Tuberculosis in Patients with Human Immunodeficiency Virus Infection*

How Often Does It Mimic Pneumocystis carinii Pneumonia?

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Adjunctive corticosteroid therapy is recommended for selected human immunodeficiency virus (HIV)-infected patients with presumed Pneumocystis carinii pneumonia. Because corticosteroids may exacerbate undiagnosed tuberculosis, we evaluated the frequency with which tuberculosis in HIV-infected patients mimics P carinii pneumonia. Over a 12-month period, we identified 105 HIV-infected patients with pleuropulmonary tuberculosis and 84 patients with P carinii pneumonia who were sufficiently hypoxic to warrant corticosteroid therapy. Of the 105 patients with tuberculosis, acid-fast smears of clinical samples were positive in 49 cases, and chest roentgenographic findings suggested tuberculosis in an additional 44 cases. The 12 patients with negative acid-fast smears and nonspecific chest roentgenographic findings presented a potential diagnostic dilemma between tuberculosis and P carinii pneumonia. Pneumocystis carinii pneumonia should not have been a presumptive diagnosis of eight of these 12 patients because of absence of pulmonary symptoms and chest roentgenographic abnormalities (four cases), a CD4 count >500/cu mm (three cases), or marked lymphadenopathy suggestive of tuberculosis (one case). Thus, only 4 percent (4/105) of HIV-infected patients with pleuropulmonary tuberculosis had clinical and chest roentgenographic features mimicking P carinii pneumonia. Two of these four patients were sufficiently hypoxic to warrant corticosteroid therapy. Thus, if corticosteroids had been routinely used during the study period, 84 patients with P carinii pneumonia would have been treated, including two patients with undiagnosed tuberculosis. We conclude that the use of corticosteroids for presumed P carinii pneumonia carries a small but acceptable risk of inadvertent exacerbation of tuberculosis, provided clinical and chest roentgenographic features do not suggest tuberculosis.

Early institution of corticosteroids in moderately to severely hypoxic human immunodeficiency virus (HIV)-infected patients with Pneumocystis carinii pneumonia reduces the frequency of respiratory failure and death.1,2 A consensus statement has therefore been published recommending that corticosteroids be given to all patients with P carinii pneumonia in whom the arterial partial pressure of oxygen is less than 70 mm Hg or in whom the alveolar-arterial gradient is greater than 35 mm Hg.4 Because therapy with corticosteroids should be initiated within 72 h of beginning antimycosystis therapy, treatment is often based on a high index of suspicion for P carinii pneumonia, before results of bronchoscopy are available. Furthermore, some patients are presumptively treated for P carinii pneumonia, and bronchoscopy is not performed. Thus, corticosteroids may inadvertently exacerbate diseases such as tuberculosis, fungal infections, and Kaposi's sarcoma,5 all of which can mimic P carinii pneumonia. Although there have been anecdotal reports of unfavorable outcomes in HIV-infected patients with tuberculosis who receive corticosteroids for presumed P carinii pneumonia,6 such adverse events have not been observed in controlled trials,1,3 and the potential risk for such an occurrence remains undefined. In order to address this question, we evaluated the frequency with which tuberculosis in HIV-infected patients presents in a manner clinically indistinguishable from P carinii pneumonia.

Materials and Methods

Patients with Pleuropulmonary Tuberculosis

We reviewed the medical records of 119 consecutive HIV-infected patients with culture-proven tuberculosis cared for at the Los Angeles County-University of Southern California (LAC-USC) Medical Center from November 1, 1989, through October 31, 1990. In three patients, growth of Mycobacterium tuberculosis from a single sputum sample was considered to represent laboratory contamination, and these patients were excluded from the study population. In one patient, autopsy revealed P carinii pneumonia, without pathologic evidence of tuberculosis, but one of six premortem sputum cultures yielded M tuberculosis. In one patient, P carinii was seen in bronchoalveolar lavage fluid, and M tuberculosis was isolated from one of nine sputum specimens, but not from broncho-

*From the Departments of Medicine and Radiology, University of Southern California School of Medicine, Los Angeles. Supported in part by a cooperative agreement CCU01877 between the Centers for Disease Control and the Los Angeles County-University of Southern California Medical Center. Manuscript received August 28; revision accepted November 20. Reprint requests: Dr. Barnes, HMR 904, USC School of Medicine, 2025 Zonal Avenue, Los Angeles 90024.
scopic specimens. In an additional patient, *M. tuberculosis* was isolated from one of 11 sputum samples, but not from bronchoscopic specimens, and no other pathogens were isolated. The latter two patients remained asymptomatic for two months without antituberculosis therapy.

