



Letter to the Editor

Circulating IgE anti-BP180 autoantibody and its correlation to clinical and laboratorial aspects in bullous pemphigoid patients



Keywords:

Bullous pemphigoid; BP180; IgE

To the Editor,

Bullous pemphigoid (BP) is an autoimmune subepidermal blister disease. The presence of IgE anti-basement membrane zone (BMZ) autoantibody in the lesional skin has been reported [1]. Some studies have also covered the relationship between clinical features of BP and IgE anti-BP180 autoantibody, while the results are controversial [2–6]. In this study, we detected the levels of IgE anti-BP180 autoantibody in Chinese patients with BP and investigated its possible relationship with clinical aspects and laboratorial parameters of these patients.

Serum samples were obtained from 41 patients with BP (19 males and 22 females, mean age 69.37 ± 11.20 , Table 1), diagnosed by typical clinical, histopathology, IgG and/or C3 deposition along the BMZ of peribullous skin by direct immunofluorescence, and positive IgG anti-BP180 autoantibody by enzyme-linked immunosorbent assay (MBL, Japan). Serum samples from 30 healthy subjects and 16 patients with pemphigus vulgaris (PV) were used as normal controls and disease controls respectively. For detecting IgE anti-BP180 autoantibody, serum samples were diluted to 1:100 and

first incubated twice in the microplate wells coated with protein G (Pierce, USA) in order to preabsorb IgG in the serum [6]. These preincubated samples were next added to the microplate wells coated with NC16A domain of BP180 according to the manufacturer's instructions (MBL, Japan). A peroxidase-conjugated goat polyclonal anti-human IgE antibody (dilution 1:50,000, Abcam, USA) was then used for the detection of IgE. The optical density at 450 nm was subsequently determined and values greater than the mean $\pm$ 2 SD values of the normal controls (0.084) were considered positive. According to the results of normal distribution test (Shapiro–Wilk test), data were expressed as mean $\pm$ SD or median [25th–75th percentile]. Independent-samples *T* test and Pearson correlation were used to analyze the normally distributed data, and Mann–Whitney *U* test and Spearman's test were used to analyze the abnormally distributed data, with the level of significance set at $P < 0.05$. The study was approved by the Ethics Committee of Peking University First Hospital.

The levels of IgE anti-BP180 autoantibody in serum samples from patients with BP, healthy subjects and patients with PV were presented in Fig. 1. IgE anti-BP180 autoantibody was detected in 24.4% (10/41) patients with BP, while neither in healthy subjects nor patients with PV. In the current study, we employed the aforementioned commercially available enzyme-linked immunosorbent assay (ELISA) kit paired with an IgE-specific secondary antibody to detect IgE anti-BP180 autoantibody in 100-fold dilution sera of patients with BP. The ELISA protocol was basically consistent with the two previous reports carried out in Japanese patients with BP, and the similar percentage of IgE anti-BP180 autoantibody (22% and 30% respectively) was found [5,6]. In another two related studies conducted in German and American patients with BP, checkerboard titrations were performed with serial dilutions of the NC16A domain of BP180 antigen to determine the optimal working conditions for ELISA strategy, and the patient sera were used as 50-fold diluted and undiluted samples respectively, as a result, increased percentages of 55% and 77% in IgE anti-BP180 autoantibody were detected [4,7]. The

Table 1
Clinical and laboratory features of patients with bullous pemphigoid (BP) positive for IgE anti-BP180 autoantibody.

Characteristics	Positive, mean (SD) (n = 10)	Negative, mean (SD) (n = 31)	P value
Sex no. (%)			
Male	7 (70)	12 (38.7)	0.174
Female	3 (30)	19 (61.3)	
Age, years	67.30 (8.51)	70.03 (11.99)	0.509
Controlling dosage of prednisone, mg/d	45.00 (21.73)	30.97 (22.67)	0.094
Duration for effective control, day	20.50 (9.55)	16.55 (7.36)	0.178
Area of skin lesions (%)	48.80 (23.69)	45.26 (24.95)	0.695
Laboratory data			
IgG anti-BP180	134.33 (63.44)	85.13 (44.44)	0.009
Abs, index			
Circulating eosinophil cell count, $10^9 L^{-1}$	1.08 (0.94)	0.74 (1.09)	0.491
Percentage of eosinophil cells	8.71 (9.47)	8.26 (9.32)	0.895
Circulating white blood cell count, $10^9 L^{-1}$	8.95 (4.47)	9.10 (3.49)	0.734

