

# Anti-230 kDa Circulating IgE in Bullous Pemphigoid: Relationship with Disease Activity

Sir,

Patients with bullous pemphigoid (BP) may have circulating IgE (1), in addition to IgG directed at hemidesmosomal proteins of 230 and 180 kDa. Such IgE have been found to be associated with the disease activity and, occasionally, to herald its exacerbation (2). More recently, they have been shown to bind the 230 kDa antigen (3).

Lately, a BP recombinant protein of 55 kDa (rBP55) has been generated from a cDNA sequence which encodes for the carboxyterminal region of the 230 kDa BP Ag (4). Such protein has been shown to be highly immunogenic and antigenic, providing a highly specific target for antibodies circulating in BP patients.

In the patients we describe, rBP55 contributed to the understanding of the relationship of circulating IgE with the disease activity.

We studied two male patients (BL and RG), 67 and 59 years old, with BP. The diagnosis was made on the basis of clinical examination, histology and direct immunofluorescence. Both patients were studied by indirect immunofluorescence (IIF) on monkey esophagus as substrate and serum levels of total IgE serum (RIA). In addition, the serum level of IgG and IgE directed to the rBP55 protein was studied by Western blot, using anti-human polyclonal IgG and monoclonal IgE. BL was followed up from 1989 to 1995 and RG from 1993 to 1995. BL was treated with 1 mg/kg/day prednisone from 1989 to 1990 and with prednisone and azathioprine in 1992. Because of iatrogenic diabetes and peptic ulcer, BL was given cyclosporin A (CyA) (5 mg/kg/day) from 1994 to 1995. RG was treated from 1993 to 1995 with CyA (5 mg/kg/day) because of diabetes.

The onset of BP in our cases was marked by high serum levels of non-specific IgE and basal membrane zone (BMZ)-bound IgG. When challenged with the rBP55 protein, specific IgG and IgE were found. Only anti-rBP55 IgE were somehow related to the disease activity, while anti-rBP55 IgG were not. The latter remained positive (over a 6-year follow-up in BL), even when anti-BMZ IgG detected by IIF were absent (RG) (Table I). In our cases, therefore, anti-rBP55 antibodies, especially IgE, proved to be more specific than anti-BMZ antibodies.

After the introduction of CyA a marked rise of total IgE was observed, fueling doubts as to their role in BP pathogen-

esis. In fact, CyA has been shown to up-regulate the IgE response at low doses such as those used in our cases, while high doses have an inhibitory effect (6). In BP, however, such up-regulation may apply only to non-specific IgE, masking the behaviour of the ones directed at the 230 kDa antigen, which in our cases were related to the disease activity.

In conclusion, we have confirmed that, at least in some BP patients, the titres of the anti-BMZ IgG have no significant relationship with the disease activity. Instead, the serum levels of specific IgE directed at the 230 kDa antigen may often be a guide for treatment, if confounding factors, such as CyA, are not introduced.

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