Lack of Utility of Bronchial Brush Biopsy in Patients Infected with the Human Immunodeficiency Virus∗

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While bronchoalveolar lavage has been shown to be more sensitive than brush biopsy (BB) for the diagnosis of Pneumocystis carinii pneumonia in AIDS patients, some have reported that BB occasionally is positive in spite of a negative BAL. Many bronchoscopists, therefore, continue to perform routine BB when doing bronchoscopy on AIDS patients. We performed a retrospective study of all fiberoptic bronchoscopies done on human immunodeficiency virus-infected patients over a one-year period at our institution to determine if the use of BB added to the diagnostic yield of bronchoscopy over that of BAL alone. Of 84 bronchoscopies in which BB was performed in addition to BAL, BB yielded no diagnoses that were not obtained by BAL. Brush biopsy added approximately $400 to the cost of bronchoscopy. We conclude that BB should not be routinely done when performing bronchoscopy on HIV-infected patients. (Chest 1992; 101:680-83)

Frequently, HIV-infected patients develop life-threatening complications involving the lung, both infectious and noninfectious.1,4 Fiberoptic bronchoscopy has been an indispensable modality for diagnosing pulmonary disease in HIV-infected patients. Early in the course of the AIDS epidemic, many bronchoscopists performed transbronchial biopsy and BB in addition to bronchial washings or BAL when performing bronchoscopy on AIDS patients.1,5 8 Recently, the excellent sensitivity of BAL for diagnosing pulmonary infection in HIV-infected patients has become apparent, and some experts recommend performing only BAL when doing bronchoscopy on HIV-infected patients with suspected pulmonary infection.3,9,10 However, performing BAL alone will result in between 2 and 21 percent of cases of PCP being missed.1,7,9,11 There have been occasional reports of diagnostic BB when BAL was negative,1,8 but in most studies, the data have been presented in such a way as to preclude determining how frequently BB yielded a diagnosis despite a negative BAL.5,7

With the increasing use of prophylactic aerosolized pentamidine, HIV-infected patients are developing PCP less frequently.12 Therefore, a patient presenting with an acute pulmonary process is now more likely to have an infection other than PCP than prior to the use of prophylactic aerosolized pentamidine.3 In addition, patients who do develop PCP while receiving prophylactic aerosolized pentamidine commonly present with atypical chest roentgenograms,13,14 and it is becoming increasingly difficult to predict whether the patient has PCP or some other pulmonary process such as tuberculosis or fungal infection. These changes are important because, unlike the large amount of experience with PCP, it has not been convincingly shown that the sensitivity of BAL alone justifies not using other modalities such as transbronchial biopsy or BB to increase the diagnostic yield for tuberculosis, cryptococcosis, and coccidioidomycosis. In fact, several studies have demonstrated an increased diagnostic yield for cryptococcosis,11 tuberculosis,11,15 and coccidioidomycosis16 from the concurrent use of transbronchial biopsy and BAL. Little information is available, however, about the utility of BB in diagnosing complications of HIV-infection other than PCP.

Many bronchoscopists do BB when performing bronchoscopy on HIV-infected patients,8,17,18 possibly because of the above-mentioned issues and the benign nature of the procedure. Because it remains unclear whether or not routine BB is useful in this context, we decided to review our experience with bronchoscopy on HIV-infected patients to determine if BB provided any diagnostic advantages.

Materials and Methods

Data Collection

The results of all fiberoptic bronchoscopies performed on HIV-infected patients at the University of California, San Diego Medical Center between January 1 and December 30, 1989, were reviewed. Only those bronchoscopies which included a BB were included in the study. Review of the medical records revealed that in most cases, the decision as to whether BB and/or transbronchial biopsy was performed was based not on the specifics of the patient's presentation, but on the opinion of the bronchoscopist regarding the utility of BB and transbronchial biopsy. The medical record of

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each patient included in the study was reviewed, and the cytologic, pathologic, microbiologic, and virologic results of the bronchoscopy were noted. In addition, the patient’s medical record was reviewed to determine if the patient’s presentation and clinical course were consistent with the diagnosis made at bronchoscopy and to ascertain if any subsequent diagnoses were made that had been missed at bronchoscopy.

