Human T-cell Lymphotropic Virus Type I and Systemic Lupus Erythematosus

**Key words:** retrovirus, autoimmune disease, pathogenesis

An association between retroviral infections and autoimmune processes has long been suspected (1). The possible pathogenic roles of infectious agents in disease development may involve molecular mimicry, polyclonal activation, and specific acceleration of latent autoimmune phenomena. In particular, viruses that persistently infect lymphocytes are attractive candidate pathogens as triggers of autoimmune diseases.

Human T-cell lymphotropic virus type I (HTLV-I) is a member of a group of mammalian retroviruses which have a relative and preferential cell tropism for CD4+ T lymphocytes (2, 3); it is well known as a prerequisite agent for the development of adult T-cell leukemia/lymphoma and HTLV-I-associated myelopathy/tropical spastic paraparesis (HAM/TSP) (4). Recently, growing empirical knowledge suggests an expanded clinical spectrum in patients with HAM/TSP and the presence of systemic manifestations in HTLV-I-infected individuals without symptoms of myelopathy (5). These include T lymphocyte alveolitis, Sjögren’s syndrome, arthropathy, uveitis, polymyositis, necrotizing vasculitis, thyroiditis, Behçet’s disease, and pseudohypoparathyroidism (4-6). The analogy of some of these clinical manifestations with known chronic inflammatory disorders, for which a viral cause has long been sought, is influencing our understanding of virus-host interactions. Importantly, both the distributional bias of HTLV-I activation between the blood flow and the affected lesions and accumulated cellular responses are documented or suggested in patients with HAM/TSP, HTLV-I-associated arthropathy, HTLV-I-associated bronchopneumonopathy, HTLV-I uveitis, and HTLV-I-associated polymyositis (6). Furthermore, expression of bcl-2 oncoprotein has been demonstrated in T lymphocytes infiltrating the spinal lesions of patients with HAM/TSP (7). Bcl-2 belongs to a growing family of proteins that can either inhibit (Bcl-2, Bcl-xL, etc.) or favor (Bax, Bcl-xS, etc.) apoptosis (8). Therefore an implication of bcl-2 related resistance to apoptosis is discussed as a mechanism for viral persistence in the spinal lesions (7).

The case presentation by Miura and colleagues suggests a possible link between systemic lupus erythematosus (SLE) and HTLV-I infection (9).

The first description of such a case was provided by Vernant et al (10), and additional 2 cases were recently reported by Takayanagui et al (11). Although the possible involvement of retroviruses in the etiopathogenesis of systemic lupus erythematosus (SLE) is controversial as in other autoimmune diseases (12), these early reports may promote further well-designed studies. A preliminary report documented that anti-nuclear autoantibodies were detected in 9.71% of the HTLV-I-infected individuals and in 3.43% of the control group (p<0.05) (13). Meanwhile, in addition to the established correlation of generalized disease activity with polyclonal B-cell activation, a non-specific T-cell function that induces polyclonal B-cell activation was demonstrated in patients with SLE (14). It was revealed that CD4+ T-cell clones derived from SLE patients can stimulate autologous B-cells to produce anti-self antibodies. Moreover, an increased expression of bcl-2 was found in T-cells but not in B-cells of SLE patients (15, 16), and defects in the apoptosis-promoting Fas gene, or its ligand (FasL), were identified in connection with the SLE-like manifestations in some spontaneous mouse models of SLE (17-19). As described above, the continuation of active and chronic cellular inflammation in the affected spinal cord of patients with HAM/TSP might be explained by the implication of a resistance to Fas ligand-induced apoptosis of the infected lymphocytes (7). In addition, polyclonal B-cell activation mediated by membrane tumor necrosis factor-α expressed on HTLV-I-infected T-cells was recently documented (20). These findings, together with the in vivo clonal expansion of CD4+ T-cells associated with HTLV-I infection (21-23), may also warrant further investigation concerning the possible partial overlap of molecular and cellular backgrounds between retrovirus infections and autoimmunity (24). To date, the rarity of the association between HTLV-I infection and SLE only raises simple questions of whether it may be a mere coincidence, whether SLE may be another disorder related to HTLV-I infection, or whether the several systemic manifestations of the infection may mimic SLE by fulfilling the criteria for its diagnosis (11).

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References

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