DEPOSITS OF IMMUNOGLOBULINS AND COMPLEMENT C3 IN CLINICALLY NORMAL SKIN OF PATIENTS WITH LUPUS ERYTHEMATOSUS

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Abstract. Deposits of immunoglobulins and/or complement C3 were found in two-thirds of biopsies from clinically normal skin of 64 patients with systemic lupus erythematosus, as judged by well defined criteria. The incidence of deposits in clinically normal skin was identical in patients with and without clinical skin lesions. IgM was found more frequently in the deposits (88%) than was IgG (36%) but equally frequently in involved and uninvolved skin, whereas C3 was found more often in patients with skin lesions (59% in involved skin, 36% in uninvolved skin) than in patients without skin lesions (14%). The occurrence of IgG and IgA was less frequent than that of C3 but the distribution was similar to that of C3. In normal skin of 20 patients with chronic discoid LE, deposits were found in one. Deposits were found in the skin of one-third of patients with nuclear antibodies in their sera and symptoms compatible with SLE but with a score of symptoms too low to meet the criteria.

Key words: Systemic lupus erythematosus (SLE); Dermo-epidermal junction of human skin; Deposits of immunological complexes; Immunoglobulins; Complement C3

In 1963 and 1964 a number of papers were published on the demonstration of deposits of immunoglobulins and complement components as a band at the dermo-epidermal junction in skin biopsies from lesions of patients with systemic lupus erythematosus (SLE) and chronic discoid lupus erythematosus (DLE) (3, 7, 13). Since the initial reports appeared, a number of papers have confirmed and extended the findings. Deposits may be found not only in skin lesions from patients with SLE but also in clinically normal skin. In DLE, however, deposits are found in the skin lesions, but rarely in uninvolved skin. Elution studies indicate that the immunoglobulins deposited are specifically directed against nuclear antigens as well as against basal membrane antigens (11, 14). Similar findings have been described in glomeruli of patients suffering from SLE, in whom mesangial deposits are found, in cases of glomerulopathy (1) and in patients without clinical or light microscopic signs of glomerular damage (9). The demonstration of deposits in the skin may be of diagnostic importance (4, 5, 15), particularly in patients without skin eruptions or with atypical skin lesions. In this study we present the finding of deposits in clinically normal skin of patients with SLE as well as DLE, in whom the diagnosis was based upon well defined criteria (6, 8, 10).

MATERIAL

Skin biopsies were obtained from 97 patients and 67 control persons. Twenty patients had DLE, according to the criteria of Lever (12). Sixty-four patients had SLE according to one or several of the definitions proposed by the American Rheumatism Association (ARA) (6), Hahn et al. (10), and Dubois (8). Thirty-one patients fulfilled all three sets of criteria. A group of 13 patients had antinuclear antibodies in their sera (all had ANF and 5 had a positive LE cell test as well), and symptoms compatible with SLE, though the score was not high enough to fulfill the criteria mentioned above. These patients are referred to as questionable SLE. Eight patients had lupoid hepatitis according to Dubois (8). Two of these met the criteria of Hahn et al. and were consequently included in the SLE group. Six patients had insufficient scores according to the ARA and Hahn et al.'s criteria and were grouped among the patients with questionable SLE. The patients with SLE have been divided in two groups according to whether or not they had, or had had skin eruptions. Biopsies were obtained from LE lesions as well as from clinically normal skin. Biopsies from clinically normal skin were taken from areas not exposed to light, usually from the thigh or the hip. Of 67 control biopsies, 18 were obtained from patients undergoing cosmetic surgery and 49 from clinically normal skin of patients with leg ulcers, psoriasis, acne vulgaris, and warts.

METHODS

Immunohistochemical staining

The biopsies were immediately frozen in liquid nitrogen, and 4-8 μm thick sections were cut in a cryostat. The sec-
Fig. 1. Deposits of IgG in a homogeneous band in the dermo-epidermal junction of skin from a patient with SLE.

Fig. 2. Deposits of complement C3 in a serpentine-like pattern in the dermo-epidermal junction of skin from a patient with SLE.

Deposits were air-dried for 15 min, washed in saline for 30 min and incubated with one drop of diluted conjugate in a moist chamber for 30 min. Fluorescein isothiocyanate labelled rabbit IgG, specific for human gamma, mu and alpha chains, and the beta component of human C3 (Dako, Copenhagen) were used. Blocking procedures with unconjugated antisera were included in each experiment. The preparations were examined in a Leitz Ortholux fluorescence microscope equipped for transmitted light illumination using an Osram HBO 200 lamp as light source, a KP 490 nm interference filter for primary light selection, a Tiyoda wide-angle, dark field condensor and a 3 mm OG 530 nm glass filter as barrier filter.

