SHORT COMMUNICATION

Circulating Anti-BP180 NC16a and Anti-BP230 Autoantibodies in Patients with Genital Lichen Sclerosus Do Not Correlate with Disease Activity and Pruritus

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MATERIALS AND METHODS

A total of 51 patients of both sexes who had GLS and attended our outpatient clinic from January 2010 to October 2012 were consecutively selected to participate in this cross-sectional study. Inclusion criteria were: subjects ≥ 18 years old with biopsy-proven GLS of any stage. Exclusion criteria were: skin conditions and treatments at baseline that would interfere with lichen sclerosus (LS) evaluation, such as immunosuppression, malignancies, subepidermal autoimmune bullous diseases, phimosis of causes other than LS, generalized pruritus of no detectable cause, bacterial, viral or fungal infection up to 2 weeks prior to inclusion and any intervention for LS (cryotherapy, laser, curettage, electrocautery, excision, immunomodulators) in the last 2 months prior to inclusion in the study. Ethics board approval and written informed consent from all patients were obtained.

Patients underwent a thorough dermatological examination and were evaluated for disease activity and genital pruritus. Disease activity was assessed by one specific dermatologist in our research team using the Investigator’s Global Assessment (IGA) score, which is a 4-point Likert scale (0: no disease – no inflammatory signs; 1: mild disease – mild erythema, infiltration, lichenification, excoriation; 2: moderate disease – moderate erythema, infiltration, lichenification, excoriation; 3: severe disease – severe erythema, infiltration, lichenification, excoriation) (1–3). Genital pruritus was assessed by the patient on a visual analogue scale (VAS) for pruritus, which is a 10-cm continuous scale (0: no itching to 10: severe itching). Based on the VAS score, the patients’ pruritus was also classified as following: no pruritus (VAS score: 0), mild pruritus (VAS score: 1–3), moderate pruritus (VAS score: 4–6) and severe pruritus (VAS score: 7–10). Patients’ age, gender, disease duration prior to inclusion in the study, IGA score, VAS score for genital pruritus and pruritus class, as well as serum levels of circulating anti-BP180 and anti-BP230 autoantibodies were recorded. The serum levels of circulating autoantibodies were detected by a well-established enzyme-linked immunosorbent assay (ELISA) test kit (commercially available MBL Kit, Japan). The cut-off value for the MBL assays was 9.0 U/ml and the upper detection range was 150.0 U/ml.

The objectives were: (i) to assess the frequency of elevated anti-BP180 and anti-BP230 autoantibody serum levels in patients with GLS; and (ii) to detect possible correlation between the serum levels of circulating anti-BP180 and anti-BP230 autoantibodies and the VAS and IGA scores.

Statistical analysis of the data was performed using the Statistical Package for Social Sciences (SPSS), version 15.0 (SPSS, Inc., Chicago, IL, USA). All tests were 2-sided, and the significance level was set at α = 0.05.

RESULTS

The median (min–max) age of the LS patients (14 men, 37 women) was 62.0 (38.0–78.0) years, the median (min–max) disease duration prior to inclusion in the study was 0.6 (0.1–7.0) years, the median (min–max) VAS score was 7.0 (0.0–10.0) and the median (min–max) IGA score was 2.0 (0.0–3.0). Only 3/51 (5.9%) of the patients had elevated anti-BP180 autoantibody serum levels (≥ 9.0 U/ml) (Table I). These 3 BP180-reactive patients did not differ from the other patients in terms of clinical features and clinical activity. None of the patients presented increased anti-BP230 autoantibody serum levels (≥ 9.0 U/ml).

DISCUSSION

A background of autoimmunity is reported in patients with GLS, especially when the onset of LS is before puberty (4, 5). There is accumulating evidence for an autoimmune basis for LS. Using antigen-specific ELISA, Oyama et al. (6) detected circulating autoantibodies to the extracellular matrix protein-1 in 80% of patients with GLS, providing data that suggest a role of these antibodies in the aetiopathology of GLS.

