SHORT REPORTS

Serum IgE Levels in Patients with Bullous Pemphigoid and Its Correlation to the Activity of the Disease and Anti-basement Membrane Zone Antibodies

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The serum levels of IgE were found to be increased in 24 of 34 patients with an acute exacerbation of bullous pemphigoid. There was no statistically significant correlation between the serum IgE level or the serum anti-basement membrane zone antibody titer and the extent of the disease during an exacerbation. There was however a positive correlation between anti-basement membrane zone antibody titers and serum IgE levels. All but 2 patients showed a normalisation or decline in serum IgE 2–4 months after an exacerbation of the disease. There was also a tendency to declining antibasement membrane zone antibody titers in many patients but changes of these titers could usually not be measured as early as alterations of serum IgE levels were found. Thus in most patients serum IgE was found to be a better laboratory parameter than indirect immunofluorescence for following the activity of the disease. (Received July 13, 1983.)

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The aetiology of bullous pemphigoid (BP) is still unknown but it is generally regarded as an autoimmune disease (1). BP is a disease that particularly affects the elderly. It is known that age-related changes occur in the immune system and it has been speculated that with increasing age disturbed immunoregulation may cause an increased incidence of autoimmune diseases (2). IgG auto-antibodies against the basement membrane zone (BMZ) and/or C3 are found in the skin and in about 70% of the patients IgG auto-antibodies are also found in the sera (3). Another sign of a disturbed immune system is the finding of elevated serum IgE levels (4, 5, 6) and increased IgE synthesis (6) in many BP patients. It is still unclear whether the tendency for increased serum IgE is caused by antigenic stimulation and/or is a result of a primary disturbance of the immune system, or whether it is merely an epiphenomenon secondary to the skin disease.

The aim of this investigation was to follow the serum IgE levels in BP patients and study whether there was any correlation to anti-BMZ antibody titers and to the extent and activity of the disease.

MATERIAL AND METHODS

The patient material was obtained from the Department of Dermatology, Södersjukhuset, Stockholm. The diagnosis was made on the basis of clinical examination, histological investigation and standard direct and indirect immunofluorescence (IF) staining. Thirty-four patients (21 females) and 13 males aged 61–99 years (mean age 81 years), with an acute exacerbation of BP were evaluated. In skin biopsy specimens from all patients direct IF examination showed a linear deposition of IgG and/or C3 along the BMZ. Monkey esophageal mucosa were used in all indirect IF tests. Two patients had the adult form of asthma but none of the patients know of any atopic disease in childhood or early adult life. All patients had an acute exacerbation of the disease when skin and serum samples were taken. Four of the patients were on maintenance therapy with low doses of oral corticosteroids when they got a flare up and these tests were conducted. The patients were divided into three groups according
Table I. Serum IgE levels and anti-BMZ antibody titers in patients with an acute exacerbation of bullous pemphigoid

<table>
<thead>
<tr>
<th>Anti-BMZ antibody titers</th>
<th>IgE (kU/l)</th>
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<tbody>
<tr>
<td>&lt;1/10</td>
<td>7</td>
</tr>
<tr>
<td>1/20-1/160</td>
<td>3</td>
</tr>
<tr>
<td>1/320</td>
<td>3</td>
</tr>
<tr>
<td>≥1/640</td>
<td>6</td>
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Statistically significant correlation between anti-BMZ antibody titers and serum IgE (p<0.01).

Fig. 1. Serum IgE levels (kU/l) in 29 patients with bullous pemphigoid. A = acute exacerbation. B = 2-4 months after the exacerbation. (In 2 patients the tests were not performed until 6 respectively 10 months after the acute exacerbation.)

to the extent of the disease during the acute exacerbation. The extent of the disease was graded as follows: localized BP (5 patients) = localized to one area (patients with localized pemphigoid of the Brunsting-Perry type were not included); moderate BP (20 patients) = some disseminated bullae sometimes combined with papules and/or an eczematous eruption on <1/4 of the body surface; severe BP (9 patients) = many disseminated bullae, sometimes combined with papules and/or an eczematous eruption on >1/4 of the body surface.

In 29 patients serum samples were taken repeatedly during several months after an acute exacerbation. Follow-up ranged from 2 to 34 months (mean 9 months). The acute exacerbation was cured or almost cured with only topical steroids in 13 patients and with oral corticosteroids alone or in combination with azathioprine, cyclophosphamide or dapsone in 15 patients. One patient with a localized BP healed without any treatment.

The conventional PRIST method (Pharmacia, Uppsala, Sweden) was used to determine the serum levels of IgE. With this method the normal value of IgE/serum in nonatopic Swedish adults is <120 kU/l.

STATISTICS
The Kruskall-Wallis one-way analysis of variance by ranks and the Wilcoxon rank sum test were used for the statistical analysis.

