

## Fine-Needle Aspiration of Peripheral Lymph Nodes in Patients With Tuberculosis and HIV

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Previous studies of fine-needle aspiration (FNA) specimens from lymph nodes of patients with tuberculosis (TB) and infection with the human immunodeficiency virus (HIV) have often involved small numbers of specimens and have produced conflicting results. We reviewed 93 FNA specimens from peripheral lymph nodes in a consecutive series of 79 patients with TB to compare results for patients with and without HIV infection. The 45 patients with HIV infection in the series were more frequently male, more likely to have negative results on a purified protein derivative tuberculin skin test, and they had more disseminated disease. Granulomatous inflammation, a positive result on a culture, acid-fast bacilli, or necrosis was found in 71% of the studies.

Identification of granulomatous inflammation occurred at a similar rate in FNA specimens from patients with HIV infection (16%) and without HIV infection (21%;  $P=.56$ ). Necrosis was the sole reported finding in a significant subset of cases (16%), occurring in patients with and patients without HIV infection. FNA of peripheral lymph nodes of patients with TB was an effective diagnostic test. Granulomatous inflammation and other FNA findings in peripheral lymph nodes of patients with TB were similar in those with and those without HIV infection. (Key words: Fine-needle aspiration; Cytology; Lymphadenopathy; Tuberculosis; Human immunodeficiency virus [HIV]; acquired immunodeficiency syndrome [AIDS]) *Am J Clin Pathol* 1997;107:317-320.

Several studies have indicated that fine-needle aspiration (FNA) is an effective diagnostic test for tuberculous lymphadenitis.<sup>1,2</sup> However, the role of FNA in patients with tuberculosis (TB) has been complicated by the epidemic of acquired immunodeficiency syndrome (AIDS). In the United States, some studies have examined FNA findings of tuberculous lymphadenitis in patients with AIDS, but these have involved small series of between 8 and 22 specimens.<sup>3-5</sup>

Some sources have maintained that granulomas may be less frequent,<sup>4</sup> poorly formed,<sup>6,7</sup> or absent<sup>8,9</sup> in some patients with AIDS and tuberculosis. Others described granulomas as rare<sup>10</sup> because of a diminished immune response or suggested that the presence of granulomatous inflammation may depend on the stage of human immunodeficiency virus (HIV) infection and the associated degree of immunological impairment.<sup>11</sup> Results of a European study suggested

that TB lymphadenitis in patients with AIDS shows a distinctive cytologic pattern on FNA specimens, with necrosis a more prominent feature.<sup>12</sup>

Others have suggested instead that granulomatous inflammation is present in most patients with AIDS and TB,<sup>3</sup> and that it is found in a significant percentage of FNA studies of patients with suspected cases of AIDS who have TB lymphadenitis.<sup>13</sup> Another source suggested that cellular immune mechanisms are not necessary for the formation of granulomas in patients with AIDS.<sup>14</sup>

We examined a larger series of FNA specimens from peripheral lymph nodes of a group of consecutive patients who had active TB reported by the microbiology laboratory of our hospital. We measured the frequency of granulomatous inflammation, necrosis, and all other reported findings in our group, and we compared results in patients with and without HIV infection. Our purposes were to analyze FNA results in peripheral lymph nodes of patients with HIV and TB and to determine whether these are different from the results in patients with TB who do not have HIV infection.

### MATERIALS AND METHODS

A database listing all cultures positive for *Mycobacterium tuberculosis* from the microbiology laboratory at Los Angeles County Hospital (Los

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Angeles, Calif) was used to begin case selection. The database included the medical record number of every patient who had at least one positive culture (from any source) confirming active TB. The period surveyed was from October 1988 to January 1992.

This list was cross-referenced with a database of all patients who had FNA results recorded in the cytology laboratory. The FNA database included information on age, sex, ethnicity, FNA site, cytology findings, and information provided by the clinician to the cytologist on the request form. All the FNA specimens from peripheral lymph nodes of patients who were documented to have active TB were selected for further review. FNA specimens were only included in the study if a positive culture for TB was confirmed within 8 weeks of the study, indicating active disease.

HIV information was obtained from cytology forms, chart review, and a database of HIV serology results at Los Angeles County Hospital. Medical record review also provided information on results of a purified protein derivative (PPD) skin test and additional information about the clinical setting of the FNA procedure.