Of the 115 HIV-infected patients with tuberculosis, 105 had pleuropulmonary disease, documented by (1) growth of *M. tuberculosis* from a pulmonary or pleural specimen, or (2) growth of *M. tuberculosis* from an extrapulmonary site and a chest roentgenogram suggestive of tuberculosis (defined below). Clinical evidence suggesting tuberculosis rather than *P. carinii* pneumonia consisted of any of the following findings: (1) acid-fast bacilli on smear of a clinical sample; (2) chest roentgenographic features suggestive of tuberculosis, ie, pleural effusion, predominant upper lobe infiltrates, cavitation, mediastinal adenopathy, or a miliary pattern; (3) CD4 cell count greater than 500/cu mm; and (4) prominent localized lymphadenopathy, suggesting tuberculous lymphadenitis.

**Patients with *P. carinii* Pneumonia**

We identified 161 consecutive HIV-infected patients cared for at the LAC-USC Medical Center in whom pulmonary specimens yielded *P. carinii* from November 1, 1989 through October 31, 1990. Arterial blood gas results for 158 patients were available, and were performed while the patient was breathing room air in 140 cases. In the remaining 18 patients, supplemental oxygen was administered because of clinical evidence of severe hypoxia. Patients in whom the arterial partial pressure of oxygen was less than 70 mm Hg or in whom the alveolar-arterial gradient was greater than 35 mm Hg were considered candidates for corticosteroid therapy.

**RESULTS**

**Patients with Pleuropulmonary Tuberculosis**

Of the 105 HIV-infected patients with culture-proven pleuropulmonary tuberculosis identified during the study period, the presence of acid-fast bacilli in sputum of clinical samples suggested the diagnosis in 49 cases (sputum, 40 cases; stool, five cases; lymph node, two cases; pleural fluid, one case; and bronchoalveolar lavage fluid, one case). Of the 56 patients in whom acid-fast smears were negative, chest roentgenograms of 50 patients were available and were reviewed to determine if they were suggestive of tuberculosis. These roentgenograms were interspersed with 50 roentgenograms of patients with *P. carinii* pneumonia, then reviewed in blinded fashion by an experienced staff radiologist (L.A.V.). In the six patients with tuberculosis for whom chest roentgenograms were not available, the radiology report in the medical record was used to determine whether the chest roentgenogram was suggestive of tuberculosis. Overall, 44 of 56 patients had chest roentgenographic findings suggestive of tuberculosis, including pleural effusion (19 cases), mediastinal adenopathy (16 cases), predominant upper lobe infiltrates (nine cases) a miliary pattern (three cases), or cavitation (two cases). More than one roentgenographic abnormality was present in some patients.

Of the 105 HIV-infected patients with tuberculosis, a positive acid-fast smear or chest roentgenographic findings suggested the correct diagnosis in 93 cases (Fig 1). In the remaining 12 patients, acid-fast smears were negative and chest roentgenographic findings were nonspecific, presenting a potential diagnostic dilemma between tuberculosis and *P. carinii* pneumonia. The chest roentgenogram was normal in six patients, bibasilar or perihilar interstitial infiltrates were present in four patients, a right lower lobe alveolar infiltrate was noted in one patient, and left basilar atelectasis was found in one patient. *Pneumocystis carinii* pneumonia should not have been a presumptive diagnosis in 8 of these 12 patients (Fig 1). Four patients had no pulmonary symptoms and normal chest roentgenograms. In three patients, the CD4 cell counts were greater than 500/cu mm, and *P. carinii* pneumonia rarely occurs in this setting. One patient had marked localized cervical lymphadenopathy suggestive of tuberculous lymphadenitis. The remaining four patients had clinical and chest roentgenographic features suggestive of *P. carinii* pneumonia.

