FasL autoantibodies in vasculitis are associated with the presence of anticonneal epithelial antibodies

E Gowen, A B Tullo, J Dixon, P J L Holt, M C Hillarby

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Eye complications are common in vasculitis, especially in Wegener’s granulomatosis (WG), where up to 90% of all cases have ophthalmic involvement. Eye involvement in the Churg-Strauss syndrome (CSS) has been reported but is rare. Corneal autoantigens have been documented in patients with WG and CSS; in particular, circulating autoantibodies to corneal specific keratin 3 (K3) are present in 60% of patients with WG. Most of these patients have peripheral ulcerative keratitis (PUK), but others have no detectable eye disease. Antibodies to a second corneal antigen, BCEA-B, are associated with CSS.

The eye is an immune privileged organ characterised by a reduced or modified immune response which protects the eye from inflammation and autoimmunity. Fas, together with its ligand FasL, has an important role in maintaining ocular immune privilege. Fas+ lymphoid cells that enter the eye are killed by apoptosis when the Fas binds with FasL present on immune privilege. Fas+ lymphoid cells that enter the eye are killed by apoptosis when the Fas binds with FasL present on ocular structures. When the Fas/FasL system is defective in mice a direct inflammatory insult to the eye triggers an inflammatory response that overwhelms the eye and causes significant damage.

Anti-FasL autoantibodies have been found in patients with systemic lupus erythematosus (SLE) and may be involved in the immune abnormalities and pathogenesis of this condition. These autoantibodies appear to protect lymphocytes from apoptosis by binding to FasL, leaving it unable to bind to Fas.

Autoantibodies to FasL may be present in patients with vasculitis. If present, these antibodies may compromise ocular immune privilege and contribute to eye complications and/or the production of antibodies to ocular antigens. Therefore the main aim of this study was to detect FasL antibodies in sera from patients with vasculitis with and without PUK.

PATIENTS AND METHODS

Three groups of patients were studied: 18 patients with WG without eye complications and seven with PUK and nine patients with CSS. Patients were diagnosed by the American College of Rheumatology criteria. Fourteen normal controls were also included. Autoantibodies to FasL, K3, and BCEA-B were detected by immunoblotting (fig 1) as described elsewhere. The significance of the results was determined using χ² contingency tables and Yates’s correlation for small sample numbers.

RESULTS

Two patients with WG without PUK (11%) and two patients with CSS (22%) were positive for FasL antibodies. However, no other patient including those with WG and PUK displayed evidence of antibodies. The 14 controls were all negative for FasL, BCEA-B, and K3 antibodies.

Table 1 shows the characteristics of the four FasL antibody positive patients. All FasL positive subjects had BCEA-B antibodies, whereas, only four (12.5%) patients without FasL antibodies had BCEA-B antibodies. The association of FasL antibodies with BCEA-B antibodies proved to be significant (p = 0.00138). However, no patient positive for antibodies to K3, carried antibodies to FasL, whereas 25% of patients negative for FasL antibodies did carry K3 antibodies.

FasL antibodies were detected in patients with both WG and CSS. However, the original hypothesis that FasL antibodies may contribute to eye disease present in vasculitis appears unsupported as none of the patients with FasL antibodies had eye complications.

DISCUSSION

At present it is unknown whether the relationship between FasL and BCEA-B antibodies is causal or coincidental. However, antibodies to FasL may block FasL function in the eye, reducing ocular immune privilege in these patients, allowing the formation of anticonneal antigens. Further studies are required to test a larger sample of patients with WG.

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Disease</th>
<th>Organ involvement</th>
<th>Sex</th>
<th>Age</th>
<th>VDI</th>
<th>Antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CSS</td>
<td>Kidney, lung, F</td>
<td>49</td>
<td>10</td>
<td>2</td>
<td>BCEA-B, K3</td>
</tr>
<tr>
<td>2</td>
<td>CSS</td>
<td>Lung, nose, F</td>
<td>46</td>
<td>7</td>
<td>2.5</td>
<td>BCEA-B, CAnCA, CRP</td>
</tr>
<tr>
<td>3</td>
<td>WG</td>
<td>Lung, nose, F</td>
<td>40</td>
<td>25</td>
<td>1</td>
<td>BCEA-B, CAnCA, CRP</td>
</tr>
<tr>
<td>4</td>
<td>WG</td>
<td>Kidney, nose, F</td>
<td>82</td>
<td>6</td>
<td>0</td>
<td>BCEA-B, CAnCA</td>
</tr>
</tbody>
</table>

RF, rheumatoid factor; CRP, C reactive protein; VDI, vasculitis damage index.

Abbreviations: CSS, Churg-Strauss syndrome; PUK, peripheral ulcerative keratitis; SLE, systemic lupus erythematosus; WG, Wegener’s granulomatosis.
and CSS in order to support the findings of this study. Additionally, it would be of interest to study FasL antibodies in patients with other types of collagen vascular disease in which patients can also have ocular manifestations, such as rheumatoid arthritis. More detailed studies to determine whether patients with SLE with FasL antibodies have an increased incidence of eye complications or other autoantibodies such as those against BCEA-B would also be worthwhile.

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