Alterations in the T-Lymphocyte Subpopulation in Patients with Rhinoscleroma

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T-lymphocyte subpopulations were studied in a group of patients with rhinoscleroma due to Klebsiella rhinoscleromatis. The data demonstrated that these patients had a significantly greater number of T-suppressor/cytotoxic lymphocytes than did clinically healthy individuals. This finding correlated with a diminished response to the T-cell mitogen concanavalin A. The evidence indicated that the T-cell response of these patients was decreased and may reflect the host's response to the bacterial invader, thus explaining the chronicity of the disease.

Rhinoscleroma is a progressive, granulomatous infectious disease, usually limited to the upper respiratory tract, induced by Klebsiella rhinoscleromatis (5, 8). Epidemiologic studies have shown that the disease affects men and women equally, with the age group 15 to 35 years having the highest incidence. It appears to be transmitted only after prolonged exposure, for example, among family members living together in close quarters (23). The disease carries a high morbidity and is endemic in some parts of the world, such as eastern Europe, north and central Africa, southern Asia, the Middle East, and some regions of South and Central America. It is not distributed uniformly among populations but, instead, seems to be centered in rural areas among less-hygienic inhabitants (13). Immunological studies have been conducted to establish whether there is an adequate humoral and cellular immune response of the host against the causal organism. Serological studies provide strong evidence for the presence of humoral antibodies directed against several mucopolysaccharide fractions of K. rhinoscleromatis, although they are not specific enough to be used in the routine diagnosis of florid scleroma (22, 23, 25, 27). In addition, the serum from some patients with active rhinoscleroma had poor in vitro bactericidal activity against K. rhinoscleromatis (15). Cell-mediated immunity (CMI) in this disease has been scantily studied. A skin window test was used to examine local inflammatory reactions and the state of immu

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TABLE 1. Determination of T-lymphocyte subpopulations in patients with rhinoscleroma and in healthy individuals

<table>
<thead>
<tr>
<th>Subpopulation</th>
<th>Patients with rhinoscleroma (mean ± SD)</th>
<th>Healthy controls (mean ± SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-rosetting cells</td>
<td>52 ± 1.60</td>
<td>59 ± 1.59</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>CD8</td>
<td>33 ± 2.69</td>
<td>22 ± 1.23</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>CD4</td>
<td>27 ± 1.92</td>
<td>33 ± 1.75</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

5396; Costar, Cambridge, Mass.) for 3 days with different concentrations of ConA, ranging from 1.0 to 100 μg/ml, as previously described (19). All cultures were performed at least in triplicate. One microcurie of [3H]thymidine (5.0 Ci/mmol; New England Nuclear, Boston, Mass.) was added to each well 28 h before termination of cultures. Cells were harvested with a cell harvester (Brandell, Rockville, Md.), and the glass fiber mats were counted in a liquid scintillation counter. Data are presented as mean counts per minute ± standard deviation.

Fisher’s test was used to determine the homogeneity or heterogeneity of the variances among groups (4). The significance of the difference among the means of the groups with homogeneous variances was determined by Student’s t test; that among the heterogeneous variances was determined by the Mann-Whitney U test (12).

The absolute count of lymphocytes was used to determine differences, if any, between the groups under investigation. Absolute counts of lymphocytes tended to be lower in the blood of patients with rhinoscleroma than in the blood of healthy individuals; however, the difference was not significant (P > 0.05). The number of lymphocytes per microliter was 1,399 ± 113 in the patients with rhinoscleroma and 1,519 ± 128 in the healthy individuals.

To determine the number of T lymphocytes present in the peripheral blood of the patients under study, the number of E-rosetting cells, as well as of CD4 and CD8 lymphocytes, was estimated. The results indicated that the number of E-rosetting cells, as well as of CD4 lymphocytes, was similar in the rhinoscleroma and control groups (Table 1). However, significant differences (P < 0.002) were observed among the rhinoscleroma and control groups when the number of CD8 cells was determined. Patients with rhinoscleroma displayed a CD4:CD8 ratio of 0.84 ± 0.04, whereas in healthy subjects the CD4:CD8 ratio was 1.40 ± 0.07, clearly indicating a higher proportion of CD8 lymphocytes in the former group tested.