RESULTS
Sera from 21 of the 34 patients (62%) showed a positive indirect IF (anti-BMZ antibody titer ≥1/20) during some period of the disease course. Of 34 patients with an acute exacerbation of BP 24 (71%) had increased (>120 kU/l) serum IgE levels (mean serum IgE value: 555 kU/l and median serum IgE value: 255 kU/l). There was a statistically significant correlation p<0.01) between high anti-BMZ antibody titers and increased serum IgE levels (Table I). Three of 5 patients with localized BP had normal serum IgE values and 4 had an anti-BMZ antibody titer <1/10. However in the group as a whole no statistically
significant correlation was found between the extent of the disease during a relapse and serum IgE levels or anti-BMZ titers.

Serial blood tests were drawn in 29 patients and they were followed 2–34 months (mean 9 months). In Fig. 1 the serum IgE level is denoted in connection with an acute BP exacerbation and after 2–4 months when the skin had healed or when there was merely a slight activity. All but 2 of the investigated patients showed a decline in serum IgE after the acute exacerbation. One patient had an unchanged IgE level and a still active BP and the other patient who developed an increased serum IgE value when the BP was cleared also suffered from an active disseminated seborrhoic dermatitis.

Concerning the anti-BMZ antibody titers only 5 patients showed a significant decrease of titers (twofold changes or more) within 2–4 months. With longer follow-up periods 6 more patients got significantly declining titers and 3 of these 6 patients got negative titers. No clear-cut correlation could be found between disease activity and anti-BMZ antibody titers.

DISCUSSION

This study confirms the reports of other investigations (4, 5, 6) that most BP patients with active disease have increased serum IgE levels. Circulating IgE levels in the elderly are reported not to be increased in comparison with the values of the younger population (7). In our study there was no statistically significant correlation between the IgE level and the extent of the disease during an exacerbation, but the serum IgE level in the individual patient followed the disease activity in all but one patient. Independent of whether the patient had received immuno-suppressive drugs or just local steroid ointments IgE declined when the disease improved. In some patients there was a period of approximately one month, with a serum IgE increase, before IgE started to decrease. In patients with atopic dermatitis and increased serum IgE levels normalization of the IgE values seem to occur first when the eczema has been in remission for a long time (8, 9). In contrast to this, the serum levels of IgE in patients with BP seem to fluctuate rather rapidly with disease activity.

Several authors have reported a bad correlation between serum anti-BMZ antibodies and clinical activity in BP (10, 11, 12). No significant correlation between anti-BMZ antibody titer and the extent of the disease during an acute exacerbation was found in this study either. Although there was a tendency to decreasing anti-BMZ antibody titers in many patients after an acute exacerbation of the disease no clear-cut correlation was found between the titers and disease activity when the individual patients were followed. A decrease in serum IgE levels could usually be measured prior to a decrease in anti-BMZ antibody titers. To some extent this can be explained by the different methods used to determine the antibodies. The PRIST method to quantitate IgE antibodies is a much more exact method than the crude method to determine anti-BMZ antibodies by indirect IF. The short half-life of circulating IgE can perhaps also result in more rapid changes of serum IgE antibodies compared to IgG antibodies. Heterogeneity of pemphigoid antigens (13) and formation of circulating immune complexes (14) may also account for lack of close correlation between anti-BMZ antibody titer and clinical activity. Thus we found that alterations in serum IgE levels were often a better guide to disease activity than determinations of serial anti-BMZ antibody titers.

In four patient we have noted an increase in the serum IgE level prior to an exacerbation of the disease, but we still do not know whether it is possible to predict a clinical relapse from a rise in serum IgE. Further studies with repeated IgE tests with short intervals during remissions are necessary to gain a better insight into this problem and the question
of whether the tendency to increased serum IgE is a result of a primary disturbance of the immune system or whether it is just secondary to the skin disease.

REFERENCES


Pseudo-Kaposi Sarcoma of the Feet: An Electron Microscopic Investigation

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A case of pseudo-Kaposi sarcoma of the feet (acroangiodermatitis) is reported. The patient showed clinical and light-microscopical signs closely resembling Kaposi’s sarcoma, but by electron microscopy of skin biopsies definite signs of degeneration of vascular walls and infiltrating cells were demonstrated. Electron microscopy should be applied when conventional histology is inconclusive or fits poorly to the anamnestic information and/or clinical appearance of the lesions. **Key words:** Acroangiodermatitis, Kaposi’s sarcoma. (Received October 7, 1983.)

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The increasing incidence of Kaposi’s sarcoma reported in recent years sharpens our attention towards possible signs of this disease in skin or mucous membranes. Thus, the need for reliable differential diagnostic criteria is enhanced. Pseudo-Kaposi sarcoma is an acroangiodermatitis. The clinical and histological findings mimic true Kaposi’s sarcoma (1.