**Tuberculosis Mimicking *P. carinii* Pneumonia**

Table 1 summarizes data on the four patients in whom clinical and chest roentgenographic findings were indistinguishable from those of *P. carinii* pneumonia. Patient 1 was thought to have bacterial pneumonia, although his clinical presentation was compatible with *P. carinii* pneumonia. Patients 2 to 4 had prominent pulmonary symptoms and underwent bronchoscopy. Patient 2 was mildly hypoxic and would not have been a candidate for corticosteroid therapy. Patients 3 and 4 had concomitant tuberculosis and *P. carinii* pneumonia, and they were sufficiently hypoxic to have been candidates for corticosteroid therapy. None of the patients received corticosteroids because they were not routinely used for *P. carinii* pneumonia during the study period. Patients 1, 2, and

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21652/ on 04/02/2017)
**Table 1—Clinical Features of Four HIV-Infected Patients with Pulmonary Tuberculosis Whose Clinical Presentations Were Indistinguishable from Those of P carinii Pneumonia**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior HIV-related diseases</td>
<td>None</td>
<td>Thrush</td>
<td><em>P carinii</em> pneumonia</td>
<td><em>P carinii</em> pneumonia</td>
</tr>
<tr>
<td>Pulmonary symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 cells/cu mm</td>
<td>246</td>
<td>76</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Serum lactate dehydrogenase, U/L†</td>
<td>268</td>
<td>272</td>
<td>560</td>
<td>250</td>
</tr>
<tr>
<td>Arterial partial pressure of oxygen‡</td>
<td>ND</td>
<td>90</td>
<td>52</td>
<td>63</td>
</tr>
<tr>
<td>Alveolar-arterial gradient</td>
<td>ND</td>
<td>16</td>
<td>46</td>
<td>35</td>
</tr>
<tr>
<td>Chest roentgenogram</td>
<td>Right lower lobe alveolar infiltrate</td>
<td>Bilateral perihilar interstitial infiltrate</td>
<td>Bilateral lower lobe interstitial infiltrate</td>
<td>Normal</td>
</tr>
<tr>
<td><em>P carinii</em> on bronchoscopy</td>
<td>ND</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presumptive diagnosis</td>
<td>Bacterial pneumonia</td>
<td><em>P carinii</em> pneumonia</td>
<td><em>P carinii</em> pneumonia</td>
<td><em>P carinii</em> pneumonia</td>
</tr>
<tr>
<td>Treatment</td>
<td>Erythromycin</td>
<td>TMP-SMX</td>
<td>TMP-SMX, pentamidine</td>
<td>Pentamidine</td>
</tr>
<tr>
<td>Outcome</td>
<td>Well until anti-TB drug therapy begin</td>
<td>Well until anti-TB drug therapy begin</td>
<td>Died after 2 weeks</td>
<td>Well until anti-TB drug therapy begin</td>
</tr>
</tbody>
</table>

*Plus sign = present; minus sign = absent; ND = not done; TMP-SMX = trimethoprim-sulfamethoxazole; TB = tuberculosis; HIV = human immunodeficiency virus.
†Normal <300 U/L.
‡All blood gas measurements were performed while the patient was breathing room air.

4 did well until antituberculosis chemotherapy was begun when cultures yielded *M tuberculosis*. Patient 3 died while receiving antipneumocystis therapy, and an autopsy was not performed. It is thus uncertain if untreated tuberculosis contributed to death in this case.

**Concomitant Pleuropulmonary Tuberculosis and P carinii Pneumonia**

During the study period, six patients had concomitant pleuropulmonary tuberculosis and *P carinii* pneumonia. Acid-fast bacilli were seen in smears of sputum in one patient, and the chest roentgenogram revealed pleural effusion or mediastinal adenopathy in an additional three patients. Thus, clinical features in two of the six patients provided no clues to the diagnosis of tuberculosis. These two patients are discussed in detail above.

**Patients with P carinii Pneumonia**

Of the 158 patients with *P carinii* pneumonia identified during the study period in whom arterial blood gas results were available, the arterial partial pressure of oxygen was less than 70 mm Hg in 63 patients, and the alveolar-arterial gradient was greater than 35 mm Hg in an additional 21 patients. Thus, a total of 84 patients were candidates for corticosteroid therapy.

