Anti-Glomerular Basement Membrane

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Nephritis due to Hydralazine

Dear Sir,

Patient A.R., aged 48 years, presented with a 3-month history of anorexia, 7 kg weight loss, and a 5-day history of arthralgia involving the hands, knees, and ankles. Two days prior to presentation, he complained of a rash commencing on his right thigh and spreading over his body. The rash was initially pruritic macules which subsequently developed into crops of haemorrhagic blisters about 2×2 mm. He had no history of cough, dyspnoea, or haemoptysis. There was no history of dark urine or peripheral oedema.

He had a background of hypertension for 7 years, well controlled by hydralazine (100 mg twice daily), pindolol (15 mg twice daily), and a combination diuretic of triam-terene (100 mg) and hydrochlorothiazide (50 mg once daily). For 5 years, he had been taking 300 mg allopurinol daily for gout.

On examination, his supine blood pressure was 130/90 mm Hg. Fundoscopy was normal. His spleen was palpable 2 cm below the left costal margin. There was no arthritis. Urinalysis showed + + + blood and + + + protein with 480,000 red blood cells/ml (50% dysmorphic), and red cell casts were visible on urine microscopy.

Initial investigations showed a urea of 34.9 mmol/l, creatinine 0.68 mmol/l, sodium 136 mmol/l, potassium 3.5 mmol/l, chloride 105 mmol/l, and bicarbonate 13 mmol/l. Albumin was 26 g/l, haemoglobin 10.8 g/dl. Blood glucose was normal, urate was 0.65 mmol/l. 24-hour urinary protein was 4.05 g. C-reactive protein was 180 mmol/l. Anti-nuclear factor was positive in a homogeneous pattern at a titre of 1:2,560. The double-stranded DNA was 20% (normal being less than 20%).

Anti-histone antibody was positive, and acetylator status was slow. Both C3 and C4 were depressed, circulating immune complexes were normal. The titre of anti-glomerular basement membrane (GBM) antibody was positive by solid-phase radioimmunoassay.

A skin biopsy showed leucocytoclastic vasculitis with positive immunofluorescence for IgG and fibrinogen. Renal biopsy showed crescentic glomerulonephritis with crescents involving almost all the glomeruli, with focal necrosis and scarring. Immunofluorescence showed a very strong linear staining of capillary walls for IgG (+ + +) and λ light chains (+). His chest X-ray was normal.

Hydralazine was ceased, and the patient was treated with daily plasmapheresis as well as prednisone (2 mg/kg/day) and cyclophosphamide (3 mg/kg/day). After 2 weeks of therapy, the latter drug was ceased temporarily due to the white cell count dropping below normal.

Cyclophosphamide was recommenced at 1 mg/kg/day, and prednisone reduced to 1 mg/kg second daily. On discharge, his creatinine was 0.41 mmol/l, and urea 26.7 mmol/l. After ceasing plasmaphoresis, the creatinine rose to 0.68 mmol/l, on weekly plasmaphoresis his creatinine was stable at 0.54 mmol/l, and the urea at 32.9 mmol/l.

The rash and arthralgia rapidly resolved on ceasing hydralazine. The anti-GBM antibody disappeared after 1 week of treatment with plasmaphoresis and immunosuppressives. Nine months later, it is still absent.

Although hydralazine-induced lupus involving the kidney is well described [1] anti-GBM renal disease secondary to hydralazine treatment has never been reported. The HLA association of hydralazine-induced lupus is

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DR 4 genotype [2], whilst that of over 80% of those with anti-GBM nephritis is DR 2 [3]. This patient's HLA typing is HLA DR2,-.

There are certain environmental factors thought to trigger the production of anti-GBM antibodies. These include infective agents such as influenza A2 virus, and chemical substances such as hydrocarbon solvents. Penicillamine, particularly at high doses of over 1 g daily, has been associated with rapidly progressive glomerulonephritis and lung haemorrhage – evidence, however, of linear staining of immunofluorescence on renal biopsy in these patients is lacking, granular IgG being noted in two cases [4].

The presence of granular IgG deposition and rapidly progressive glomerulonephritis has been well described with hydralazine [1, 5, 6]. This is the first time that the coexistence of linear staining of IgG on renal biopsy and anti-GBM antibody in the serum has been reported in the same patients [Bjorck, pers. commun.]. In the patient described above, the anti-GBM disease and hydralazine-induced lupus could be occurring as two separate diseases with similar times of onset, but as both conditions are rare, this is extremely unlikely.

We believe that this patient demonstrates the induction of anti-GBM renal disease by the administration of hydralazine.

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