

Reprints or correspondence: Dr. Cornelia Lass-Flörl, Dept. of Hygiene, Microbiology and Social Medicine, Innsbruck Medical University, 6020 Innsbruck, Austria (cornelia.lass-flörl@i-med.ac.at).

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HIV-1 Infection in Persistently HIV-1–Seronegative Individuals: More Reasons for HIV RNA Screening

TO THE EDITOR—The World Health Organization (WHO) has recently released updated guidelines for HIV diagnosis that recommend serum antibody testing by either EIAs or rapid tests and that encourage the identification of unrecognized HIV infections [1]. However, this approach may fail to identify subjects with acute infection. In consideration of the potential public health benefits of not missing individuals in the most contagious phase of infection, implementation of routine HIV RNA screening has been suggested [2]. We want to stress that there are other situations in which viral load is detectable in the absence of reactive antibody tests and in which the introduction of nucleic acid testing may be beneficial. This is the case for HIV-infected subjects in whom specific antibody responses are absent, as for the case reported here.

A 28-year-old man was hospitalized in November 2005 because of severe respiratory insufficiency. He presented with cutaneous Kaposi sarcoma and reported a 4-month history of thrush. His CD4⁺ cell count was of 4 cells/mm³. *Pneumocystis jiroveci* pneumonia was diagnosed. Surprisingly, second- and third-generation EIAs and 2 rapid tests of serum samples were nonreactive for HIV antibodies. HIV-1 Western blot showed indeterminate results (isolated weak p24 reactivity), which had already been documented in a test performed 2 months earlier. No abnormalities in serum immunoglobulin concentrations were found. Fourth-generation HIV assays yielded positive results,

and the patient's p24 antigen level was 17.2 pg/mL. His plasma HIV RNA level was 122,000 copies/mL. Genetic analysis confirmed that the patient was infected with a clade B strain. Tropism studies showed that the virus was R5. The patient began antiretroviral therapy, and after 3 weeks, the viral load had decreased to 12,000 copies/mL. Despite this laboratory improvement, his clinical status worsened, and Kaposi sarcoma rapidly progressed, accompanied by refractory pulmonary insufficiency. The patient died 2 weeks later.

A total of 16 cases of seronegative HIV-1 infection have been reported in the literature. All diagnoses were made for subjects with profound immunodeficiency and high-level viremia and who were therefore potentially contagious. Host characteristics, rather than specific HIV features, seem to be the main determinants of these “occult” HIV infections [3]. The implications of this phenomenon in public health and vaccine development are obvious [4, 5]. An approach that combines pooling of HIV antibody EIA-negative samples with HIV RNA screening on a routine basis has shown excellent performance and cost-effectiveness [5]. Our case, albeit rare, further supports the use of HIV RNA testing to exclude HIV infection in HIV-seronegative individuals.

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Raúl Ortiz de Lejarazu,¹ Vincent Soriano,²
José M. Eiros,¹ Manuel Arias,³
and Carlos Toro²

¹Service of Microbiology, Hospital Clínico, Valladolid, ²Service of Infectious Diseases, Hospital Carlos III, Madrid, and ³Hospital “Río Carrión” Palencia, Spain

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Reprints or correspondence: Dr. Carlos Toro, Dept. of Infectious Diseases, Hospital Carlos III, Calle Sinesio Delgado 10, Madrid 28029, Spain (carlostororueda@hotmail.com).

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