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Short communication

Progressive multifocal leukoencephalopathy in a HIV/HTLV co-infected patient

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ABSTRACT

Many HIV infected patients are at risk for HTLV-I co-infection worldwide. These patients exhibit abnormally high CD4+ T lymphocyte counts that are not a reliable parameter of the immune status. We report a HIV/HTLV co-infected patient who developed progressive multifocal leukoencephalopathy despite of a high CD4+ T lymphocyte count emphasizing that this situation can be observed in regions around the world where HTLV-I infection is prevalent.

1. Introduction

A growing number of Human Immunodeficiency Virus (HIV) infected patients are at risk for Human T-cell Lymphotropic Virus-I (HTLV-I) co-infection worldwide, since both viruses share the same transmission routes [1]. HIV/HTLV-I co-infected patients usually exhibit CD4+ T lymphocyte count higher than HIV infected patients [2], which represents a nonspecific CD4+ T lymphocyte proliferation induced by HTLV-I and not a satisfactory immune status. Consequently, CD4+ T lymphocyte count is not a reliable marker of immunosuppression in these patients and opportunistic infections can occur elevated counts. In this report, we describe a HIV/HTLV co-infected patient with progressive multifocal leukoencephalopathy (PML), an opportunistic infection often observed in the setting of advanced immunosuppression, and a high CD4+ T lymphocyte count, emphasizing that this situation can be observed in regions around the world where HTLV-I infection is prevalent.

2. Case report

A forty-two year old man with a previous diagnosis of HIV reported a 3-month history of constant headache associated with progressive left side weakness. The neurological examination showed cognitive impairment, an ataxic gait, brisk reflexes and left hemiparesis. He had been diagnosed with HIV infection seven years before but he had never been prescribed antiretroviral therapy because CD4+ T lymphocyte cell count had remained high (792 cells/mm^3 two months before). A brain magnetic resonance imaging (MRI) showed multifocal non-enhancing T2-weighted and FLAIR hyperintense lesions in periventricular region and right parietal white matter, associated with global cortical atrophy. CSF analysis revealed 2 cells/mm^3, protein 55 mg/dl, and glucose 51 mg/dl. Staining and cultures for bacteria, mycobacteria and fungi were negative. CSF JC virus polymerase chain reaction (PCR) was positive and the PML was diagnosed. Since HTLV-I infection is endemic in Brazil and often causes an elevation of abnormal CD4+ T lymphocytes, HTLV-I serology was ordered and the result was positive. He was started on highly active antiretroviral therapy soon after the diagnosis of PML and, a month later, the HIV load reduced to less than 400 copies, while the CD4+ T lymphocyte count remained stable. During the next months, the patient gradually improved and he is still alive ten years after diagnosis of PML. Nowadays, he has mild memory impairment and an ataxic gait but is fully independent. The HIV viral load is currently suppressed with tenofovir, lamivudine and efavirenz and his most recent CD4+ T cell count is 1162/mm^3. Lesions remained stable in the follow-up MR studies (Fig. 1).

3. Discussion

HTLV-I is a retrovirus associated with adult T-cell leukemia/lymphoma (ATLL) and HTLV Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP). The recognized routes of infection are sexual, parenteral (blood transfusion, needle sharing or percutaneous exposure) and vertical (congenital or via breastfeeding). These routes are also shared with HIV and the major risk factor associated with coinfection is intravenous drug use (IDU). This virus is endemic in a number of geographic areas such as Japan, Central Africa, the Caribbean, and some Latin America regions [3]. In Brazil, there is a wide geographic diversity in the prevalence ranging from 0.4% to 1.8% in different states [4]. In Europe and in the US HTLV infection is mainly seen in immigrants from endemic areas and in intravenous drug users, especially in association

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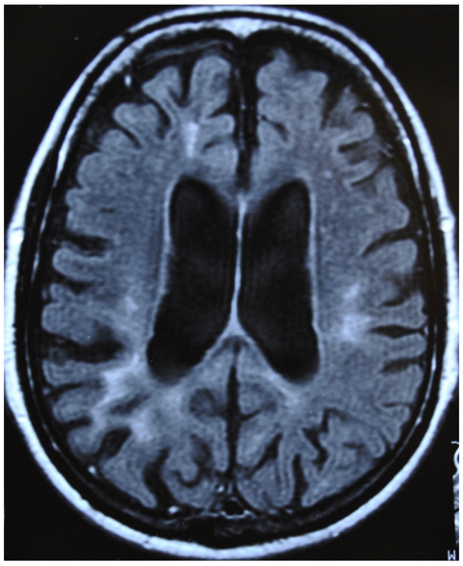

