



Case Report

HTLV-1 and HIV-1 co-infection: A case report and review of the literature

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ABSTRACT

HTLV type 1 and 2 are both involved in actively spreading epidemics, affecting over 15 million people worldwide. HTLV-1 has been described as the more clinically significant one, being associated with diseases such as adult T-cell leukemia and tropical spastic paraparesis. We report here a case of tropical spastic paraparesis in an HIV-positive patient who did not report any history of travel or residence in an HTLV endemic area.

A 57 year old African-American male was admitted to the hospital due to bilateral upper and lower extremity weakness associated with stiffness. He had recently been diagnosed with HIV. His physical examination showed mild to moderate decreased motor strength, in both upper extremities and marked loss in both lower extremities. This was associated with hyperreflexia and clonus. Sensory function was intact. He looked cachectic and had several psoriatic plaques on both lower and upper extremities. Laboratory work-up showed a CD4 count decreased to 94 cells/mm³ and a HIV viral load of 273,000 copies/mL. Based on serum positivity for HTLV type 1 and the patient's clinical presentation suggestive of upper and lower motor neuron dysfunction, the diagnosis of tropical spastic paraparesis was made.

HTLV and HIV share the same routes of transmission and the same tropism for T-lymphocytes. Co-infection occurs probably more frequently than we are aware, since testing for HTLV is not routinely performed in outpatient HIV clinics.

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Background

Human T-cell lymphotropic virus (HTLV) was initially identified in 1979 and it represents the first human retrovirus ever described [1]. It belongs to the Retroviridae family, in the genus Deltaretrovirus, and predominantly affects T lymphocytes. Its genome is a positive single-stranded RNA [2]. So far, 4 types of HTLV have been established, but specific illnesses have been associated only with type 1 and 2. HTLV type 1 and 2 are both involved in actively spreading epidemics, affecting over 15 million people worldwide [3]. HTLV-1 has been described as the more clinically significant one, being associated with diseases such as adult T-cell leukemia and tropical spastic paraparesis. HTLV and HIV share the same routes of transmission and the same tropism for T-lymphocytes. Co-infection occurs probably more frequently than we are aware,

since testing for HTLV is not routinely performed in outpatient HIV clinics [4]. We report here a case of tropical spastic paraparesis in an HIV-positive patient who did not report any history of travel or residence in an HTLV endemic area.

Case report

A 57 year old African-American male was admitted to the hospital due to bilateral upper and lower extremity weakness associated with stiffness, more severe in his lower extremities. His symptoms had started several months prior to this presentation and had gradually worsened to the point that he was no longer able to ambulate. He denied any fever, chills, seizures or any history of trauma.

His past medical history was significant for psoriasis and HIV, diagnosed eight months prior. He was not enrolled in HIV care and he was not on any medications at home. He had no past surgical history. The patient denied tobacco use, alcohol abuse or any illicit drug use. He was born in Florida, United States, and had never

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traveled outside this state. He had been sexually active in the past with female partners only and his last sexual contact was about one year prior. Review of systems was positive for bilateral upper and lower extremity weakness and stiffness, with generalized pain upon movement, and increased urinary frequency. His physical examination was remarkable for mild to moderate decreased motor strength, in both upper extremities and marked loss in both lower extremities. This was associated with hyperreflexia and clonus. Sensory function was intact. He looked cachectic and had several psoriatic plaques on both lower and upper extremities.

Magnetic resonance imaging of the brain, with and without intravenous contrast, showed only non-specific bilateral symmetric white matter changes. Magnetic resonance imaging of the cervical, thoracic and lumbosacral spine, with and without intravenous contrast, was interpreted as normal.

Laboratory work-up showed a CD4 count decreased to 94 cells/mm³ and HIV viral load by PCR of 273,000 copies/mL. His white blood count was 4×10^3 /mm³ and hemoglobin was 11.6 g/dL. Platelets were within normal limits at a level of 186×10^3 /mm³. Renal, hepatic and thyroid function, as well as electrolytes, were all within normal limits. Cerebrospinal fluid analysis showed 102 red blood cells/mm³, 42 white blood cells/mm³ with 100% lymphocytes, normal protein, normal glucose and negative bacterial, fungal and mycobacterial cultures. VDRL, CMV PCR, JC PCR, HSV PCR, Cryptococcal antigen and West Nile virus IgM and IgG were all negative in the cerebrospinal fluid. HTLV-1 antibodies were negative in CSF, but positive in serum by enzyme-linked immunosorbent assay and confirmed by Western blot.

Based on serum positivity for HTLV type 1 and the patient's clinical presentation suggestive of upper and lower motor neuron dysfunction, the diagnosis of tropical spastic paraparesis was made. He was started on symptomatic treatment with muscle relaxants and gabapentin. He was also started on HIV treatment with tenofovir/emtricitabine, atazanavir and ritonavir. He was also started on opportunistic infection prophylaxis with daily trimethoprim-sulfamethoxazole and weekly azithromycin. He was discharged to a physical rehabilitation center. One year after initial presentation he had gained over 50 lbs and his lower extremity weakness and stiffness had improved. He was able to walk with a rolling walker. His CD4 count had increased to 169 cells/mm³ and HIV viral load had decreased to less than 20 copies/mL.

Discussion

Human T-cell virus type 1 (HTLV-1) is well recognized as the cause of tropical spastic paraparesis (TSP), disease that is also known as HTLV-1-associated myelopathy (HAM) [5]. TSP/HAM is an upper motor neuron syndrome that primarily affects the lower extremities. It presents as a slowly progressive spastic paraparesis and the sensory signs are generally less evident. This syndrome can develop as early as three months after infection with HTLV-1 [6], but an average of three years of latency is more typical, and 20–30 years is possible [2]. An age of onset at 50 years or older is usually associated with a more rapid progression to a severe disability.