**DISCUSSION**

The data presented in this report indicate that tuberculosis in HIV-infected patients is unlikely to present in a manner clinically indistinguishable from *P carinii* pneumonia. In the vast majority of HIV-infected patients with pleuropulmonary tuberculosis, positive acid-fast smears, chest roentgenographic findings, a CD4 cell count of greater than 500/cu mm, or prominent localized lymphadenopathy suggested the correct diagnosis. Only four (4 percent [90 percent CI 1 to 7 percent]) of the 105 patients had clinical and chest roentgenographic findings suggestive of *P carinii* pneumonia. Two of these four patients were sufficiently hypoxic to warrant corticosteroid therapy, and both had coexistent *P carinii* pneumonia. During this same period, 84 patients with *P carinii* pneumonia would have been candidates for corticosteroid therapy. Thus, the use of corticosteroids for presumed *P carinii* pneumonia carries at most a small risk of inadvertent exacerbation of tuberculosis, provided there are no clinical or chest roentgenographic features suggestive...
of tuberculosis. A high proportion of the HIV-infected patients served by our medical center are medically indigent blacks and Hispanics in whom the incidence of tuberculosis is higher than that in other HIV-infected individuals. In other clinical settings, the risk of inadvertent exacerbation of tuberculosis during corticosteroid therapy for presumptive P. carinii pneumonia should be correspondingly lower.

Our findings emphasize that clinical features other than the chest roentgenogram and the acid-fast smear of sputum are valuable for identifying HIV-infected patients with tuberculosis. In five patients, a positive acid-fast smear of stool suggested the correct diagnosis. Although acid-fast organisms in stool are commonly ascribed to M. avium complex infection, this finding is present in 40 percent of HIV-infected patients with tuberculosis.9 Because tuberculosis often causes clinically significant pulmonary disease in HIV-infected patients, whereas M. avium complex generally does not,10 acid-fast organisms in stool should be considered evidence of tuberculosis in all patients who present with pulmonary disease, including those who receive corticosteroids for presumed P. carinii pneumonia.

The CD4 cell count is also valuable in estimating the likelihood of P. carinii pneumonia vs tuberculosis in a given patient. Pneumocystis carinii pneumonia characteristically occurs when the CD4 cell count is below 200/cu mm, and rarely when it is greater than 500/cu mm.7 In contrast, tuberculosis occurs at all stages of HIV infection.8,11 Thus, a markedly depressed CD4 cell count does not rule out tuberculosis, whereas a CD4 cell count greater than 500/cu mm makes P. carinii pneumonia unlikely.

The results of our retrospective study must be interpreted with some caution. First, it is possible that some patients with tuberculosis were not included in our population because samples were never obtained for mycobacterial culture. Second, the chest roentgenograms in this study were interpreted by an experienced radiologist who was more attuned to findings suggestive of tuberculosis than the average physician. For both of these reasons, the risk of undiagnosed tuberculosis in patients with presumed P. carinii pneumonia may be higher than we noted. Prospective investigations should provide a more accurate estimate of the magnitude of this risk.

In regions where tuberculosis is common, one could consider administration of antituberculosis medications to HIV-infected patients who receive corticosteroids for P. carinii pneumonia and who are at increased risk for tuberculosis, eg, ethnic minorities and intravenous drug users.12 Because these groups constitute a large proportion of the HIV-infected population in many cities, we do not favor this approach as it would expose many patients to antituberculosis agents in order to provide potential but unproven benefit to a few. In view of reports that antituberculosis agents cause significant adverse reactions in as many as 18 percent of HIV-infected patients,13 we believe that the risks of antituberculosis therapy in this situation outweigh its potential benefits.

In many of our patients, the clinical evidence suggesting tuberculosis consisted of chest roentgenographic findings of pleural effusion, mediastinal adenopathy, predominant upper lobe infiltrates, and miliary pattern, or cavitation. Although these findings were initially considered extremely atypical in P. carinii pneumonia, they have been more frequently noted in recent reports, particularly among patients who receive aerosolized pentamidine as antipneumocystis prophylaxis.13,14 When these chest roentgenographic features are present, the risk of inadvertent exacerbation of tuberculosis by corticosteroids for presumed P. carinii pneumonia may be significant. Additional studies will be necessary to determine the optimal methods to distinguish tuberculosis from P. carinii pneumonia in this setting.

ACKNOWLEDGMENT: We thank Drs. Joseph Indenbaum and Om Sharma for their critical comments and suggestions, and Dr. Fred Sattler, Martin Holmes, P.A., and Claire Hughlett, R.N., for providing us with chest roentgenograms on patients with P. carinii pneumonia. We are also indebted to Gayle Gutierrez, B.S.N., Ann Easley, R.N., Belen Marcos B.S.N., and Latonia Garrett for assistance in identifying the patients included in this study.

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