**Bronchoscopic Procedure**

All bronchoscopies were performed by second year pulmonary and critical care fellows at the University of California, San Diego, under the direction of an attending physician in the Division of Pulmonary and Critical Care Medicine. Bronchoalveolar lavage was performed with each bronchoscopy, although the technique used varied according to the preference of the bronchoscopist. Brush biopsy and transbronchial biopsies were performed at the discretion of the bronchoscopist. Either a Pentax 15 A or a Pentax 19 D fiberoptic bronchoscope was used for all procedures. For BB, a 7 mm Harrell brush was used. With the exception of bronchoscopies performed in the intensive care unit, all BBs were performed under fluoroscopic guidance peripherally in an area of abnormality seen on chest roentgenogram. The BALs were sent for the following studies: cytology with Comori methenamine silver, Gram and acid-fast stains, bacterial, viral, fungal and Legionella culture. The BB was sent for cytology with Comori methenamine silver stain, acid-fast stain, and Legionella direct fluorescent antibody. Transbronchial biopsy specimens were sent for histologic studies with special stains and cultures as indicated.

**RESULTS**

During the period under study, 139 fiberoptic bronchoscopies were performed on HIV-infected patients. Of these, 52 were excluded because the procedure did not include BB, and three were excluded because the complete medical record was not available, leaving 84 bronchoscopies on 80 patients. Table 1 demonstrates the results of the bronchoscopies and the final diagnosis or diagnoses given to the pulmonary process for which the bronchoscopy was performed. Of note, cytomegalovirus was not considered a pulmonary pathogen, with the exception of one patient in whom the clinical course in addition to the positive culture of cytomegalovirus suggested the diagnosis. Transbronchial biopsy was done infrequently (17 times) and in no cases provided diagnoses not obtained by BAL (results not shown).

The were 36 bronchoscopies which yielded a diagnosis of PCP (including two which yielded both PCP and Cryptococcus). There were two negative bronchoscopies which were shown to be false-negatives as both of the patients in question were subsequently diagnosed as having PCP, one at post-mortem exam and the other by examination of induced sputum. There were an additional six negative bronchoscopies on six patients who had a clinical course consistent with PCP and were treated empirically without a definitive diagnosis being made. In the analysis of our results, it was assumed that all six of these patients did in fact have PCP. Thus, the sensitivities that we report reflect the lower limit, and the true sensitivities may be somewhat higher. Bronchoscopy had a sensitivity of 82 percent (36 of 44) for PCP. All 36 of these had positive BALs, while BB was positive in 24 of 44 (55 percent). In no case was there a diagnosis of PCP that was made by BB alone.

Bronchoscopies were performed on patients with a wide range of infectious diseases other than PCP, including mycobacterial, fungal and bacterial infections. There were seven bronchoscopies performed on six patients who had proven mycobacterial disease (six bronchoscopies on five patients with *Mycobacterium tuberculosis*, and one bronchoscopy on a patient with *M. bovis*). Four BALs were positive by either smear or culture, while no BB was positive. Of the three patients with tuberculosis who had false-negative bronchoscopies, one was diagnosed by a second bronchoscopy, one by a subsequent sputum and one at post-mortem exam. All five of the patients with cryptococcosis were diagnosed by bronchoscopy, although one patient had a negative BAL and a negative BB but a positive transbronchial needle aspirate. The one patient with coccidioidomycosis was diagnosed by serology and response to therapy, as he had a negative bronchoscopy. There were three bronchoscopies performed on two patients who were diagnosed with Legionella pneumonia, all of which were negative (all were performed after the patients had been started on empiric therapy with erythromycin). Both of these patients were subsequently diagnosed by sputa which had been obtained prior to the initiation of antibiotics. The three patients with bacterial pneumonia were receiving empiric antibiotics prior to the bronchoscopy, accounting for the false-negative results obtained with two of the patients. Similar to the results