The diagnosis of TSP/HAM is based mainly on history and physical exam, in context of positive HTLV-1 serology. HTLV infections are detected with enzyme-linked immunosorbent assay (ELISA), which then must be confirmed with Western blot, immunofluorescence assay (IFA), or polymerase chain reaction (PCR). Spine imaging studies are done mostly to rule out other causes of myelopathy. Magnetic resonance imaging of spine may show evidence of demyelination in patients with TSP/HAM and similar changes can be seen also in the periventricular white matter. However, these lesions also occur in patients with asymptomatic HTLV-1 infections, and comparisons with controls

have not been adequate [7]. The mainstay of treatment for TSP/HAM is symptomatic. No standard treatment is currently available.

The interaction of HIV and HTLV remains poorly understood, and there is clearly need for further research into the epidemiology, pathogenesis and treatment of this co-infection. Both HTLV-1 and HTLV-2 appear to have an effect on the clinical progression of HIV disease, and HIV infection has an influence on the clinical manifestations of HTLV.

It is estimated that rates of HTLV-1 or 2 co-infection in HIV infected individuals are at least 100–500 times greater than in general population. There are some geographic areas where up to 20% of HIV infected individuals may be co-infected with HTLV-1 [8].

HTLV-1 and HIV-1 co-infection

HTLV-1 predominantly affects CD4 lymphocytes. In vitro, HTLV-1 is also capable of infecting other cell types and this has been attributed to the fact that one of its host-receptors is GLUT-1, an ubiquitous glucose transporter.

HTLV-1/HIV-1 co-infection is more frequently reported in South America, the Caribbean and Africa [8–10]. Studies suggest that HTLV-1/HIV-1 co-infection is associated with a modification of the natural history of HIV-1, with a faster clinical progression to AIDS and a shorter survival time [11]. HIV-1 appears to up-regulate HTLV-1 expression, leading to a higher risk of HTLV-1 associated diseases, such as TSP/HAM and adult T-cell leukemia. However, clinical evidence remains controversial due to methodological problems in the majority of currently published studies [12].

An early study of HIV and HTLV-1 co-infection done by Leung et al. in 1988 [13] reported that co-infection with HTLV-1 led to increased production of specific host cell proteins which results in stimulation of HIV replication. In 1994 Schechter et al. published a case-control study of 27 patients with HIV/HTLV-1 co-infection [14] and concluded that co-infection was associated with higher CD4 counts, but at the same time with evidence of more advanced HIV clinical disease. A case-control, retrospective study, published in 2001 by Brites et al. [8] of 198 HIV-1 infected patients, of which 63 cases were co-infected with HTLV-1 concluded that HIV-1/HTLV-1 co-infected patients had a shorter mean survival than the HIV-1 mono-infected patients, regardless of sex or baseline CD4 cell count. Sobesky et al. found an increased risk of death for HIV-1/HTLV-1 co-infected patients from French Guiana, compared to HIV-1 mono-infected ones, but the power of their conclusion was limited by small sample size. Out of 151 HIV-infected patients that were included in this study, only 18 patients were co-infected [15].

In 2004 Beilke et al. published a longitudinal study, done in New Orleans, that looked at 62 patients with HIV/HTLV-1 co-infection and compared them to a group of 824 HIV-mono-infected patients. They found no significant differences in progression to AIDS, presence of opportunistic infections or death between these two groups [16]. There were though some methodological issues that may have influenced their results. This study included patients that were on antiretroviral medications, while some of the prior studies were done in the pre-HAART era. Beilke et al. mention that they adjusted the analysis for the use of antiretroviral drugs, but there is no description in the article on the duration of HAART therapy, patient follow-up or time when antiretroviral medication was started in HIV mono-infected patients, as compared to co-infected ones [17].

HTLV-2 and HIV-1 co-infection

HIV-1/HTLV-2 co-infection predominates in North America and Europe, especially among IV drug users [18]. The available evidence suggests a possible protective role of HTLV-2 co-infection

with a slowing of progression to AIDS [19]. HIV/HTLV-2 co-infected patients had lower levels of T-cell activation with lower rate of HIV replication [18]. In the retrospective study published by Beilke et al., 141 patients with HIV/HTLV-2 co-infection were compared to 824 patients who were HIV-mono-infected. Their conclusion was that HIV/HTLV-2 co-infection was statistically associated with delayed progression to both AIDS and death [16]. A longitudinal study by Turci and al. of 2371 HIV-1 infected Caucasian, intravenous drug users from Italy, of whom 6.7% were co-infected with HTLV-2, found that the co-infected patients were older aged, had higher baseline CD4 counts and delayed progression to AIDS [20].

Conclusions

HIV and HTLV-1/2 co-infection may occur more frequent than we are aware of, since routine testing for HTLV-1/2 in outpatient HIV clinics is not currently recommended. HTLV-1 and HTLV-2 co-infection seem to have different effects on HIV infected individuals. It appears that HTLV-1 may accelerate clinical progression to AIDS and the HIV virus may promote a higher risk of HTLV-1 associated diseases. However, some of the available data is contradictory. HTLV-2 co-infection seems to have a protective role, decreasing progression to AIDS. One common denominator between HTLV-1 and HTLV-2 co-infection in HIV patients, is that both have been linked to higher CD4 counts. The higher CD4 counts may have resulted in a delay in introduction of antiretroviral therapy in these co-infected patients [12].

There is definitely a need for larger, well designed studies in order to clearly determine the impact of HIV/HTLV-1/2 co-infection.

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