Interface dermatitis, commonly seen in biopsies of GLS, was interpreted by Howard et al. (7) as a reaction to autoantigens of the basement membrane zone, namely the

Table I. Information regarding the 3 female patients with reactivity against BP180 NC16A

<table>
<thead>
<tr>
<th>Patient/ Disease</th>
<th>Age, years</th>
<th>Disease duration, years</th>
<th>IGA score</th>
<th>VAS score</th>
<th>Anti-BP180, n.d.</th>
<th>Anti-BP230, n.d.</th>
<th>Direct IF microscopy</th>
<th>Indirect IF microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/52</td>
<td>4</td>
<td>5</td>
<td>38.9</td>
<td>2.5</td>
<td>negative</td>
<td>n.d.</td>
<td>negative</td>
<td>n.d.</td>
</tr>
<tr>
<td>2/61</td>
<td>7</td>
<td>3</td>
<td>36.3</td>
<td>3.3</td>
<td>negative</td>
<td>n.d.</td>
<td>negative</td>
<td>n.d.</td>
</tr>
<tr>
<td>3/40</td>
<td>1</td>
<td>2</td>
<td>12.1</td>
<td>7.6</td>
<td>negative</td>
<td>n.d.</td>
<td>negative</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

The cut-off value for the MBL assays was 9.0 U/ml and the upper detection range was 150.0 U/ml. IGA: Investigator’s Global Assessment; VAS: visual analogue scale; IF: immunofluorescence, n.d.: not done.
bullous pemphigoid antigen 2 (BPAg2 or BP180NC16a). The same group demonstrated that, in 30% of adult women with GLS, circulating autoantibodies against components of the basement membrane are detected (7).

Baldo et al. (8, 9) suggested that autoreactivity to basement membrane proteins in the skin may contribute to the pathogenesis of GLS. They demonstrated that in 6/14 patients (>40%) with vulvar LS, the NC16A domain of BP180 was a target for circulating T cells, and that vulvar LS was associated with circulating autoantibodies to BP180 in 3/14 patients. This was a small study with only 14 LS, 5 vulvar LP and 4 healthy controls (8). A second study of the same group demonstrated circulating BP180 autoantibodies in 4 out of 9 girls with GLS. None of the 9 patients had anti-BP230 autoantibodies (9).

In our study, elevated anti-BP180 autoantibody serum levels were found in 5.9% (3/51) of patients with GLS; anti-BP230 autoantibodies were undetectable. Therefore, no correlation between the serum levels of circulating anti-BP180 autoantibodies and the VAS or IGA score is suggested.

Our results are in accordance with the study of Gambichler et al. (10), in which, among the 149 patients with LS studied, only 4 had increased BP180 and 1 BP230 autoantibody levels. The authors conclude that anti-basement membrane autoantibodies detected with ELISA techniques are not significantly increased in patients with LS compared with healthy controls.

The hypothesis that pruritus followed by scratching may reveal hidden antigens of the basement membrane and induce an autoimmune process with the formation of targeted autoantibodies (mainly anti-BP180), is a possible explanation for the evolution of circulating autoantibodies in patients with GLS (11).

In the normal population we do not expect to find BP180 or BP230 antibodies, as confirmed in the study by Gambichler et al. (10). Yet, in the study by Wieland et al. (12), in a sample of unaffected patients, BP180 or BP230 antibodies were detected in 7.5% of tested patients. In another study by Fourer et al. (13, 14), BP180 antibodies were detected in 3.6% of elderly patients without clinical signs of bullous pemphigoid (BP).

Based on the results of the current study, we conclude that the detection of circulating anti-BP180 autoantibodies in patients with GLS represents an epiphenomenon rather than a true component of LS pathogenesis, because the percentage of patients with positive circulating anti-BP180 antibodies appears not to exceed the number found in the general population (10, 12–14).

REFERENCES