Tuberculosis and the Acquired Immunodeficiency Syndrome at a New York City Hospital: 1978-1985*

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Recent reports have described an increase in cases of tuberculosis in several urban centers. To investigate the possible relationship between tuberculosis and the acquired immunodeficiency syndrome (AIDS), we reviewed case records at a New York City hospital between 1978 and 1985. During this period, tuberculosis occurred in 15.1 percent of AIDS patients with a history of parenteral drug use and 4.4 percent of all other patients with AIDS. The yearly rate of tuberculosis more than doubled during the study period; this increase was entirely attributable to cases among patients with AIDS or AIDS-related complex and parenteral drug users, a group at high risk for the development of AIDS. Patients with AIDS and tuberculosis were younger and more frequently men than other patients with tuberculosis, and were more likely to have extrapulmonic disease. In the majority of patients, tuberculosis occurred prior to confirmation of CDC-defined AIDS. Forty-four percent of patients with AIDS-related complex at the time of diagnosis of tuberculosis subsequently developed AIDS. Mycobacterium tuberculosis appears to be yet another opportunistic agent to which patients with AIDS retroviral-induced immunodeficiency are susceptible.

An ever-widening spectrum of disease is being reported in association with the acquired immunodeficiency syndrome (AIDS). The Centers for Disease Control (CDC) definition of the syndrome has been expanded so that in patients without known cause of reduced resistance, the presence of infection with such diverse organisms as the protozoa Pneumocystis carinii, Toxoplasma gondii, and cryptosporidia, the fungi Cryptococcus and Candida, and members of the herpes viruses are considered indicative of cellular immunodeficiency. More recently, Histoplasma and Isospora have been added as opportunists diagnostic of the syndrome, in the presence of a positive serologic test for the AIDS retrovirus. Among the mycobacteria, only infections due to the atypical organisms are included in the CDC surveillance definition of AIDS. Infections due to Mycobacterium tuberculosis have been reported to occur rarely among United States-born patients with AIDS; however, among patients with AIDS who reside in or have emigrated from Haiti, tuberculosis occurs frequently, often in disseminated form.

Despite an overall decline in tuberculosis nationwide, recent reports suggest that in some urban areas, the incidence of tuberculosis is increasing. The present investigation was undertaken to determine the relationship between the occurrence of tuberculosis and AIDS at Beth Israel Medical Center over the last eight years.

METHODS

Since mid-1977, Beth Israel Medical Center has maintained an active tuberculosis surveillance program, identifying all cases of mycobacterial infection from microbiology laboratory culture results. Records of hospitalized, adult (age 18 years or older) patients with tuberculosis were included for the present review if cultures were positive for M tuberculosis. Disease was classified as pulmonary or extrapulmonary; pulmonary tuberculosis was defined by the presence of positive sputum, bronchial washing, transbronchial biopsy, and/or pleural cultures.

An active surveillance system for AIDS was established in the institution at the onset of the epidemic in 1981. Records of adult hospitalized patients meeting the CDC surveillance definition of AIDS were included for review. AIDS-related complex (ARC) was diagnosed in the presence of oral candidiasis, generalized lymphadenopathy (two or more noninguinal lymph node groups enlarged six months or more), chronic diarrhea, and/or weight loss greater than 10 percent of body weight.

Parenteral drug use was defined as any history of illicit subcutaneous or intravenous use of narcotics or cocaine. Alcohol abuse was defined as a history of alcohol intake which required hospitalization for detoxification or withdrawal symptoms.

Results are given as the mean ± SD. The statistical significance of associations was tested using methods of chi square analysis applied to contingency tables and to assess linear trends. Analysis of variance was used to determine the significance of differences between means, which were further assessed by Fisher's least significant difference test.

RESULTS

A total of 305 cases of M tuberculosis infection were identified between January 1978 and September 1985. Table 1 shows the yearly incidence of AIDS and tuberculosis. The incidence of tuberculosis more than doubled during the period, increasing from 1.17 to 2.53 per 1,000 medical-surgical admissions. During the period, 386 cases of AIDS were identified; none was
Table 1—AIDS and Tuberculosis at Beth Israel Medical Center, 1978-1985

