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Factors Affecting the Yield of Acid-fast Sputum Smears in Patients With HIV and Tuberculosis*

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Objective: To evaluate the sensitivity of acid-fast sputum smears in the diagnosis of pulmonary *Mycobacterium tuberculosis* (MTB).

Design: Retrospective chart and radiographic film review.

Setting: Department of Veterans Affairs Medical Center in New York City.

Patients: All patients with positive sputum cultures for MTB during 1989 to 1991, including 100 with HIV, and 76 without HIV infection.

Parameters: The likelihood of a positive acid-fast sputum smear, related to chest radiograph findings, CD4 cell counts, drug sensitivity, and the presence of disseminated disease.

Results: Overall, 60 percent of patients with HIV had positive acid-fast smears, compared with 57 percent of non-HIV-infected patients. A relative absence of cavitary infiltrates did not substantially reduce the fre-

quency of acid-fast smears in patients with and without HIV. Patients with HIV and CD4 count <50, 50 to 200, and >200 had positive acid-fast smear rates of 58 percent, 60 percent, and 56 percent, respectively; HIV-infected patients with drug-resistant organisms had 65 percent positive smears. Smear positivity was 96 percent in patients with HIV infection and disseminated MTB.

Conclusions: Positive acid-fast sputum smears in culture-proven MTB occur with similar frequency in patients with and without HIV. The absence of cavitary disease did not significantly reduce the frequency of positive acid-fast smears. For patients with HIV, the likelihood of a positive smear was also independent of CD4 cell counts and drug resistance. Patients with HIV and disseminated MTB had positive sputum smears in nearly all cases. (Chest 1994; 106:684-86)

MTB=*Mycobacterium tuberculosis*

The resurgence of *Mycobacterium tuberculosis* (MTB) in association with human immunodeficiency virus (HIV) infection has focused attention on rapid diagnosis in high-risk patients. Several investigators have reported on the sensitivity of sputum smears in patients with HIV infection and pulmonary MTB.¹⁻⁴ Most reports have shown a similar frequency of positive sputum smears in pulmonary MTB for patients with and without HIV infection.¹⁻³ The expectation that infection with HIV would reduce the sensitivity of acid-fast smears, due to a decreased frequency of cavitary pulmonary MTB, has not been substantiated.^{3,5} To determine what influence the appearance of the chest radiograph, the CD4 cell count, the presence of drug resistance, and the presence of disseminated infection have on the likelihood of positive acid-fast smears, we reviewed data on 76 non-HIV-infected and 100 HIV-infected patients with a positive sputum culture for MTB, admitted to the New York Veterans Administration Medical Center during 1989 to 1991.

MATERIAL AND METHODS

Inclusion in the study required an isolate of MTB from sputum culture and at least three specimens smeared for acid-fast organisms, identified from records in the mycobacteriology laboratory during 1989 to 1991. The medical records of the study patients were reviewed and the following data were recorded: (1) the sites other than sputum which grew MTB; (2) drug sensitivities of the isolates; and (3) CD4 cell counts and HIV serology, when available. Patients were included in the non-HIV group if their HIV serologic findings were known to be negative or, in the absence of a serologic test, no known risk factors for HIV infection were present. Chest radiographs, when available, were reviewed by all authors.

Sputum, blood, other body fluids, and tissue were processed according to standard mycobacteriology laboratory procedures.⁶ After digestion and concentration of sputum with N-acetyl-L-cysteine and a final concentration of 1 percent sodium hydroxide, specimens were inoculated onto Middlebrook 7H11 agar and Lowenstein-Jensen medium or mycobacterial medium. Slides for the detection of acid-fast bacilli were prepared with auramine-o-fluorochrome stain.

Statistical comparison between groups was performed by χ^2 analysis.

RESULTS

A total of 176 patients were identified who met the criteria for inclusion in the study. One hundred patients had a positive HIV serologic result; all were men with a mean age of 47 years (range, 27 to 67 years). Seventy-six patients had either a negative HIV

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Table 1—Chest Radiographic Findings and Acid-Fast Smear Positivity in Patients With and Without HIV Infection

Chest Radiographic Findings	Non-HIV (n=69)		HIV (n=88)	
	No. of Patients	+Smears (%)	No. of Patients	+Smears (%)
Cavitary	25	21 (84)	13	11 (85)
Infiltrates	36	18 (50)	48	28 (58)
Adenopathy only	2	0	4	2 (50)
Pleural effusion	1	0	5	2 (40)
Normal	5	1 (20)	18	7 (39)

serologic finding or lacked risk factors for HIV infection; all were men with a mean age of 56 years (range, 29 to 87 years).

Of the non-HIV-infected patients, 43 of 76 (57 percent) had positive acid-fast smears, compared with 60 of 100 (60 percent) of the HIV-infected patients. Among the latter group, 26 of 100 (26 percent) had disseminated disease, including isolation of MTB from blood (n=10), extrathoracic lymph nodes (n=5), urine (n=5), cerebrospinal fluid (n=4), bone marrow (n=1), and stool (n=1); 25 of 26 (96 percent) of HIV-infected patients with disseminated disease had positive acid-fast sputum smears. None of the non-HIV-infected patients had disseminated disease.

