Remarkable Increase in CD26-Positive T Cells in Patients with Human T Lymphotropic Virus Type I (HTLV-I) Associated Myelopathy

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We used two-color flow cytometric analysis to investigate CD26+ (Tα1+) cells in peripheral blood T lymphocytes from patients with human T-lymphotropic virus type-I (HTLV-I) – associated myelopathy (HAM). The percentage of CD26+ cells among CD3+ cells was markedly increased in patients with HAM, compared with anti-HTLV-I seropositive carriers (p < 0.001) and seronegative controls (p < 0.01). Within the subpopulation of T cells, a significantly high percentage of CD26+ cells was detected in both CD4+ and CD8+ cell populations. Furthermore, analysis of HLA-DR+ T cells revealed similar results. In contrast CD4+CD45RA+ cells were significantly decreased in comparison with controls. These results suggest that immunologically activated or memory T cells found in peripheral blood may be etiologically relevant to HAM.

Key words: activated T cells, memory T cells

Introduction

At present, both “human T-lymphotropic virus type-I (HTLV-I) – associated myelopathy (HAM)” (1) and “HTLV-I-associated tropical spastic paraparesis” (2) are considered identical (3). However, regarding the pathogenesis of HAM/TSP, the mechanism by which HTLV-I infection causes chronic progressive myelopathy is still not known. Hafler et al have reported that Tα1+ (CD26+) cells include T memory cells (4) and that the number of CD26+ cells is related to the disease activity of multiple sclerosis (MS) (5). Tα1 (CD26) is a 105kD antigen (Ag) which is markedly expressed on activated T cells but not on macrophages or B cells (6). Various immunological activated states have been demonstrated in patients with HAM/TSP (7–9). Using two-color flow cytometric analysis Itoyama et al have reported increases in helper inducer T cells and activated T cells in HAM (9). Here, we report a study using two-color flow cytometric analysis of CD26+ cells in peripheral blood lymphocytes (PBL) from patients with HAM.

Subjects and Methods

Subjects

Peripheral blood lymphocytes (PBL) from 15 patients with HAM (4 men, 11 women, age: 26–66) were studied. The diagnosis of HAM was based on the criteria described by Osame et al (10). For controls the PBL of anti-HTLV-I antibody seropositive carriers (2 men, 5 women, age: 41–77) and anti-HTLV-I antibody seronegative normal subjects (6 men, 9 women, age: 22–51) were studied.

Analyses of the surface markers on T cells

Peripheral blood mononuclear cells were separated from heparinized venous blood by Ficoll-Conray density gradient centrifugation. After washing them 3 times, cells (2 × 10^6) were stained with 5 μl of monoclonal antibodies to human lymphoid cells. For monoclonal antibodies, FITC-labeled anti-CD3, CD4, CD8 (Coulter Immunology, Hialeah, FL) and phycoerythrin (PE)-labeled anti-DR, CD26 (Tα1), CD45RA (2H4) (Coulter Immunology, Hialeah, FL) were used. The labeled cells were analyzed by Epics III (Coulter Electronics, Hialeah, FL). Statistical analysis was done with Student’s t-test.
Results

**CD26+ T cell subsets in PBL**

Phenotypic analyses of PBL are listed in Table 1. In HAM patients, the percentage of CD3+CD26+ cells among the CD3+ cells (33.4 ± 19.0%) was significantly increased compared with that for normal subjects (13.8 ± 3.2%, p < 0.01); it was also significantly increased as compared with that for HTLV-I carriers (10.0 ± 2.4%, p < 0.001). Furthermore, the percentage of CD4+CD26+ cells among the CD4+ cells was significantly increased (p < 0.001), and the percentage of CD8+CD26+ cells among the CD8+ cells was increased as well (p < 0.05), in comparison to the values for the normal subjects.

**HLA-DR+ T cell subsets in PBL**

In HAM patients, the percentage of CD3+HLA-DR+ cells among the CD3+ cells (22.1 ± 13.0%) was markedly increased in comparison to the percentage for normal subjects (2.4 ± 0.5%, p < 0.001), and as compared with the percentage for HTLV-I carriers (4.4 ± 2.1, p < 0.001). Furthermore, the percentage of CD4+HLA-DR+ cells among the CD4+ cells was significantly increased (p < 0.001) and the percentage of CD8+HLA-DR+ cells among the CD8+ cells was also increased (p < 0.001) as compared to the values for normal subjects.

**CD4+CD45RA+ subsets in PBL**

In HAM patients, the percentage of CD4+CD45RA+ cells among the CD4+ cells was significantly decreased in comparison to the value for normal subjects.

Discussion

We found a marked increase in CD26+ T cells in the PBL from patients with HAM, together with a higher percentage of HLA-DR+ T cells in the PBL from HAM patients. Recently it was reported that CD45RA+ cells among T cells indicate naive cells, and CD29+ cells indicate memory cells (11). In the current study, patients with HAM contained a decreased percentage of CD45RA+CD4+ cells compared with both normal subjects and HTLV-I carriers. These results support the possibility that PBL from HAM patients have a higher percentage of activated or memory T cells.

Hafler et al reported that an increase in CD26+ cells from patients with multiple sclerosis (MS) implies systemic immune activation in the pathogenesis of MS (12). They also demonstrated that CD26+ cells, which constituted only 10–15% of the circulating T cells in normal subjects.
CD26-Positive T Cells in HAM

subjects had an enhanced proliferative response to soluble recall Ag (for example, tetanus toxoid and mumps Ag) (4). In a study of Graves’ disease, Eguchi et al reported that CD26+ cells may include antigen-triggered memory cells that react with thyroid-specific Ag (13). From the above findings, a possible explanation is that the increase in CD26+ cells in HAM patients may indicate an expansion of the memory T cell population which recognize neuronal tissue-related Ag in the immunologically activated T cells. Another explanation is that the increase in this population may be related to a hyperimmune response to HTLV-I (14). Further investigation of the functional role of the activated or memory T cells in PBL from HAM patients will be necessary.

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References