RESULTS

Deposits of immunoglobulins and/or complement C3 were found in the dermo-epidermal junction in a total of 87 biopsies. In some cases the deposits formed a narrow, homogeneous or stippled band. In others, a wide zone or a serpentine-like pattern could be demonstrated (Figs. 1, 2).

Table 1 presents the findings in skin biopsies obtained from clinically normal skin of 97 patients and 67 controls. Deposits were found in 67% of 64 patients with SLE of which 40 patients had skin lesions and 24 patients had none. Deposits in normal skin were found in 67% of both groups of patients. Four of 13 patients with questionable SLE had deposits in normal skin while one of 20 patients with DLE had deposits in clinically unaffected skin. This patient had had discoid lesions for about 6 years and arthralgias for 3 months. Nuclear antibodies were not found in her serum. Two of 67 control persons had deposits in clinically normal skin (IgM in both cases). They were females of 19 and 16 years, who had the biopsies taken during cosmetic surgery. Both were on birth control pills. One gave a history of a rash on sun exposure. She had an elevated IgM, but no antinuclear antibodies in her serum. The other patient had normal serology and an unremarkable history. A biopsy from another area of her skin confirmed the finding of IgM-deposits in the dermo-epidermal junction.

Forty-seven of the patients with SLE met the criteria of Hahn et al., 38 those of the ARA, and 61 those of Dubois. Deposits were found in 72, 68, and 66%, respectively (Table II). Three of the 8 patients with lupoid hepatitis had deposits in clinically normal skin. Two of them had SLE accord-
Table I. Deposits of immunoglobulins and complement C3 in the dermo-epidermal junction of clinically normal skin from 97 LE patients and 67 controls

<table>
<thead>
<tr>
<th>SLE</th>
<th>Deposits in dermo-epidermal junction</th>
</tr>
</thead>
<tbody>
<tr>
<td>without skin lesions</td>
<td>24</td>
</tr>
<tr>
<td>with skin lesions</td>
<td>40</td>
</tr>
<tr>
<td>SLE questionable</td>
<td>13</td>
</tr>
<tr>
<td>DLE</td>
<td>20</td>
</tr>
<tr>
<td>Controls</td>
<td>67</td>
</tr>
<tr>
<td>Total</td>
<td>164</td>
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</table>

Table III. Deposits of immunoglobulins and/or complement C3 in skin lesions of LE patients

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Deposits</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE</td>
<td>20</td>
</tr>
<tr>
<td>Questionable SLE</td>
<td>1</td>
</tr>
<tr>
<td>DLE</td>
<td>19</td>
</tr>
</tbody>
</table>

Table IV. The immunoglobulin classes, IgG, IgM, and IgA, and complement C3 in the skin deposits

<table>
<thead>
<tr>
<th>No.</th>
<th>Patients</th>
<th>C3</th>
<th>IgG</th>
<th>IgM</th>
<th>IgA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin lesions</td>
<td>37</td>
<td>22</td>
<td>16</td>
<td>30</td>
<td>13</td>
</tr>
<tr>
<td>Clinically normal skin</td>
<td>28</td>
<td>10</td>
<td>12</td>
<td>26</td>
<td>6</td>
</tr>
<tr>
<td>Patients with skin lesions</td>
<td>31</td>
<td>14</td>
<td>14</td>
<td>19</td>
<td>1</td>
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<tr>
<td>Patients without skin lesions</td>
<td>22</td>
<td>3</td>
<td>3</td>
<td>21</td>
<td>2</td>
</tr>
</tbody>
</table>

DISCUSSION

The finding of deposits in clinically normal skin of more than two-thirds of patients with definite SLE, compared with one-third in patients with questionable SLE, stresses the value of the diagnostic criteria and of the immunopathological examination of skin. The diagnostic value of immunofluorescence microscopy of normal skin in SLE is unrelated to the presence or absence of clinical signs of skin involvement. The finding that one of 20 patients with discoid LE had deposits in normal skin corresponds to the findings of other authors (2, 4, 5, 15) and stresses the localized nature of the disease. The finding that 77 deposits (88%) contained IgM whereas only 31 deposits (36%) contained IgG differs from previously published results in which IgG has been a more frequent finding than IgM (2, 5). This discrepancy may be due to differing conjugates. The incidence of IgG and C3 was similar, and, unlike the incidence of IgM, varied according to whether or not the patients had skin lesions.

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REFERENCES


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