Correspondence

A case of severe bullous pemphigoid treated with plasmapheresis

Sir,

We describe a case with severe bullous pemphigoid complicated by diabetes mellitus and septicemia, in whom the daily corticosteroid dose could only be tapered to acceptable, effective, maintenance levels following treatment with plasmapheresis.

A 51-year-old woman presented with a 5-month history of generalized pruritic vesicles and bullae. She had been admitted to another hospital and treated with oral prednisolone 30 mg/day for 2 months, but the skin lesions progressed and a spiking temperature had been sustained for 1 week. She had had non-insulin-dependent diabetes mellitus for a year, which had been poorly controlled with oral hypoglycaemics. Examination revealed multiple, variably sized tense vesicles and bullae on erythematous bases and erosions on the whole body surface area (Figure 1A). The oral mucous membranes showed superficial erosions. Skin biopsy, and direct and indirect immunofluorescence examination showed features compatible with bullous pemphigoid. In addition, immunoblotting with the BP180 NC16a domain fusion protein was positive. The laboratory studies revealed leukocytosis, eosinophilia, elevated ESR, elevated fasting blood glucose level, and decreased protein and albumin levels. Staphylococcus aureus was cultured from the blood.

She was diagnosed with bullous pemphigoid complicated with non-insulin-dependent diabetes mellitus and septicemia, and was commenced on prednisolone 70 mg/day in combination with tetracycline 2 g/day, niacnimide 2 g/day and intravenous cephalzoline 4 g/day. After 2 weeks of treatment new blister formation decreased and the fever subsided, but attempts to lower the dose of prednisolone to below 50 mg/day resulted in the reappearance of bullae. In addition, she did not respond to the combined treatment with prednisolone 50 mg/day and either azathio-prine 150 mg/day or dapsone 100 mg/day.

About 1 month after admission, we decided to perform the average-volume plasma exchanges every other day, in combination with oral corticosteroid (50 mg/day). Each exchange removed 1.51 of the total theoretical plasma volumes (60 ml/kg of body weight), replaced by an equal volume of human albumin diluted 4% in isotonic saline solution. Following four plasmaphereses during a period of 9 days, the skin lesions were dramatically improved (Figure 1B). New blister formation was controlled, and the daily prednisolone dose was tapered to 20 mg/day over a period of 8 weeks; at present, 10–20 mg of prednisolone is sufficient to suppress blistering. The only problem attributed to plasma exchange procedures was transient fever, but this quickly normalized.

Although bullous pemphigoid is a disease that is usually easily controlled with moderate doses of corticosteroids in combination with dapsone or immunosuppressants, there are some patients whose disease is severe or who are intolerant of the standard therapies. Recent studies have demonstrated that patients who have circulating autoantibodies directed against BPAG2 (180 kD) have a poor prognosis with an increased likelihood of dying in the first year of treatment. Our patient had more severe disease with BPAG2 antibodies, complicated by sepsis and diabetes mellitus, allowing us to tailor our therapy more effectively. A controlled, randomized trial of plasmapheresis in the treatment of 41 patients demonstrated a steroid-sparing effect. However, a rebound in antibody titre has been noted after plasma exchange in other cases in which neither corticosteroids nor immunosuppressive drugs were given concurrently. Plasmapheresis is not associated with serious side effects. The potential difficulties with this treatment include maintaining venous access, a bleeding tendency from the addition of anticoagulants and clotting factor depletion, electrolyte imbalance, allergic reaction to foreign proteins, pulmonary oedema, cardiac arrhythmia and septicemia, but they have rarely developed. The milder side-effects of fever, chills and hypotension are relatively common. Plasmapheresis is useful in the treatment of antibody-mediated diseases, such as idiopathic thrombocytopenic purpura and autoimmune diseases. But recently, a case of bullous pemphigoid with a marked reduction of serum interleukin-6 levels after successful treatment with plasmapheresis was reported. Therefore, the removal of immune complexes, complement and inflammatory mediators may play a role in clinical improvement. Although it would be unwise to recommend the use of plasma exchange in the routine therapy of every patient with bullous pemphigoid, when adjuvant immunosuppressants fail to provide a steroid-sparing effect or for patients with severe disease who require high doses of corticosteroid, plasmapheresis offers an alternative.

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**Figure 1**
Bullous pemphigoid with generalized erythematous vesicles, tense bullae and erosive areas (A) before and (B) at 10 days after commencement of plasmapheresis.