<table>
<thead>
<tr>
<th>Year</th>
<th>AIDS (Rate)*</th>
<th>TB (Rate)*</th>
<th>TB and AIDS†</th>
<th>TB and ARC† (% of all TB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1978</td>
<td>0 (—)</td>
<td>25 (1.17)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1979</td>
<td>1 (.04)</td>
<td>35 (1.53)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>1980</td>
<td>1 (.04)</td>
<td>39 (1.66)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1981</td>
<td>6 (.23)</td>
<td>33 (1.29)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1982</td>
<td>20 (.74)</td>
<td>42 (1.55)</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>1983</td>
<td>87 (3.34)</td>
<td>44 (1.69)</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>1984</td>
<td>141 (6.41)</td>
<td>43 (1.95)</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>1985 (6 mo)</td>
<td>130 (7.49)</td>
<td>44 (2.53)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>386</td>
<td>305</td>
<td>30</td>
<td>14</td>
</tr>
</tbody>
</table>

*Rate per 1,000 medical-surgical admissions.
†By year of tuberculosis diagnosis.
‡Hospital admissions were decreased in 1984.

recognized prior to 1979. The yearly incidence of AIDS increased steadily, to 7.48 per 1,000 medical-surgical admissions during the first eight months of 1985. Sixty-one percent of AIDS patients were homosexual or bisexual men, 33 percent were parenteral drug users, and 6 percent were members of other risk groups. During the study period, the relative proportion of parenteral drug users among AIDS patients increased: 28 percent of patients diagnosed prior to 1984 were parenteral drug users, while during the following 20 months, 35 percent of patients were parenteral drug users.

Figure 1 shows the rate of tuberculosis per 1,000 medical-surgical admissions during the study period. Overall, parenteral drug users accounted for 36 percent of patients with tuberculosis. This proportion increased significantly throughout the period (p<0.01) (Fig 1A). Concomitantly, the proportion of patients who were alcohol abusers declined (p<0.001). There was no significant change in the frequency of tuberculosis in patients without a history of substance abuse. Patients with AIDS and ARC accounted for 14.4 percent of all cases of tuberculosis during the period. This proportion also rose significantly over the period (p<0.001), to 45.5 percent during the first eight months of 1985 (Fig 1B). Thus, the increase in tuberculosis could be accounted for by cases occurring in parenteral drug users, and most significantly, in patients with AIDS or ARC.

Thirty cases were identified during the period in which both AIDS and tuberculosis were diagnosed, representing an overall rate of tuberculosis among patients with AIDS of 7.8 percent. In 1985, Pneumocystis carinii pneumonia was diagnosed in 64 percent of patients with AIDS, infections with Mycobacterium avium intracellulare in 18 percent, with Mycobacterium tuberculosis in 7.7 percent, and with cytomegalovirus in 6.8 percent. Central nervous system toxoplasmosis and esophageal candidiasis each were diagnosed in 5.1 percent of AIDS patients, and cryptococcosis and cryptosporidiosis each in 4.3 percent. Thus, tuberculosis was one of the most common infections among AIDS patients at our institution.

Nineteen of the 30 patients (63 percent) with AIDS and tuberculosis were parenteral drug users. Of the 25 male patients, nine were homosexual or bisexual (including one Haitian patient), 15 were parenteral drug users, and one United States-born patient denied...
any known risk factor for AIDS. Of the five female patients, one was Haitian and four were parenteral drug users. Thus, tuberculosis was diagnosed in 19 (15.1 percent) of 127 AIDS patients with a history of parenteral drug use and in 11 (4.3 percent) of 259 AIDS patients belonging to all other risk groups (p<0.001).

In addition to the 30 patients meeting the CDC surveillance definition of AIDS, 14 patients with tuberculosis had signs and symptoms compatible with AIDS-related complex (ARC). Eight patient had oral candidiasis, six had generalized lymphadenopathy, five had weight loss, two had diarrhea, and one patient had multidermatomal herpes zoster. Only one patient had generalized lymphadenopathy as the only evidence of ARC. Lymph node biopsies were not routinely performed. Twelve of these patients were parenteral drug users, two were homosexual; all were men.

The mean age of patients with AIDS or ARC at the time of diagnosis of tuberculosis was 36.0 ± 6.9 years (range 24 to 50 years), similar to that of patients with a history of only parenteral drug use (mean 35.8 ± 8.8 years). Patients with AIDS or ARC were significantly younger (p<0.01) than patients with a history of alcohol abuse (mean 46.7 ± 11.2 years) or those with no history of substance abuse (56.4 ± 20.1 years).

Male patients accounted for 88.6 percent of all AIDS and ARC patients with tuberculosis, as compared to 67.8 percent of all other patients with tuberculosis (p<0.005). Among parenteral drug users, 87 percent with AIDS or ARC were men, and 75 percent of patients without AIDS or ARC were men (NS).