The FNA results in patients with TB were categorized according to the presence of acid-fast bacilli (AFB), granulomatous inflammation, necrotic inflammation, mixed inflammation, reactive lymphadenopathy, an inadequate study, or no specific abnormality. Granulomatous inflammation was indicated by the presence of epithelioid macrophages and multinucleated giant cells. Acid-fast bacilli were identified on the basis of Ziehl-Neelsen stains applied to aspirate smears. Reactive lymphadenopathy was indicated by a polymorphous pattern of lymphoid cells.

Comparisons of patient characteristics and cytologic findings were made between patients with HIV infection and patients without HIV infection. An independent samples *t* test was used to compare mean values, and a  $\chi^2$  test (or Fisher's exact test) was used to compare incidence rates.

## RESULTS

A total of 93 FNA specimens from the peripheral lymph nodes of 79 patients with TB were reviewed. The patients were predominantly male, most were HIV positive, and the most common ethnic background was Hispanic (Table 1).

Patients with HIV infection were more likely to be male and less likely to have a positive PPD skin test. Their median CD4 count was 56. Patients with HIV infection also had, on average, more sites with cultures positive for *M tuberculosis*, suggesting more disseminated

disease. Pulmonary involvement was confirmed in the majority of patients with HIV. Involvement of the central nervous system or urinary tract was infrequent, but it occurred more often than in patients without HIV infection. These results are shown in Table 2.

Of the 93 FNA specimens, 89 were cultured, and *M tuberculosis* was found in 43 (48%) of the cultures. The frequencies of different cytologic findings are presented in Table 3. Some patients had more than one of the findings under study present or had a positive cytologic finding and a positive culture result. Acid-fast bacilli were identified in 21% of the studies, granulomatous inflammation in 18%, and necrosis in 21%. If these findings are grouped as results suggesting TB, then 63 (71%) of the FNA results were positive. Another 7 FNA results (8%) had nonspecific inflammation without evidence of necrosis, granuloma, or AFB.

In 26 cases, the cytology report did not suggest a diagnosis of TB. These cases were distributed evenly between patients with and without HIV infection (24% of FNA specimens of patients without HIV infection;

TABLE 1. CHARACTERISTICS OF PATIENTS WITH TB EXAMINED WITH FNA (N = 79)

	Number	%
HIV positive	45	57
Male	59	75
Ethnicity		
Hispanic	49	62
Black	18	23
Caucasian	9	11
Asian	3	4

TB = tuberculosis; FNA = fine-needle aspiration; HIV = human immunodeficiency virus.

TABLE 2. COMPARISON OF PATIENTS WITH TB WITH AND WITHOUT HIV INFECTION

Characteristic	HIV Negative or Untested (n = 34)	HIV Positive (n = 45)	P*
Male, no. (%)	16 (43)	43 (96)	<.001
Mean age, y	31	34	.25
Positive PPD skin test	19 (56)	8 (18)	<.001
Culture positive for TB			
No. of sites, mean	1.4	2	<.01
Pulmonary site, no. (%)	11 (32)	28 (62)	<.01
Urine, no. (%)	1 (3)	8 (18)	.04
Cerebrospinal fluid, no. (%)	0 (0)	4 (9)	.07

TB = tuberculosis; HIV = human immunodeficiency virus; PPD = purified protein derivative.

\*P Determined by  $\chi^2$  or Fisher's exact test for incidence rates, *t* test for comparison of means.

31% of FNA specimens of patients with HIV infection;  $P=.44$ ,  $\chi^2$ ). In these cases, no specific abnormality was reported, a reactive lymph node was described, or the study was considered inadequate. However, in six of the cases the culture of the FNA specimen was positive for *M tuberculosis*. An additional 5 of these studies were associated with follow-up lymph node biopsy results that indicated TB, so a total of 11 of the 26 negative cytologic reports can be confirmed as false-negative reports for tuberculous lymphadenitis.

Table 3 compares positive cytology results in patients with known infection and those not known to be HIV positive. FNA specimens in patients with HIV infection identified AFB more frequently on smear, and necrosis was identified more often in patients without HIV infection, but neither of these differences reached statistical significance. Similar rates of granulomatous inflammation and positive cultures were found in the two populations.

## DISCUSSION

This series of 98 FNA specimens in patients with TB represents the largest in the United States comparing patients with HIV infection with patients who do not have HIV infection. The two groups showed similar cytologic results. The majority of FNA specimens (71%) provided information useful for a diagnosis of TB.

Many patients with TB, especially those with HIV infection, have undergone complicated evaluations with cultures at many sites. Examination of the peripheral lymph node may have a relatively high yield and should be considered when possible as an alternative to the more invasive studies that are often performed on these patients.

