Correspondence

The Diagnosis of Latent Tuberculosis in HIV-Infected Persons

To the Editor—We read with interest the article by The Antiretroviral Therapy Cohort Collaboration [1] on the incidence of tuberculosis among patients receiving antiretroviral therapy. The authors note that the effectiveness of the tuberculin skin test (TST) for detecting latent tuberculosis appears to be increased among patients receiving effective antiretroviral therapy. The TST uses purified protein derivative of tuberculin, a crude mixture of >200 antigens that cross-react with Mycobacterium bovis bacille Calmette-Guérin (BCG), and many environmental mycobacteria and, therefore, has a very low specificity.

The 6 kDa early secretory antigenic target of M. tuberculosis (ESAT-6) and the 10 kDa culture filtrate protein (CFP-10) are peptides that are present only on M. tuberculosis and a few rare environmental mycobacteria (Mycobacterium kansasi [2], Mycobacterium marinum [2], Mycobacterium szulgai [2], and Mycobacterium leprae [3]). These peptides have been incorporated into 2 new commercially available diagnostic tests (T-SPOT.TB [Oxford Immunotec] and QuantiFERON-TB Gold [Cellestis]) that measure the release of IFN-γ following stimulation of T lymphocytes with these peptides. These tests are not only more specific than the TST but also have the advantage that a non-specific T cell stimulant (phytohaemagglutinin) may be used as a positive control. This enables true-negative results to be distinguished from those that fail as a result of anergy or for technical reasons. It has recently been shown that the performance of the T-SPOT.TB test appears to be independent of the CD4+ T lymphocyte count [4]. Thus, tests incorporating ESAT-6 and CFP-10 peptides, rather than the TST, should be better for the diagnosis of latent tuberculosis, regardless of the patient’s CD4+ T lymphocyte count or use of antiretroviral therapy.

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References


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Molecular Epidemiology of Tuberculosis

To the Editor—The Antiretroviral Therapy Cohort Collaboration’s recent article about the incidence of tuberculosis (TB) during HAART [1] describes the current features of HIV–Mycobacterium tuberculosis coinfection in high-income countries and confirms TB’s role as the most prevalent opportunistic infection to affect HIV-infected individuals—even those who present with relatively high CD4+ cell counts [2]. A more obvious explanation for this phenomenon is that a relevant percentage of cases of TB in patients with high CD4+ cell counts are simply attributable to recent infections by Mycobacterium tuberculosis. Unfortunately, the authors were not able to corroborate this hypothesis, because they lacked the epidemiological data required to differentiate between recent infection and reactivation of latent TB.

In the absence of clear clinical epidemiological data proving the origin of TB (i.e., whether infection was recent or re-activated), molecular biological analysis has played a substantial role in clarifying the picture. Use of restriction fragment–length polymorphism (RFLP) DNA fingerprinting to distinguish between epidemiologically related and unrelated M. tuberculosis strains has opened up the field of molecular epidemiology in TB transmission. Patients whose strains exhibit an identical fingerprint pattern during a defined period of time are considered to be “clustered” and are assumed to belong to a chain of recent transmissions. Patients whose M. tuberculosis isolates have unique patterns (i.e., they are unmatched) are assumed to have reactivated disease. With these methods and definitions, we compared HIV-infected patients with CD4+ cell counts ≤100 cells/μL who developed TB disease with coinfected patients with CD4+ cell counts >100 cells/μL on the basis of the patients’ clustering patterns.

We had at our disposal M. tuberculosis cultures useful for RFLP analysis for 119 patients with HIV infection and con- comitant TB; the patients had been treated at our clinic during the period of 1993–2003. We used a molecular epidemiology database of M. tuberculosis strains to determine which cases belonged to clusters.