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Infrequent Detection of Lipoarabinomannan Antibodies in Human Immunodeficiency Virus-Associated Mycobacterial Disease

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A commercially available test for the serologic diagnosis of tuberculosis was evaluated for its applicability in human immunodeficiency virus (HIV)-positive patients. Antibodies to lipoarabinomannan were detectable in sera from only 9 of 85 HIV-positive patients with a confirmed diagnosis of tuberculosis. Given the low degree of sensitivity of the assay with sera from HIV-infected patients, the study does not support the use of this serologic assay for the diagnosis of tuberculosis in HIV-infected patients.

Patients with human immunodeficiency virus (HIV) infection are at increased risk for the development of tuberculosis and other mycobacterial diseases (7). The clinical picture of tuberculosis is atypical, and extrapulmonary disease is more frequently diagnosed in this population. Fast and inexpensive methods for the establishment of the diagnosis of tuberculosis would improve the rapid identification of patients with a communicable disease. So far no serologic test is available to support the diagnosis of tuberculosis. In HIV-infected patients, the purified protein derivative used in vivo has unacceptably low levels of sensitivity and specificity. Lipoarabinomannan (LAM) is a membrane-associated lipopolysaccharide and one of the dominant antigens of *Mycobacterium tuberculosis* (2). LAM can frequently be detected in up to 67% of patients with tuberculosis (6). Consequently, serologic assays that can be used to detect antibodies against LAM for the indirect diagnosis of tuberculosis have been developed (1).

The study described here was conducted to evaluate an inexpensive, commercially available test as a diagnostic tool for the detection of tuberculosis in HIV-infected individuals. We used frozen sera from the repository of the Swiss HIV Cohort Study (SHCS). SHCS is a multicenter, prospective cohort including more than 6,000 HIV-infected patients (4). Stored serum samples frozen at −20°C were used. We selected all patients from SHCS with a culturally confirmed diagnosis of tuberculosis for whom serum samples at the time of diagnosis or 6 months prior to the time of diagnosis were available (n = 85). An HIV-infected cohort of patients matched for sex, risk category, and CD4 count was used as a control group (n = 85). A third group (n = 104) consisted of patients with the diagnosis of mycobacterial disease other than tuberculosis (MOTT).

Thawed serum samples were tested by a commercially available serologic assay (MycoDot; Genelabs, Geneva, Switzerland) according to the manufacturer's procedure. The MycoDot test uses LAM antigen bound onto plastic combs which are incubated with diluted serum, heparin-derived plasma, or whole blood. After washing, the combs are incubated with a suspension of colored particles which bind to the specific immunoglobulin G (IgG) and leave a red spot on the comb. The results are summarized in Table 1. Only 9 serum samples from 85 patients with tuberculosis (10.6%) were reactive. Two serum samples from patients with MOTT were weakly reactive. Additional serum samples obtained 6 months prior to the diagnosis of tuberculosis were available from 27 patients. In 2 of 27 patients antibodies against LAM were detectable 6 months prior to the clinical diagnosis.

Using stored sera for the evaluation of a commercially available test for the detection of antibodies to LAM, we found a low level of sensitivity for the indirect detection of tuberculosis in HIV-infected individuals. Multiple factors might be responsible for this low level of sensitivity of the assay with sera from HIV-infected patients. Mycobacterial LAM as well as other polysaccharide antigens stimulate a humoral immune response of the IgG2 subclass (5). The humoral immune response of the IgG2 subclass is impaired in patients with HIV infection (3). This particular defect in the humoral immune response of HIV-positive patients might explain in part the low level of sensitivity of the assay with sera from this population as well as

TABLE 1. Results of LAM antibody testing

Patient category	No. of patients tested	No. (%) positive
Patients with tuberculosis		
CD4 count, <200	58	7 (12)
CD4 count, 200–400	17	2 (12)
CD4 count, >400	10	0 (0)
All patients with tuberculosis	85	9 (12)
Sample 6 mo prior to tuberculosis diagnosis	27	2 (7)
HIV-positive controls[a]	85	0 (0)
Patients with MOTT	104	2 (2)

[a] Matched for sex, risk category, and CD4 count.

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the poor reactivity of the assay with sera from HIV-positive patients with MOTT. We conclude that serologic testing for LAM antibodies is not useful for the diagnostic workup of HIV-positive patients with suspected tuberculosis.

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