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HIV and HTLV-1 Coinfection: The Need to Initiate Antiretroviral Therapy

Eduardo Ticona, MD, MScBT[1,2], **Moises A. Huaman, MD, MSc**[3], **Omar Yanque, MD**[1,2], and **Joseph R. Zunt, MD, MPH**[4]

[1] Infectious Diseases and Tropical Medicine Unit, Hospital Nacional Dos de Mayo, Lima, Peru

[2] Universidad Nacional Mayor de San Marcos, Lima, Peru

[3] Department of Medicine, Division of Infectious Diseases, Vanderbilt University, Nashville, TN, USA

[4] Departments of Neurology and Global Health, University of Washington, Seattle, WA, USA

According to the latest Department of Health and Human Services guidelines for the use of antiretroviral therapy (ART) in HIV-1-infected persons, initiation of ART is recommended for all HIV-infected persons regardless of the CD4 count. In resource-limited settings where ART is not available for all patients, treatment should be prioritized for those with the following conditions: pregnancy, CD4 count <200 cells/mm^3 or AIDS-defining illness, HIV-associated nephropathy, HIV-associated dementia, hepatitis B virus coinfection, and acute HIV infection.[1] We suggest that coinfection with human T-cell lymphotropic virus type 1 (HTLV-1) should be added to this prioritized list for the following reasons:

The predictive value of CD4 count as a marker of HIV-related immunosuppression and disease stage for persons coinfected with HIV and HTLV-1 is likely not the same as for persons infected with HIV alone. Human T-cell lymphotropic virus type 1 promotes the clonal expansion of CD4-infected T lymphocytes, causing an artificially elevated CD4 count in coinfected persons.[2] Compared to HIV-infected patients with CD4 counts greater than 200 cells/mm^3, HIV/HTLV-1-coinfected individuals with similar CD4 counts are at increased risk for developing opportunistic infections.[3,4] Thus, a high CD4 count in coinfected persons does not necessarily reflect a competent immune system.

HIV/HTLV-1 coinfection is associated with accelerated progression to AIDS and worse outcomes of HIV-related opportunistic infections.[5-7] Human T-cell lymphotropic virus type 1 induces HIV viral replication and the transition from M- to T-tropic HIV phenotype, which is often a marker of HIV disease progression.[8] In addition, compared to individuals infected with only HIV, HIV/HTLV-1-coinfected individuals have higher production of proinflammatory cytokines, most notably interleukin 2 and interferon-γ, suggesting that metabolic and cardiovascular complications mediated by chronic immune activation could be more pronounced among coin-fected individuals.[9]

Corresponding Author: Eduardo Ticona, Hospital Nacional Dos de Mayo, Parque Historia de la Medicina Peruana s/n, Cuadra 13 Av. Grau, Lima 1, Peru. eticonacrg@gmail.com.

In countries with a high burden of tuberculosis, tuberculosis is more common in persons infected with both HIV and HTLV-1.[10] The risk of tuberculosis is about 2.5-fold higher in HIV/HTLV-1-coinfected patients compared to patients with HIV infection alone, and both morbidity and mortality are higher in patients with HIV/HTLV-1 coinfection.[11,12]

Using quantitative HTLV-1 proviral load (PVL) as an indicator of when to initiate ART in asymptomatic HIV/HTLV-1-coinfected individuals with preserved CD4 counts is often impractical due to limited laboratory capacity in countries where HTLV-1 infection is endemic. In addition, HTLV-1 PVL varies widely in asymptomatic carriers and in persons with HTLV-associated disease[13]; and the relationship between HTLV-1 PVL and HIV-associated manifestations in HIV/ HTLV-1-coinfection has not been well established. Hence, neither quantitative HTLV-1 PVL nor CD4 count is a clinically useful indicator of disease or immune status in the setting of HIV/HTLV-1 coinfection.

In contrast, limited evidence suggests that coinfection with HTLV-2, common among HIV-infected injection drug users in the United States and Europe, has a protective effect against progression of HIV infection to AIDS.[14] Human T-cell lymphotropic virus type 2 has been associated with increased CCL3L1 expression, a chemokine that inhibits HIV-1 cell entry by binding to CCR5.[6] Furthermore, HIV/HTLV-2-coinfection has been linked to a “long-term nonprogressor” phenotype. Therefore, the effect of HTLV-1 and HTLV-2 coinfection upon HIV infection may be different, and our recommendation for considering earlier initiation of ART in persons with HIV/ HTLV-1 coinfection may not apply to people with HIV/ HTLV-2 coinfection.

In conclusion, compared to a CD4 count greater than 200 cells/mm^3 in persons infected with HIV alone, a similar CD4 count in persons coinfected with HIV and HTLV-1 may mask immunosuppression, and if used as an indicator for determining when to initiate ART in resource-limited settings, may delay initiation of ART, resulting in a missed opportunity to slow the progression to AIDS, decrease the risk of tuberculosis, and lessen complications related to chronic immune activation. Therefore, initiating ART earlier in HIV/HTLV-1-coinfected persons, independent of CD4 count, should be considered, especially in areas where tuberculosis is endemic.

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