The Role of Host T-Cell Lymphocyte in Immunopathogenesis of HTLV-I-Associated Myelopathy/Tropical Spastic Paraparesis

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Abstract

Human T-cell lymphotropic virus type 1 (HTLV-1) is associated with adult T-cell leukemia/lymphoma (ATL) and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). Only a limited percentage of infected individuals develop disease in response to the virus while the majority remain asymptomatic and HAM/TSP is the most common clinical manifestation of the virus. HAM/TSP is an inflammatory disease of the central nervous system (CNS). The mechanism by which HTLV-1 induces HAM/TSP is not clear yet. Several factors have been hypothesized to contribute to an HTLV-I-infected individual’s progress to HAM/TSP. One of the most important factors is the host immune response against HTLV-I and T cell lymphocytes plays a key role in the immune response against HTLV-I virus. HTLV-I attacks different types of cells in the body but CD4(+) T lymphocytes are the main target of HTLV-I that have an important role in the immunological response to this retrovirus. HTLV-I-infected CD4+ T lymphocytes migrate to the CNS tissues and CD8+ HTLV-I specific cytotoxic T lymphocyte (CTL) attack HTLV-I-infected lymphocytes. Recent data indicate that HTLV-I and its expression are localized in infiltrated lymphocytes within the spinal cord lesions of HAM/TSP patients rather than in resident central nervous system (CNS) parenchymal cells. Hyperactive CD8(+) cytotoxic T lymphocytes (CTL) that generate in response to HTLV-I-infected lymphocytes likely play a key role in the genesis of pathologic abnormalities associated with HAM/TSP and also a high HTLV-I proviral load in peripheral blood lymphocytes (PBL) increase this pathological response and cause spinal cord lesions in HAM/TSP patients. Although the exact mechanism underlying the high HTLV-I proviral load in PBL in HAM/TSP patients is still unknown, we must consider therapeutic approaches in HAM/TSP that eliminate HTLV-I-infected CD4+ T lymphocytes and also the regulation of efficiency and activity of hyperactive CD8(+) cytotoxic T lymphocyte (CTL).

Keyword: HTLV-1, htlv-1-associated myelopathy/tropical spastic paraparesis (HAM/ TSP), cytotoxic T lymphocytes (CTL)

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