Fig. 1. Fluid attenuation inversion recovery (FLAIR) MRI sequence showing multiple hyperintense lesions in the subcortical and periventricular white matter with no mass effect.

with HIV infection. It is established that in HIV/HTLV-I co-infected patients there is dissociation between CD4 + T lymphocyte count and HIV clinical stage. However, it is not known to date how chronic activation induced by HTLV-1 could affect the progression to AIDS. In clinical settings, the anomalous CD4 + T lymphocyte count in HIV/HTLV-I infected individuals postpones the diagnosis of AIDS. On other hand, complications such as thrombocytopenia, respiratory and urinary tract infections occur more frequently in co-infected patients [5]. Therefore, it is possible that CD4 + T lymphocyte function is defective in co-infected subjects, which may render this parameter less useful. Possibly the higher CD4 + T lymphocyte counts in co-infected patients reflects HTLV-I-associated nonspecific lymphocyte proliferation, as first demonstrated by Schechter et al. [2].

PML is a demyelinating disease that was first described by Astrôm et al. in three hematological patients [6]. Later an association with JC virus infection was established. The primary infection occurs during childhood and remains latent in kidney tubular cells, B-lymphocytes and probably in the brain. Although PML has been observed in patients with CD4 T cell count >200 [7], it usually happens in patients with advanced immunosuppression. In this scenario, JCV can reactivate and infect oligodendrocytes and astrocytes leading to demyelination. Since the late 1980's, PML has gained clinical visibility with AIDS. Nowadays, it has also been associated with immunomodulatory drugs used in the treatment of autoimmune diseases, such as natalizumab, rituximab, efalizumab and mycophenolate mofetil [8].

The PML clinical presentation is extremely wide-ranging, but the most common symptoms include visual disturbances, behavioral alteration and motor signs. Although the gold standard diagnosis is stereotactic brain biopsy, a positive JCV PCR-CSF associated to characteristic images on brain MRI is considered diagnostic nowadays. Reestablishment of immunocompetence is the mainstay of treatment, either starting or changing antiretroviral therapy in HIV patients or reduction/interruption of immunomodulatory and immunosuppressive drugs in patients with autoimmune diseases or cancer. In HAART era, PML mortality in AIDS patients dropped from 90% to approximately 50% during the first three months as a result of recovery of the immune system [9]. In a recent study, 58% of patients who had survived five years from PML diagnosis had no disability or slight disability and were living independently [10].

PML has been rarely reported in HTLV-I infected individuals [11–15]. Although it is possible that HTLV-I itself may activate JCV promoter sequence as observed with HIV [11], a concurrent source of immunosuppression was established in all six patients (hematological malignancies in five and cirrhosis in one).

Interestingly, HIV, JCV and HTLV-I can lead to demyelinating lesions in the brain. The characteristic PML MRI findings are single or multiple asymmetric white matter lesions, which are hypointense on T1 and hyperintense on T2-weighted sequences with no mass effect or contrast enhancement. The HIV encephalitis is shown as periventricular symmetric non-enhancing white matter abnormality without mass effect, associated with brain atrophy and sparing of subcortical white matter [16]. Although the thoracic spinal cord is most affected by HTLV-I, small white matter lesions are frequently seen in subcortical and periventricular areas in HAM/TSP patients.

This case is important to demonstrate important aspects of the HIV patient care: the CD4 + T lymphocyte should not be considered an absolute parameter of the immune status in HIV-infected individuals and HTLV-I serology should be ordered routinely at the initial work-up of HIV patients from endemic areas or in HIV infected intravenous drug users.

Finally, this report sustains that patients harboring HIV and HTLV-I co-infection may present unusual clinical course of the HIV infection or opportunistic diseases in the central nervous system despite of relatively high CD4 + T lymphocyte counts. This fact can mislead physicians when to start antiretroviral therapy and/or opportunistic infections prophylaxis.

Conflict of interest

None.

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