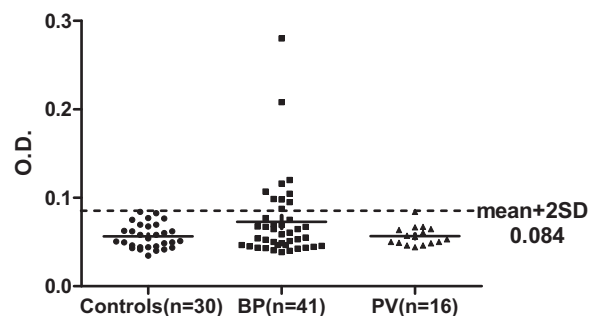


Fig. 1. IgE anti-BP180 antibody levels in serum samples from patients with bullous pemphigoid (BP), healthy subjects and patients with pemphigus vulgaris (PV).

dilution of patient sera and different manners in which the ELISA assays were performed possibly caused the discrepancies in these studies [7,8].

With regards to the disease severity of BP, correlations of the following clinical items, namely controlling dosage of prednisone, duration for remission and area of skin lesions, have been investigated with the presence or levels of IgE anti-BP180 autoantibody in four previously reported studies, while the results were not consistent [2,3,5,6]. In our present study, we did not get any positive correlation between the presence or levels of IgE anti-BP180 autoantibody with the above items, though, to some extent, patients with higher IgE anti-BP180 autoantibody levels required a larger prednisone dosage, a longer duration for effective control, and had a broader area of skin lesion (Table 1). On the other hand, there was a significant difference in IgG anti-BP180 autoantibody levels between patients with positive IgE anti-BP180 autoantibody and those with negative values ($t = 2.734$, $P = 0.009$), which suggests that increased IgE anti-BP180 autoantibody levels may also associate with a higher titer of IgG anti-BP180 autoantibody.

Regarding correlation of IgE anti-BP180 autoantibody with laboratorial parameters, the circulating eosinophil count may be the most putative one. Two recent related studies have revealed that neither the presence of IgE anti-BP180 autoantibody nor its increased levels correlated with the circulating eosinophil count [5,6]. In this study, we observed a similar result ($r = 0.297$, $P = 0.06$ and $r = -0.089$, $P = 0.807$, respectively), though the eosinophil counts of patients with BP positive for IgE anti-BP180 autoantibody were indeed higher than those of the other patients with BP (1.08 ± 0.94 vs. 0.74 ± 1.09 , Table 1). In addition, the increased IgE anti-BP180 autoantibody levels did not associate with eosinophils infiltration around edematous erythemas and blisterings of skin biopsy specimens ($r = -0.283$, $P = 0.461$). To clarify the possible relationship between increased circulating eosinophil count and IgE autoantibody in BP, some studies also focused on another major target antigenic site in BMZ, namely BP230. No positive correlation was found between circulating eosinophil count and IgE anti-BP230 autoantibody [5,6], though a significant correlation with circulating eosinophil count was observed in IgG anti-BP230 autoantibody [6]. So whether there is a positive relationship between circulating eosinophil count and IgE autoantibody specific for BMZ antigen need further research.

In conclusion, the present study demonstrates that IgE anti-BP180 autoantibody level is increased in some Chinese patients with BP and may associate with their higher titers of IgG anti-BP180 autoantibody, although no significant correlations of this IgE autoantibody with various clinical and laboratorial aspects were observed.

Acknowledgments

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Letter to the Editor

Possible correlation of IgE autoantibody to BP180 with disease activity in bullous pemphigoid



Keywords:

Bullous pemphigoid; BP180 antibody; IgE; BPDAI

To the Editor,

Bullous pemphigoid (BP) is an autoimmune blistering disease characterized by circulating serum immunoglobulin G (IgG)

antibodies against type XVII collagen/BP180 (BP180), forming tense subepidermal blisters [1]. While IgG BP180 antibodies play an essential role for the development of BP, serum IgE BP180 antibodies are also detected in some BP cases [2]. The involvement of the IgE class of anti-BP180 antibodies remains to be elucidated in the pathogenesis of BP. Here, we report a refractory BP case having a high level of IgE BP180 antibodies. The IgE BP180 antibody level appeared to fluctuate in association with the disease severity of BP.

A 47-year-old Japanese man with refractory BP, who had been treated with 60 mg of oral prednisolone and 200 mg of cyclosporine per day for one month, was referred and admitted to our