Our results agree with those of other research suggesting that evidence of granulomatous inflammation on FNA may be found with similar frequency in patients with TB, with or without HIV infection.<sup>3</sup> Reports suggesting that granulomas were less common in patients with HIV may have included patients with more advanced disease,<sup>6,8,9</sup> which may be associated with less granuloma formation. Variations of reported results in the literature may also be related to sample size, with previous studies in the United States identifying series of 8 to 22 FNA specimens.<sup>3-5</sup> One European study examined a group of 57 FNA specimens from patients with HIV infection but did not compare results with those of patients without HIV infection.<sup>12</sup>

Differences in reported results can also be due to methods of selection of FNA specimens. Finfer et al<sup>4</sup> reported a higher frequency of granulomatous inflammation (7 [32%] of 22 FNA specimens), but the

TABLE 3. FNA RESULTS IN PATIENTS WITH TB\*

Cytology/Microbiology Report	Without HIV Infection (n = 38)	With HIV Infection (n = 55)	P†
AFB identified‡	6 (16)	14 (25)	.26
Granulomatous inflammation‡	8 (21)	9 (16)	.56
Necrosis present‡	13 (34)	11 (20)	.12
Necrosis only (no AFB or granuloma)‡	8 (21)	5 (9)	.10
Culture positive for <i>Mycobacterium tuberculosis</i> ‡	20 (53)	23 (42)	.30
No cytological evidence of TB§	9 (24)	17 (31)	.44

FNA = fine-needle aspiration; TB = tuberculosis; HIV = human immunodeficiency virus; AFB = acid-fast bacilli.

\*Data are reported as no. (%).

†P determined by  $\chi^2$ .

‡An overall yield of 71% for FNA was determined as the percent of studies having at least one of these findings.

§Of these 26 studies, 11 were subsequently shown to be false negatives for tuberculous lymphadenitis.

FNA specimens were selected on the basis of cytologic findings instead of the diagnosis of the patients. Only FNA specimens with granulomatous inflammation, acute inflammation, or both were reviewed.<sup>4</sup>

In our study, the frequency of granuloma, when considered only as a percentage of the FNA specimens with inflammation, was similar to that found by Finfer et al<sup>4</sup> (38% vs 32%, respectively). However, Table 3 provides the frequency of granuloma and other results among all FNA specimens of peripheral lymph nodes in our series. It includes some FNA results that were negative. Documentation of positive and negative results in patients with TB is relevant to the clinician considering FNA as a diagnostic test.

The false-negative results in 11 of our specimens included cases in which tuberculous lymphadenitis was later diagnosed after an FNA report of benign reactive lymphadenopathy. This demonstrates that lymph node biopsy results can provide a diagnosis of TB that was missed by FNA.

At the same time, a minority of patients with AIDS and TB may have lymphadenopathy due to other causes. In 16% of our FNA studies we did not have subsequent biopsy specimens to exclude this possibility. In our review medical records, we found no reports of lymphadenopathy progressing despite the administration of antituberculous medications.

The results of this study are consistent with observations that necrosis alone, without identification of granulomatous inflammation or AFB, is an important cytologic indicator of tuberculous lymphadenitis.<sup>12</sup>

Our estimated 71% yield included several FNA results showing only necrosis. This finding should suggest TB if no evidence of malignancy is present. However, FNA results showing only necrosis were not uniquely characteristic of patients with TB and AIDS. Patients without AIDS had this finding on FNA specimens with a similar or greater frequency.

An increase in the identification of AFB on the cytologic smears of patients with TB and AIDS has been noted elsewhere,<sup>4</sup> and it may reflect an increased organism burden. In our study, AFB was also identified on cytologic smears more frequently in patients with HIV, but the trend was not statistically significant.

Inherent difficulties in establishing the diagnosis of TB limited patient selection to those with culture confirmation. Even if patients met clinical criteria for TB,<sup>15</sup> they were not included in the study if all culture results were negative. Culture confirmation is essential in patients with HIV because they may harbor atypical mycobacteria.

Other limitations of the study are due to the differences in patient populations. We identified differences in sex, PPD skin test status, and dissemination of disease between patients with and patients without HIV infection. It is possible that underlying histologic differences may be obscured by some of these differences in patient populations. However, a purely consecutive series was studied, and as a result there was no selection bias for patient characteristics or the quality of FNA results.

In our population of patients with TB, FNA specimens from peripheral lymph nodes frequently provided useful diagnostic information. The frequencies of granulomatous inflammation and positive culture results were similar in those with and without HIV infection.

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