Drug-resistant organisms were found in 13 of 69 (18 percent) of the non-HIV-infected patients, including 7 with multidrug-resistant organisms. Among the HIV-infected patients, 38 of 89 (42 percent) had resistant organisms, including 25 with multidrug resistance. Overall, 25 of 38 (66 percent) of HIV-infected patients with resistant organisms had positive acid-fast smears.

Table 1 compares chest radiographic findings of patients with and without HIV infections, along with the frequency of a positive acid-fast smear. Significantly more non-HIV-infected patients had cavitary infiltrates ($p < 0.01$) than HIV-infected patients; more HIV-infected patients had normal chest radiographs, however ($p < 0.05$). No significant differences between the HIV-infected and non-HIV-infected patients were found in the frequency of positive acid-fast sputum smears, stratified by chest radiographic findings.

Among the HIV-infected patients, no significant differences were found in the frequency of positive

Table 2—The Relationship Between CD4 Cell Counts and Acid-Fast Smear Positivity in Patients With HIV

CD4 Cell Count	No. of Patients	+Smears (%)
<50 (mean, 22)	26	15 (58)
50-200 (mean, 121)	25	15 (60)
>200 (mean, 395)	33	17 (56)

acid-fast sputum smears between groups stratified by CD4 cell counts (Table 2).

DISCUSSION

Infection with HIV is known to alter the presentation of pulmonary MTB. Prior reports have emphasized a radiographic picture characterized by less cavitary disease and more adenopathy, compared with the typical radiographic picture found in patients with pulmonary MTB without HIV infection.^{1,5} Since cavitation is associated with increased numbers of extracellular acid-fast bacilli, and thus a greater likelihood of a positive smear in non-HIV-infected patients with typical reactivation MTB, the diagnostic yield of acid-fast smears in HIV-infected patients, with less cavitary disease, has been questioned. Klein et al⁴ showed a decreased sensitivity of sputum smears in culture-positive MTB among patients with HIV infection (45 percent vs 81 percent among patients without HIV).⁴ Other investigators, however, have shown a similar frequency of positive acid-fast sputum smears in patients with and without HIV infection. Long et al² observed a 66 percent frequency of positive acid-fast sputum smears in HIV-infected patients, compared with 78 percent in patients without HIV infection. Modilevsky and co-workers⁷ found an 83 percent frequency of positive acid-fast smears. Pitchenick et al¹ and Theuer et al⁸ also observed no differences in the frequency of positive acid-fast smears between HIV-infected and non-HIV-infected patients.

Our data confirm the finding that positive acid-fast sputum smears are found as frequently in patients with, as in those without, HIV infection and pulmonary MTB. Although cavitary disease was significantly less frequent among the HIV-infected patients, this form of disease, when present, resulted in the highest frequency of acid-fast smear positivity, similar to that observed among the patients without HIV infection (84 percent vs 85 percent). In addition, the frequency of acid-fast sputum smears in association with noncavitary infiltrates was similar for patients with and without HIV infection (58 percent vs 50 percent).

Patients with HIV infection did have a significantly greater number of normal chest radiographs, in the presence of pulmonary MTB, than those without HIV. However, the absence of parenchymal infiltrates on chest radiographs did not substantially reduce the likelihood of a positive sputum smear in the patients with HIV infection. Seven of the 18 patients with HIV infection and normal chest radiographs still demonstrated sputum smears positive for acid-fast bacilli. The finding that lack of parenchymal tissue destruction, and cavitation in particular, does not substantially reduce the yield of acid-fast

smears has been observed previously.^{1,9} Long et al⁹ suggested that, in cases of pulmonary MTB associated with profound immunosuppression from HIV, caseation necrosis may be less relevant to the yield of acid-fast smears than the unchecked proliferation of bacilli as seen with other opportunistic infections. Our data support this explanation; the frequency of positive acid-fast smears was 56 and 58 percent in the subgroups of patients with the highest and lowest CD4 cell counts, respectively.

Drug sensitivity also did not influence the likelihood of a positive acid-fast smear in HIV-infected patients with MTB. Overall, drug resistance was found in 42 percent of HIV-infected patients and multidrug resistance was found in 28 percent. The 65 percent frequency of a positive acid-fast smear in the 25 HIV-infected patients with resistant MTB was not significantly different from the frequency of a positive smear in the HIV-infected group overall. This finding is consistent with the study of Fischl et al¹⁰ that reported 58 percent of patients with multidrug-resistant MTB had positive acid-fast smears.

The presence of disseminated MTB, however, did increase the likelihood of a positive acid-fast smear in patients with HIV infection. Of the 26 patients with disseminated MTB, 25 (96 percent) had positive acid-fast smears. This finding may be due to the general increase in organism burden in disseminated disease and, specifically, to the lung's place as the original site of infection.

In conclusion, positive acid-fast sputum smears in culture-proven MTB occurred with similar frequency in patients with and without HIV infection. Chest radiographs with cavitory or noncavitory infiltrates were also associated with similar rates of acid-fast smear positivity in both patient groups. In patients with HIV infection, the frequency of positive acid-

fast smears was independent of CD4 cell counts and drug resistance. Lastly, in patients with HIV infection and disseminated MTB, acid-fast sputum smears were positive in nearly all cases.

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