

Plasmapheresis Treatment for Bullous Pemphigoid Induces Marked Reduction of the Serum IL-6 Level Rather than the Titre of Circulating Autoantibodies

Sir,

Plasmapheresis has been used for treatment of autoimmune bullous disease, principally for cases with high titres of autoantibodies that have proved to be uncontrollable by systemic steroid treatment (1–3). We report here a case of bullous pemphigoid (BP) in which marked reduction of the serum IL-6 level was observed after successful treatment with double-filtration plasmapheresis (DFPP).

CASE REPORT

A 60-year-old Japanese man had developed widespread erythemas with bullae on his trunk and extremities. He was diagnosed as having BP on the basis of the skin manifestations, histopathological findings and the results of immunofluorescence staining. The serum was found to have an antibody titre of 1:60 on cryostat sections of guinea pig oesophagus substrate, and showed a typical basement membrane zone (BMZ) pattern of IgG and C3 deposits by direct immunofluorescence. Epidermolysis bullosa acquisita was ruled out by exclusive staining for IgG on the epidermal side of 1 M NaCl-treated split skin substrate revealed by indirect immunofluorescence. DFPP was attempted because blisters emerged continuously in spite of systemic prednisolone administered at 70 mg/day. DFPP was carried out twice a week, and skin lesions such as erosions and blisters subsided dramatically during the 11 courses of DFPP.

We examined the titres of autoantibody and serum levels of IFN- γ (enzyme amplified sensitivity immunoassay; Biosource, Belgium), TNF- α (enzyme-linked immunosorbent assay; Japan Immuno Research Lab., Japan) and IL-6 (chemiluminescent enzyme immunoassay; Fujirebio Inc., Japan) before and after DFPP. Although plasmapheresis has been thought to work by removing pathogenic autoantibodies, a marked reduction in the serum IL-6 level from 34 to 8 pg/ml (normal <4) was noticed in this case, whereas anti-BMZ antibodies showed little decrease. Furthermore, slight enhancement of IFN- γ was also observed after the treatment, whereas TNF- α was unchanged.

DISCUSSION

The molecular weights of IgG and IL-6 are 150,000 and 12,000, respectively, and 70% of IgG and 20% of IL-6 should theoretically be removed by the filtration membrane used in DFPP. As an explanation for the paradoxical decrease in serum IL-6 in comparison with IgG, we speculated that certain molecules which upregulate IL-6 production or an immune complex containing IL-6 might be removed. Moreover, the slight increase in IFN- γ after DFPP might be a phenomenon caused by interaction of cytokine, thus mutually regulating their production.

It has been assumed that several factors besides autoantibodies are involved in blister formation in BP, because the activity of BP is not always correlated with the titres of anti-BMZ antibodies, in contrast to pemphigus. Indeed, complement activation and inflammatory cell infiltration are usually observed in BP skin lesions, and the effects of various mediators, such as interleukins and eosinophil chemotactic factors, on blister formation have been discussed. With regard to the

involvement of cell-mediated immunity in the pathogenesis of BP, several investigators have already reported an increase of cytokines including IL-6 in serum and/or blister fluid in BP patients (4–6). Although it has not been elucidated whether the increase in IL-6 is a pathogenic event or a consequence of blister formation, the role of IL-6 has been emphasized in several immunological disorders treated with plasmapheresis. One case similar to the present one was antiglomerular basement membrane antibody-induced glomerulonephritis in which treatment with plasmapheresis resulted in a marked decrease in the levels of both IL-6 and circulating antibody (7). The effect of plasmapheresis on an immune complex composed of IL-6 and soluble IL-6 receptor has also been discussed in a case of Crow-Fukase syndrome (8).

In addition to its effect on antibody production, many biological activities of IL-6 are known. IL-6 is thought to be an important cytokine involved in inflammatory processes, along with IL-1 β and TNF- α . The present case also appears to support the hypothesis that IL-6 is involved in the pathogenesis of BP, and cytokines could be involved in the severity of BP.

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Accepted December 23, 1998.

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