In 18 of the 30 patients (60 percent) with both tuberculosis and AIDS, tuberculosis preceded the diagnosis of AIDS by a mean of 6.8 ± 4.9 months (range one to 17 months). In six patients with tuberculosis and AIDS, tuberculosis was diagnosed from one to four months after AIDS (mean 2.5 ± 0.9 months). In the remaining six patients, tuberculosis and AIDS were diagnosed within the same month; in four of these, both pulmonary tuberculosis and a pulmonary opportunistic infection were present.

Tuberculosis was solely pulmonary in 12 of the 30 patients (40 percent) with AIDS. In four of these patients, bronchial washings yielded M tuberculosis and Pneumocystis carinii concomitantly. Tuberculosis was solely extrapulmonary in seven patients (23.3 percent) and both extrapulmonary and pulmonary in 11 (36.7 percent). Extrapulmonary disease was present in 12 of 18 patients in whom tuberculosis preceded AIDS, in two of six in whom AIDS and tuberculosis were diagnosed concurrently, and in four of six in whom tuberculosis occurred after AIDS (NS). Sites of extrapulmonary M tuberculosis included lymph nodes (nine), blood (five), urine (three), bone (one), bone marrow (three), liver (two), peritoneum (two), and neck (one) and psoas (one) abscesses. One patient with blood cultures positive for M tuberculosis developed tender skin nodules which upon biopsy revealed many acid-fast bacilli.

Six of the 14 ARC patients (42.8 percent) had extrapulmonary tuberculosis, including isolates from bone, lymph nodes, and urine. Among all other patients with tuberculosis, extrapulmonary disease occurred in 15.7 percent. One fifth of these cases occurred in immigrants from the Far East or Europe. Extrapulmonary tuberculosis was thus significantly more frequent among patients with AIDS (p<0.001) or ARC (p<0.01) than in other patients with tuberculosis. The frequency of extrapulmonary tuberculosis among parenteral drug users without AIDS or ARC (13.8 percent) was not significantly different from that among patients without a history of substance abuse.

To assess the relative likelihood for the development of AIDS, patients with tuberculosis and AIDS risk were stratified by the presence of ARC and/or extrapulmonary disease. Signs or symptoms of ARC were present in 11 of the 18 patients in whom tuberculosis occurred prior to AIDS. Seven patients had oral candidiasis, six had generalized lymphadenopathy, and three had chronic diarrhea. Of the 14 additional patients with tuberculosis and ARC identified during the study period, three have been lost to follow-up, and the remaining 11 have not yet developed CDC-defined AIDS after one to 12 months of observation (mean 4.5 ± 3.2). Thus, of 25 patients identified with ARC at the time of tuberculosis, 11 (44 percent) subsequently developed AIDS. In contrast, AIDS subsequently occurred in seven of 87 parenteral drug users without ARC at the time of tuberculosis (8 percent) (p<0.001). When patients with ARC were further stratified by extent of disease, seven of 13 (53.8 percent) with extrapulmonary disease subsequently developed AIDS, as compared to four of 12 (33.3 percent) with pulmonary disease (NS). When parenteral drug users without evidence of ARC were grouped by extent of tuberculosis, five of 16 (31.3 percent) with extrapulmonary disease subsequently developed AIDS, as compared to two of 71 (2.8 percent) with solely pulmonary disease (p<0.001).

**Discussion**

M tuberculosis infection has been described only infrequently in patients with AIDS in the United States. A significant exception is the high incidence of tuberculosis among patients with the syndrome who were born in Haiti, where the overall prevalence of tuberculin positivity is 80 to 90 percent. 2 Pape et al.
reported tuberculosis in 11 of 31 (35 percent) patients with AIDS in Haiti. This was the second most common infection noted in their study sample, following only mucocutaneous candidiasis in frequency of occurrence. Among Haitian immigrants in Florida, tuberculosis is seen in up to 60 percent of patients diagnosed with AIDS.7 In the United States, two large surveys of pulmonary infections among patients with AIDS, consisting largely of homosexual men and parenteral drug users, have reported the incidence of tuberculosis as 2 and 4 percent.8-10 Maayan et al11 cited four cases of tuberculosis among 40 patients with the syndrome from economically disadvantaged areas of New York City. Three of the patients were parenteral drug users.

