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Review

Virological aspects of tropical spastic paraparesis/ HTLV-I associated myelopathy and HTLV-I infection

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TSP/HAM, a chronic spastic paraparesis or paraplegia with sphincter disturbances and minimal sensory loss, is characterized pathologically by a meningo-myelitis of the lower thoracic cord with axonal degeneration and demyelinisation of the lateral and anterior spinal tracts. High titer specific anti HTLV-I antibody is present in the serum and in the cerebrospinal fluid with specific intrathecal IgG synthesis, elevated IgG index and intra blood-brain barrier IgG synthesis. Most TSP/HAM patients also exhibit IgG oligoclonal bands in the CSF (also sometimes in the serum), some of those being HTLV-I specific, directed against p24 or against various antigens of the disrupted virus. HTLV-I specific cytotoxic T lymphocytes (CTL), mainly CD8+HLA class I restricted, and recognizing several HTLV-I epitopes especially of the *tax*, the *rex* and *env* proteins are present at high levels in the blood and CSF of TSP/HAM patients. These findings of high CTL activity have led some authors to suggest that these specific CD8 cells may play a major role in TSP/HAM pathogenesis by destruction of HTLV-I infected cells within the central nervous system. Such an hypothesis remains a matter of controversy since some groups have shown that such CTL (both CD8+ or CD4+) are also present in asymptomatic HTLV-I carriers. Recent data have confirmed the high proviral load in PBMC of TSP/HAM patients (as compared to asymptomatic HTLV-I carriers); however viral expression is very low. There is also recent evidence that more than one copy of HTLV-I proviral DNA may be present in an individual PBMC. One major unanswered question is whether HTLV-I can infect central nervous system cells (neurons, or astrocytes) or if the only HTLV-I infected cells present in the CNS are the infiltrating CD4+ cells. There are published reports supporting both hypotheses. Futhermore, no specific HTLV-I sequences have been related to a given disease outcome, whereas several molecular studies have clearly demonstrated that nucleotide changes in some parts of the HTLV-I genome are correlated with the geographical origin of the patients.

Keywords: HTLV-I; chronic myelopathy; TSP/HAM; neurotropism

Introduction

In 1985, we first reported the high prevalence of serum antibodies against the Human T Cell Lymphotropic virus type I in neurological patients in Martinique (French West Indies) with a chronic progressive myelopathy (named Tropical Spastic Paraparesis-TSP) and suggested that either this virus is neurotropic or that this virus or a related one contributes to the pathogenesis of TSP (Gessain *et al*, 1985). In 1986, a similar association was documented in Southern Japan and this neurological entity was called HTLV-I associated myelopathy (HAM) (Osame *et al*, 1986). Soon after it was recognized that HTLV-I associated TSP and HAM were the same disease and the name TSP/HAM was retained (Roman and Osame, 1988; Gessain and Gout, 1992). At that time, HTLV-I, the first human exogenous oncoretrovirus (Poiesz *et al*, 1980), was considered to be the causative agent of only adult T cell leukemia/lymphoma, an aggressive CD4+ lymphoproliferative disorder (Takasuki *et al*, 1977). In this article, we shall first review the main virological aspects of HTLV-I infection in TSP/HAM disease. We shall then raise

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