Expression of MHC Class II Antigens and Other T Cell Activation Antigens on T Cells and Salivary Duct Epithelial Cells in the Salivary Gland of Cases of Sjögren’s Syndrome

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We studied infiltrating T cells and salivary duct epithelial cells in the sublingual glands of 10 patients with primary Sjögren’s syndrome (SS) using monoclonal antibodies (MoAb) to T cell subsets (OKT-series), natural killer cells (Leu7) and activation antigens of T cells such as OKT10, OKT9, interleukin 2 receptor (anti-Tac antibody) and major histocompatibility complex (MHC) class II antigens (anti-DR and anti-DQ antigens).

DR antigens were identified on salivary duct epithelial cells, suggesting that the cells might function as antigen-presenting cells (APC).

Among the salivary duct epithelial cells, OKT8 + cells, which are known to be suppressor/cytotoxic cells, were found in 9 out of 10 patients.

Three types of mononuclear cell infiltrations were also evaluated separately: (1) periductal foci, (2) periacinal foci and (3) lymph follicles.

We found that the majority of the infiltrating cells in the central portion of the periductal foci were activated T cells (OKT3 + , OKT4 +, OKT8 +, DR + and DQ +), but OKT9, OKT10 and Tac antigens were rarely found in this portion. However, most of the infiltrating cells in the peripheral portion of the periductal foci were OKT10 +, and some of them were also positive for OKT9 antigen (transferrin receptor). The results indicated that the T cells in the peripheral portion of the periductal foci are at an early or intermediate phase of activation, whereas the T cells around the salivary ducts are at a later phase. Infiltrating cells in the periacinal foci resembled the cells on the peripheral portion of the periductal foci.

Cells within lymph follicles were mainly B cells although scattered OKT4 + or OKT8 + cells were also present.

(Key Words: major histocompatibility complex class II antigens, activated antigens, T cells, salivary glands, Sjögren’s syndrome)

INTRODUCTION

Sjögren’s syndrome (SS) is a chronic inflammatory disease characterized by lymphocytic infiltration in the salivary and/or lacrimal glands. SS is generally considered as an autoimmune disease although the exact mechanism of glandular destruction is still unknown. It appears, however, that infiltrating lymphocytes play an important role in the tissue damage.

Recently, several monoclonal antibodies (MoAb) to T cells and their functional subsets have become available. In patients with SS, abnormal levels of peripheral blood T cells and their subsets have been reported (5, 8, 15). Studies on the lymphocytes in the salivary glands of SS have shown that helper/inducer T cell subsets are predominant (1, 20).

In the present study, we examined cell surface antigens expressed on infiltrating lymphocytes and duct epithelial cells in the sublingual glands from primary SS using MoAb directed to major histocompatibility complex (MHC) class II antigens or other antigens associated with T cell activation.

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Fig. 3 Scheme of the infiltrating cell foci: periductal area, periacinal area and lymph follicles.

Table 1 Surface characteristics of lymphocytes infiltrating the salivary glands of ten patients with primary Sjögren's syndrome.

<table>
<thead>
<tr>
<th>Periductal foci</th>
<th>Periacinal foci</th>
<th>Lymph follicles</th>
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<tbody>
<tr>
<td></td>
<td>central</td>
<td>peripheral</td>
</tr>
<tr>
<td>Periductal foci</td>
<td>portion</td>
<td>portion</td>
</tr>
<tr>
<td>OKT3</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>OKT4</td>
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<td>++</td>
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<td>OKT6</td>
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<td>OKT8</td>
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<tr>
<td>Tac</td>
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<tr>
<td>OKT9</td>
<td>-</td>
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</tr>
<tr>
<td>OKT10</td>
<td>+</td>
<td>+++</td>
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<tr>
<td>Hu-11 + Hu-18</td>
<td>+++</td>
<td>++</td>
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<tr>
<td>Hu-20</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>anti-IgM</td>
<td>+</td>
<td>+</td>
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<td>Leu7</td>
<td>+</td>
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Positively stained cells accounted for more than 50% (+++), 10–50% (++), 5–10% (+) or less than 5% (−).
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Fig. 4 Lymphocytes in the central portion of periacinal foci: Lymphocytes stained with DQ (dark blue) or OKT8 antibodies (red), and those stained with both antibodies (dark purple) in the central portion of the periductal foci are shown.

