The patients who had palpable lumps had been receiving fluspirilene for an average of 26 months, whereas the others had been receiving it for an average of only eight months (Student's *t* test: $P < 0.001$). All eight patients with palpable lumps but only three of the other 16 had been on fluspirilene for over a year. At the time of assessment the patients with lumps were receiving a higher weekly dose (11 mg compared with 7 mg: $P < 0.05$).

Comment

Sporadic unpublished reports of "subcutaneous nodules" at the site of fluspirilene injection have been made to the manufacturers. Our findings suggest that the occurrence of deeply placed swellings is more than sporadic but is instead a probable outcome in a patient maintained on the drug for more than 12 months. The cause of the necrosis is not certain. Nevertheless, it seems reasonable to speculate that after injection the aqueous vehicle for fluspirilene is rapidly absorbed, thus allowing precipitation of crystals, which exert a toxic effect. As there was little cellular response the necrosis was almost certainly not due to sensitivity to the drug. A pure pressure effect is also unlikely.

Fluspirilene is an effective antipsychotic with few extrapyramidal side effects.¹ But unless it can be administered in a more acceptable form its value in long-term maintenance treatment may be limited.

We thank the nursing staff of Gartnavel Royal Hospital, especially Sister M Condie, Mr J Lang, and Sister A McLachlan, for drawing our attention to the problems of administering fluspirilene.

¹ Malm, V, et al, *Acta Psychiatrica Scandinavica*, 1974, suppl No 249, p 94.

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Minocycline-induced acute interstitial nephritis

The tetracyclines are associated with several renal complications, mainly through their anti-anabolic action. We report here, for the first time, a hypersensitivity-like acute interstitial nephritis associated with tetracycline treatment.

Case report

A 43-year-old housewife presented to her general practitioner two weeks before admission with an upper respiratory tract infection which was treated with minocycline (Minomycin) 250 mg four times a day for five days. Ten days later she developed fever, lethargy, bilateral loin pain, and nausea. The general practitioner prescribed a further course of minocycline but noted proteinuria (++) and microscopic haematuria (165 erythrocytes/ μ l). Two days later an intravenous pyelogram showed smooth, slightly enlarged kidneys but with very poor dye excretion at 30 minutes.

The patient was referred to the renal unit at Prince Henry's Hospital with a provisional diagnosis of acute glomerulonephritis. On admission she was feverish (38.8°C) and normotensive (150/80 mm Hg) with no evidence of oedema. Her fundi were normal and there was mild bilateral loin tenderness. There was no rash and no clinical evidence of uraemia. Investigations showed a haemoglobin concentration of 12.6 g/dl; leucocytosis (14.3×10^9 /l) with eosinophilia (9%); severe renal failure (serum creatinine concentration 700 μ mol/l (7.9 mg/100 ml)); proteinuria (0.2 g/24 h); and microscopic haematuria without casts. Obstructive uropathy was excluded on ultrasoundography. Percutaneous renal biopsy was performed.

The renal biopsy specimen showed intense interstitial inflammation consisting of histiocytes, lymphocytes, and plasma cells. Some tubules were infiltrated particularly by lymphocytes. Glomeruli appeared essentially normal although scattered mononuclear inflammatory cells were present in some capillary loops.

Immunofluorescence—IgA (Burroughs-Wellcome) was deposited along the

Dense interstitial infiltrate of mononuclear inflammatory cells with occasional cells infiltrating tubular epithelium. (Periodic-acid Schiff. $\times 160$.)

brush border of some proximal convoluted tubules and in some arteriolar walls. C3 was seen in glomerular capillary loops and arteriolar walls.

Apart from withdrawing minocycline and rigidly controlling fluid balance we gave no further treatment. Throughout her stay in hospital the daily urine output exceeded 2 l. Her renal function improved spontaneously immediately after admission, and the serum creatinine concentration fell to 150 μ mol/l (1.7 mg/100 ml) within six days. At outpatient review two weeks later, renal function was normal (serum creatinine concentration 60 μ mol/l (0.7 mg/100 ml)), as was urine analysis and urine microscopy.

Comment

Through their anti-anabolic action tetracyclines (except for doxycycline) may induce severe azotaemia often associated with acidosis and polyuria. A Fanconi-like syndrome of aminoaciduria, glycosuria, acidosis, and proteinuria has also been reported after the use of degraded tetracyclines,¹ and nephrogenic diabetes insipidus has been described after tetracycline treatment.² The anti-anabolic effects of tetracycline are particularly seen in pregnant women and in patients with pre-existing renal impairment. Although these effects are usually reversible, occasional deaths and cases of irreversible renal damage needing long-term dialysis have occurred.²

The isolated hypersensitivity-like acute interstitial nephritis suffered by our patient has not been reported as a complication of tetracycline treatment. Hypersensitivity interstitial nephritis is well documented in association with other antibiotics, such as methicillin and ampicillin.⁴ The typical fever, eosinophilia, polyuria, and renal failure of drug-induced interstitial nephritis were seen in our patient, though she did not develop a rash, which is often reported in this allergic reaction.

The exact pathogenesis of this type of reaction remains undetermined. In methicillin-induced interstitial nephritis a penicilloyl haptenic group may alter the antigenicity of the tubular basement membrane, resulting in the formation of antibodies which react with the tubular basement membrane and stimulate an interstitial inflammatory reaction. IgG and C3 have been shown along the tubular basement membrane in methicillin-induced interstitial nephritis.⁵ In our patient IgG was not shown, although IgA was observed along the tubular brush border. The importance of this finding is uncertain.

¹ Frimpter, G W, et al, *Journal of the American Medical Association*, 1963, **184**, 111.

² Phillips, M E, et al, *British Medical Journal*, 1974, **2**, 149.

³ Casbell, D O, and Sparks, H A, *Journal of the American Medical Association*, 1965, **193**, 237.

⁴ Gilbert, D N, et al, *Annals of Allergy*, 1970, **28**, 378.

⁵ Border, W A, et al, *New England Journal of Medicine*, 1974, **291**, 381.

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