Beth Israel Medical Center serves the Greenwich Village and lower East Side areas of Manhattan, and maintains a large outpatient methadone maintenance program and an inpatient drug detoxification service; the catchment area of the hospital thus includes among persons at risk for AIDS, primarily homosexual men and parenteral drug users. The yearly rates of both AIDS and tuberculosis rose during the study period. The increase in AIDS far exceeded that of tuberculosis: in 1985, the incidence of AIDS per 1,000 admissions was approximately three times that of tuberculosis. During the eight-year study period, infections due to M tuberculosis occurred in 7.8 percent of patients with AIDS, a frequency higher than that reported in earlier large surveys in the United States. At our institution, tuberculosis was diagnosed more often in patients with AIDS than central nervous system toxoplasmosis, esophageal candidiasis, cryptococcosis, or cryptosporidiosis. However, tuberculosis occurred disproportionately more frequently in parenteral drug users with AIDS. Sixty-three percent of AIDS patients with tuberculosis were drug users, although only 33 percent of all patients with AIDS at this hospital gave a history of parenteral drug use.

Recent reports from large urban centers suggest that the occurrence of tuberculosis is increasing, particularly in New York City, California, and Florida, areas where the greatest number of AIDS cases have been reported.4,11-12 The data from our hospital support these observations. Between 1978 and 1985, the increase in tuberculosis has been accompanied by a change in the population of affected patients from one comprised largely of alcohol abusers to one primarily of drug users. Furthermore, the yearly increment in tuberculosis cases could be accounted for by the increase in cases among parenteral drug users, since the rate among patients without a history of substance abuse remained constant, and the rate among alcohol abusers declined. Overall, parenteral drug users accounted for 36 percent of all patients with tuberculosis. In 1985, the figure rose to 45 percent. The most significant trend, however, was the increase in cases among patients with AIDS or ARC. During 1984 and 1985, the majority of the parenteral drug users in whom tuberculosis was diagnosed also had AIDS or ARC. Thus, the observed increase in tuberculosis is entirely attributable to cases among patients with documented AIDS or ARC and those at risk for AIDS.

When compared to other patients with tuberculosis, patients with AIDS or ARC were younger and more frequently men. These characteristics likely reflect those of the group most at risk for AIDS and tuberculosis, as the gender and age distributions were similar to those of parenteral drug users without AIDS or ARC. As has been recently reported, extrapulmonic disease occurred more frequently in patients with AIDS.13 In addition, extrapulmonary tuberculosis was also more common among ARC patients, irrespective of substance abuse history. Patients with AIDS or ARC and extrapulmonary tuberculosis often had widely disseminated disease with multiple sites of involvement. However, tuberculosis was also found to be solely pulmonary in one-half of patients at the time of or after the diagnosis of AIDS.

When patients at risk for AIDS were grouped by clinical criteria at the time of tuberculosis diagnosis, the presence of ARC was identified as the factor most strongly associated with the subsequent development of AIDS. One-third of all patients with ARC and pulmonary tuberculosis, and 54 percent of those with ARC and extrapulmonary disease subsequently developed infections or neoplasms fulfilling the CDC surveillance definition of AIDS. Among parenteral drug users without ARC, the presence of extrapulmonary involvement was more strongly associated with the subsequent development of AIDS than was pulmonary involvement alone. It seems clear that in the presence of ARC, infection due to M tuberculosis is a poor prognostic sign, even if disease is solely pulmonary. Since the interval between diagnoses was as long as 17 months in those patients who had tuberculosis prior to AIDS, continued observation of patients at risk will be necessary to determine the proportion of cases in which tuberculosis represented a first AIDS-associated infection.

Although classically described as a primary pathogen, disease due to M tuberculosis has been associated with diminished cell-mediated immunity in patients with carcinoma, lymphoreticular malignancies, renal failure, and in patients receiving corticosteroids. Extrapulmonic disease occurs frequently in such immunodeficient patients.13-16 Our findings suggest that this organism may also be acting as an opportunist in patients with AIDS retroviral-induced immunodeficiency. Thus, patients with tuberculosis who are members of high risk groups should be evaluated for AIDS retroviral infection and development of CDC-defined AIDS. In addition to appropriate precautions for
exposure to blood and body fluids from patients in high risk groups, respiratory isolation should be maintained for patients with AIDS or ARC and undiagnosed pulmonary infections. Since tuberculosis may coexist with other opportunists, the finding of another pulmonary infection should not preclude attempts to isolate M tuberculosis. The preponderance of parenteral drug abusers in this study suggests that, as in other AIDS associated infections, host factors determine the spectrum of opportunistic agents encountered. Although the increase in tuberculosis cases we observed is presently confined to patients with AIDS and those at risk for AIDS, ongoing surveillance will be necessary to determine the potential effect of this increment on the reservoir of active tuberculosis in the community at large.

References
1 Revision of the case definition of acquired immunodeficiency syndrome for national reporting—United States. MMWR 1985; 34:373-75
11 Update: Acquired immunodeficiency syndrome—United States. MMWR 1984; 33:337-39

Tuberculosis and AIDS (Handwerger et al)

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