In addition, experiments were performed to determine the ability of T cells to respond to different concentrations of ConA. Lymphocytes from the patients under study reacted differently to the mitogen compared with those from healthy individuals (Fig. 1). The data show that in both groups the optimal response was observed at the dose of 10 μg/ml and that, at this ConA concentration, the proliferative response was significantly lower in the patients with scleroma than it was in the control group (P < 0.005). However, the data also showed that higher proliferative responses were obtained in the rhinoscleroma group than in healthy controls when doses of 100 μg/ml were used; the difference was also significant (P < 0.002).

The present data show an abnormality in the T-lymphocyte population of patients with rhinoscleroma. The irregularly consisted of an increased number of CD8 cells as well as a low response to a mitogen specific for T cells, namely ConA (17), as compared with healthy individuals. It is interesting to note the proliferative response of the rhinoscleroma group to the highest dose of ConA. It is known that high concentrations of ConA induce suppressor cells (7); therefore, at this high dose of the mitogen, the suppressor cells that appeared in higher proportion in the patients with rhinoscleroma may have proliferated optimally, giving the highest [3H]thymidine incorporation. The diminished response to the T-cell mitogen is particularly important since it indicates an abnormal CMI, which may prevent patients from eliminating the bacteria.

In studies performed with other infectious diseases produced by intracellular microorganisms, such as leprosy, similar findings have been reported (3). Thus, patients with lepromatous leprosy have a depressed cellular immune capacity to respond to antigens from Mycobacterium leprae, a reduction in the number of effector and CD4 cells, an increase in the number of CD8 cells (1, 24), and a reduction in the synthesis of interleukin-2 (9). Furthermore, the lymphocytes of individuals with leprosy suppressed the response to ConA of lymphocytes from healthy individuals (3), a finding that has been observed in infections caused by other acid-fast bacilli, namely Nocardia brasiliensis (18). The observations described above indicate the important role that CD8 cells play in regulating the immune response of individuals infected with intracellular microorganisms. In this regard, it is known that immune homeostasis results from a delicate balance of inducer and suppressor subsets within the human T-cell circuit. Perturbation in subset dynamics may initiate a variety of immunopathological disorders (20). The changes in the T-cell populations reported here may help to explain some of the pathology observed in patients with rhinoscleroma.

The granuloma particular to patients with rhinoscleroma is similar to that observed in lepromatous leprosy and is characterized by the presence of histiocytes (14). It has been postulated that the intimate contact of both helper and suppressor cells with mononuclear phagocytes may impede the immune response in patients with rhinoscleroma, thereby preventing the maturation of histiocytes into bacteriolytical epithelioid cells and allowing florid bacillary proliferation and extensive nasopharyngeal tissue destruction.
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Our data showing an altered ratio in the lymphocytes engaged in CMI may explain the chronicity of the disease due to the inability of the infected individuals to eliminate the microorganism. The increased number of CD8 cells may result in the inability of the infected individuals to activate the mononuclear phagocytic system (11). In infections, the activity of this accessory phagocytic system must be heightened. T-cell products secreted after immune recognition cooperate to effect this heightened activity. Such products promote increased bone marrow activity and resultant production of macrophages, and they also cause a heightened functional activity in the final effector cells (16).

The heterogeneity of the results obtained in the patients with rhinoscleroma reported here is very probably due to the different stages of evolution of the disease, which in the present study varied from 3 to 15 years. Nevertheless, the results pointed to a modification in the T-cell population.

In summary, in this investigation we found that patients with rhinoscleroma showed an alteration in the ratio of CD4:CD8 cell subsets and an abnormal proliferative response to ConA, which may reflect the host’s response to the bacterial invader and help to explain the chronicity of the disease.

LITERATURE CITED