E. Fenoprofen nephropathy: lipid nephrosis and interstitial nephritis. *Am J Med* 1982; **72**: 81-7.