Fig. 5 OKT9+ lymphocytes in the periacinal foci: OKT9+ cells are scattered in the periacinal foci (arrows)

Fig. 6 OKT10+ cells in the periacinal foci: Numerous OKT10+ lymphocytes (blue) are seen in the periacinal foci and OKT8+ lymphocytes (red) are observed in the periductal foci.
DISCUSSION

A similar autoimmune mechanism has been suggested in Sjögren's syndrome and autoimmune thyroiditis because of the similar histopathological findings. In thyroid disease, DR antigens have been expressed on epithelial cells of the thyroid follicles and it was suggested that these cells were active in antigen presentation (2). In the salivary glands, Oxholm et al (18) also found OKT6+ cells in SS and indicated that these cells might be Langerhans cells, one of antigen-presenting cells (APC). However, they did not determine if OKT6+ cells expressed MHC class II antigens. In other reports (1), few OKT6+ cells were identified in the salivary glands and their results were compatible with those obtained in the present study. DR antigens were also found on the salivary duct epithelial cells in SS although the cells did not express DQ antigens. MHC class II antigens are essential for antigen presentation by APC to T cells and most APC are positive for both DR and DQ antigens. A small number of monocytes which function as APC, however, do not express DQ antigens (16). Antigen-presenting function has been reported to be restricted to DR antigens but not to DP or DQ antigens (14, 17). It is possible, therefore, that salivary duct epithelial cells in SS might present antigens to T cells.

OKT8+ cells were detectable among the salivary duct epithelial cells in nine of 10 patients studied, whereas, OKT4+ cells were identified in only two patients. The findings suggested that the invading T cells are cytotoxic to the epithelial cells.

Mononuclear cell infiltration in the salivary glands is a characteristic feature of SS. Most of these cells consist of activated helper/inducer T cells in the minor salivary glands in primary SS (1, 5). We also confirmed this in the major salivary glands (sublingual glands) and no difference was found in the characteristics of infiltrating cells between primary and secondary SS (20). In the major salivary glands of SS, however, large foci of infiltrating cells containing lymph follicles are frequently found (20). In the present study, we examined mononuclear cell infiltration using MoAb to several activation antigens including MHC class II antigens in three regions: (1) the periductal area, (2) periacinal area and (3) lymph follicles.

In the central portion of the periductal foci, most of the cells were OKT4+, DR+, DQ+, OKT9−, OKT10−, and Tac−, and the remaining cells were OKT8+, DR+, DQ+, OKT9−, OKT10−, and Tac+. In the peripheral area of the foci, however, OKT10+ and/or OKT9+ cells were identified. Many OKT10+ cells were also found in the periacinar foci and some of cells were OKT9+. Activated T cells express antigens recognized by OKT9 and OKT10 antibodies (7, 24). Tac antigen (25) or MHC class II antigens (Ia-like antigens, DR antigen and DQ antigen) in vitro (13, 23). When T cells are activated by mitogens, both transferrin receptor and Tac antigen appear at an early phase, whereas HLA DR antigens appear later. Expression of OKT10 antigen was found to occur between the two activation stages (4). It has also been confirmed that activated T cells express Tac antigen in the early G1 phase and transferrin receptors appear in the late G1 phase. Ia and OKT10 determinants are expressed in the S phase of the cell cycle or later (22).

The present study, therefore, demonstrated that the T cells in the central part of the periductal foci are in the S phase or a later phase. The majority of the T cells in both the peripheral region of the periductal foci and periacinar foci are also in the S phase or a later phase, but a few T cells are in the late G1 phase.

From this evidence, the following speculations can be made: if antigen(s) such as viral antigen(s) are expressed on the surface of duct epithelial cells, the antigen(s) are presented to T cells with DR molecules, and then activate them. Subsequently, the activated helper T cells induce antigen-specific cytotoxic T cells and aid in the activation of B cells. The T cells cytotoxic for the antigen(s) expressed on duct epithelial cells invade the epithelial cells. Activated B cells proliferate, form lymph follicles and produce autoantibodies. More T cells might be supplied from the peripheral blood and migrate to the periductal area. In this connection, we found an increase in T cells in the early or relatively early stages of activation in the peripheral blood of SS patients, suggesting that the activated T cells are ready to migrate to the target tissues (submitted for publication).
REFERENCES


