Recurrent Goodpasture’s disease with severe renal involvement after initial successful treatment

Sir,

Goodpasture’s disease is an autoimmune disorder characterized by the development of autoantibodies to the NC1 domain of the α3 chain of type IV collagen, found in glomerular, pulmonary and other basement membranes. Patients present with a rapidly progressive crescentic glomerulonephritis and also, in approximately two-thirds of cases, pulmonary haemorrhage. The disease is usually monophasic, and the autoantibodies disappear, even without treatment, within 18–24 months in most cases [1]. We report the case of a patient with renal disease who was initially treated with partial success, such that dialysis was withdrawn, but who relapsed more severely 1 month after treatment was withdrawn.

Case. A 47-year-old female, non-smoking, IT manager presented in March 2000 with a 7-month history of arthralgia, night sweats, a weight loss of 4 kg, nausea, amenorrhoea, and epistaxis. She had been investigated elsewhere, and was found to have a microcytic anaemia (MCV 78.7 fl), with a raised ESR (111 mm/h) and CRP (148 mg/l). Other investigations included a normal chest radiograph, abdominal ultrasound, CT abdomen and pelvis, upper gastrointestinal endoscopy, colonoscopy, isotope bone scan, blood, urine, and viral cultures, thyroid and liver function tests, ECG, and echocardiogram. ENT review was also unremarkable. Her rheumatoid factor and antinuclear antibodies were weakly positive, however, anti-dsDNA and ANCA (PR3 and MPO) titres were negative. In February 2000 her renal function tests were normal, but on transfer to our centre her creatinine had risen to 402 μmol/l (creatinine clearance 8 ml/min) and she had microscopic haematuria and low-grade proteinuria.

Her past medical history was of Graves disease in 1967, for which she underwent a thyroidectomy in 1971. She commenced thyroxine therapy in 1982, which was her only regular medication. Examination revealed a thin (52 kg), pale lady with extensive vitiligo. There were no rashes or stigmata of vasculitis. A renal biopsy confirmed the presence of a focal segmental necrotizing glomerulonephritis with crescents in 88% glomeruli, many with rupture of Bowman’s capsule. There was no evidence of vasculitis. Anti-glomerular basement membrane antibody titre (GBM-Ab) was significantly raised at 34 kU/l (upper limit normal: 2.5 kU/l), thus confirming the diagnosis of Goodpasture’s disease.

She received treatment with steroids (methylprednisolone 500 mg intravenously for 3 days followed by oral prednisolone 1 mg/kg), cyclophosphamide (5 mg/kg fortnightly intravenously), and plasma exchange (eleven 60 ml/kg exchanges in total). After four sessions of haemodialysis, her renal function improved and she became dialysis-independent. Six weeks after commencing treatment, serial measurements of GBM-Ab became negative. By 10 weeks, her creatinine was 117 μmol/l, creatinine clearance 40 ml/min, and her menstruation resumed. At 14 weeks, her steroid therapy (prednisolone 5 mg) was withdrawn.

Two weeks after stopping steroid therapy she became unwell again with myalgia, loss of appetite, nausea, night sweats, and deteriorating renal function (creatinine 470 μmol/l). A repeat renal ultrasound was normal. Further biopsy showed a necrotizing crescentic glomerulonephritis with linear IgG staining. Fifty per cent glomeruli were sclerosed, and all the remainder had crescents. The GBM-Ab titre had significantly increased (250 kU/l), thus confirming recurrent Goodpasture’s disease. Further treatment was given with steroids, cyclophosphamide and plasma exchange (10 sessions), causing GBM-Ab to fall over the ensuing 4 weeks. Although urine output returned, she remained dialysis-dependent.

Comment. Recurrent Goodpasture’s disease is uncommon. Relapses more commonly present after 3–5 years with pulmonary manifestations, and renal involvement tends to be less aggressive [2]. Cases have been described where the disease is chronic and recurrent [3,4], relapses occurring when immunosuppressive therapy is withdrawn [4]. Our patient is unusual in that she achieved good renal function after the initial phase of her illness, despite being dialysis-dependent and having more than 88% crescents on her first biopsy. In a series of 40 patients, Daly et al. [5] concluded that patients with high serum creatinine concentrations and more than 80% crescents on biopsy usually required long-term dialysis therapy. It is also interesting that our patient had previous evidence of autoimmune disease including thyrotoxicosis, vitiligo, and strongly positive gastric parietal cell antibodies. This altered immune status may have increased the likelihood of recurrent Goodpasture’s disease in the event of recovery of renal function after the initial phase of the illness.

Renal Unit, Dorset County Hospital, P. Giri
Williams Avenue, Dorchester, UK J. E. Taylor