Comment

As shown by the H max:M max amplitude ratio study, latent neuropathy seems to be common in patients receiving perhexiline, affecting two-thirds of the treated population. This study also shows that the H reflex latency and the distal motor latencies are useful indices for detecting subclinical nerve disease and for estimating its severity.

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Interstitial nephritis in a case of phenylbutazone hypersensitivity

Phenylbutazone is a commonly used drug, and gastrointestinal and haematological side effects and sodium retention are well documented. Acute renal failure, and particularly interstitial nephritis, is a less well known effect and only a few cases have been recorded. We report here a case of acute interstitial nephritis associated with fever, rash, hepatitis, and eosinophilia after phenylbutazone ingestion.

Case report

A 48-year-old housewife received phenylbutazone 200 mg three times a day for a painful right elbow. Two days after the end of a three-week course she developed fever, rigors, lymphadenopathy, and a diffuse, erythematous, purpuric rash. On admission to hospital the rash was still florid, blood pressure was 120/85 mm Hg, and there was mild hepatomegaly. Investigations showed: haemoglobin 13.9 g/dl; platelets $80 \times 10^9/l$; total WBC $19.4 \times 10^9/l$ with a 36% eosinophilia. Blood urea concentration was initially 14.3 mmol/l (86 mg/100 ml) but fell to 4.5 mmol/l (27 mg/100 ml) after intravenous fluid replacement. Serum creatinine was 118 $\mu\text{mol/l}$ (1.3 mg/100 ml); γ -glutamyltranspeptidase 140 IU/l; serum aspartate aminotransferase 312 IU/l; alkaline phosphatase 607 IU/l; bilirubin 17 $\mu\text{mol/l}$ (1 mg/100 ml). Urine microscopy showed leucocytes, epithelial cells, and granular casts with no appreciable proteinuria. Bone marrow aspiration showed hyperactivity only. Skin biopsy showed dilatation of dermal capillaries and perivascular infiltration by lymphocytes together with some nuclear fragments. There was also focal extravasation of red cells and a picture compatible with an allergic drug reaction. She was negative for autoimmune antibodies, DNA antibody binding was 28 U/ml (Amersham radioimmune assay 0-25 U/ml); C3 1040 mg/l (normal 700-1800 mg/l); C4 350 mg/l (normal 140-700 mg/l); and there was no anticomplementary activity. IgG was 19.5 g/l (normal 5-18 g/l), IgM 2.4 g/l (normal 0.5-2.5 g/l), IgA 10.5 g/l (normal 0.5-2.5 g/l); total IgE by the Prist method 8540 U/ml (mean $\pm$ 2 SD = 122 U/ml $\pm$ 275 $\mu\text{g/l}$).

The rash faded, but on the 16th day of her illness she developed further pyrexia and associated loin tenderness. Midstream urine examination showed a significant growth of *Streptococcus faecalis*, and amoxycillin was started. Despite this proteinuria increased and red cells appeared in the urine and over the next two days she became anuric. Blood urea concentration was 15.7 mmol/l (95 mg/100 ml) and serum creatinine 530 $\mu\text{mol/l}$ (6 mg/100 ml). Peritoneal dialysis was started on day 23 when blood urea concentration was 30.1 mmol/l (181 mg/100 ml) and serum creatinine 1003 $\mu\text{mol/l}$ (11.3 mg/100 ml), and this was followed by haemodialysis. Abdominal radiographs showed two 15-cm kidneys, and a renal biopsy performed on day 26 showed considerable interstitial inflammatory infiltrate of plasma cells with occasional polymorphonuclear cells. There was a diffuse interstitial fibrosis with dilatation and localised loss of tubules. Glomeruli showed no hypercellularity or basement membrane abnormality (see figure).

Immunofluorescence studies showed no localisation of immunoglobulins of components of complement within the tubular basement membrane or walls of the vessels. Haemodialysis was discontinued on day 46, when effective urine volumes had been achieved. Two months later her urea concentration was 12.5 mmol/l (75 mg/100 ml), creatinine 174 $\mu\text{mol/l}$ (1.9 mg/100 ml), and IgE 1137 U/ml.

Intense interstitial infiltration and areas of tubular necrosis. (H and E. $\times 50$.)

Comment

The episode of acute interstitial nephritis was thought to be a hypersensitivity reaction to phenylbutazone. This is in keeping with the additional manifestations of hypersensitivity found in this patient, such as fever, eosinophilia, rash, and abnormal liver function values. At the time of developing these abnormalities she was receiving no other medication. Acute interstitial nephritis has been described before,¹ mainly with methicillin and phenindione.² One report reviews a few cases associated with phenylbutazone,³ although these were mainly cases of acute renal failure without the additional features seen in our patient. This syndrome has been reported with ampicillin, and our patient did have amoxycillin, but the drug was given for only two days 16 days after the development of her illness and after the clinical and urinary evidence of renal disease was apparent.

The hypersensitivity reaction in the kidney in this condition is said to be directed against the tubules and there are reports of anti-tubular basement membrane antibodies and linear deposition of IgG along the tubular basement membrane.⁴ We were unable to show this in our patient. We were, however, able to confirm that measurement of IgE helps to differentiate between acute interstitial nephritis and other causes of acute renal failure.⁵ We would suggest, in view of the other features of hypersensitivity and in the absence of any other causal agent, that this case of acute interstitial nephritis was caused by phenylbutazone treatment.

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