**Table 1—Results of 84 Fiberoptic Bronchoscopies Performed on HIV-Infected Patients**

<table>
<thead>
<tr>
<th>Final Diagnosis</th>
<th>Positive BAL (%)</th>
<th>Positive BB (%)</th>
<th>Positive BB With Negative BAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>42 (81)</td>
<td>22 (52)</td>
<td>0</td>
</tr>
<tr>
<td>Kaposi's sarcoma</td>
<td>9 (0)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>9 (0)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Mycobacteria†</td>
<td>7 (4)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Cryptococcus</td>
<td>3 (2)</td>
<td>2 (67)</td>
<td>0</td>
</tr>
<tr>
<td>Bacterial pneumonia</td>
<td>3 (1)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Legionella</td>
<td>3 (0)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Bronchogenic cancer</td>
<td>2 (0)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Cryptococcus +</td>
<td>2 (1)</td>
<td>1 (50)‡</td>
<td>0</td>
</tr>
<tr>
<td>PCP</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nocardia</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Coccidioidomycosis</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Influenza</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>84</td>
<td>54 (25)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Positive by either cytology or culture.
†Mycobacterium avium-intracellulare was not considered a pulmonary pathogen.
‡One BB detected only PCP while the other one detected both pathogens.
seen with PCP, the yield of bronchoscopy on patients with diseases other than PCP was not increased by the use of BB.

Discussion

The HIV-infected patient frequently develops life-threatening pulmonary complications, most commonly opportunistic infections.1,2-4 Fiberoptic bronchoscopy, because of its safety, efficacy, and relatively low cost is generally agreed to be the best method of diagnosing these infections if aerosol-induced sputum is nondiagnostic.3 While there is general agreement regarding the utility of fiberoptic bronchoscopy in this setting, there is significant controversy in the literature as to whether BAL should be done alone, or whether other modalities such as transbronchial biopsy or BB should be done in addition.1,3-6,8-11

Before the AIDS epidemic, there were several reports concerning the use of BB for the diagnosis of opportunistic infection in immunocompromised patients. One group reported that BB had an 80 percent sensitivity for PCP in 21 immunocompromised pediatric patients,19 while another reported a 67 percent sensitivity for PCP in adults receiving immunosuppressive therapy.20 However, other studies have reported sensitivities of only 38 percent21 and 45 percent22 in similar patient populations.

Studies of the yield of BB for the diagnosis of PCP in AIDS patients have also yielded disparate results. One group found that BB detected PCP in 20 of 27 (74 percent) patients.8 Because of the rapidity with which slides from BB can be processed, this group recommended that BB should routinely be done in addition to BAL. Another group, using BB both via a bronchoscope and blindly via an endotracheal tube, reported an 86 percent sensitivity for PCP.27 They suggested that BB be used as an independent modality for diagnosing PCP. In contrast, Mones et al9 reported that BB detected only 12 of 21 (57 percent) cases of PCP in AIDS patients and suggested that BB does not add to the diagnostic yield of transbronchial biopsy for PCP. This group did not perform BAL as part of their bronchoscopic procedure.

Several studies have shown that BAL has a sensitivity for PCP of 89 percent or better in AIDS patients,7,9-11 higher than reported for BB. However, what cannot be determined from the studies published to date is how often performing BB allows detection of cases of PCP missed by BAL alone. If the use of BB increased the diagnostic yield by only a small percentage, its use might be warranted, given the extremely low morbidity associated with the procedure.

In the present study, there were 44 bronchoscopies on patients with proven or probable PCP in which BB was performed in addition to BAL. Brush biopsy was positive in 24 (55 percent) of these cases while BAL was positive in 36 (82 percent). Importantly, there were no cases in which a positive BB for PCP was seen with a negative BAL. Therefore, BB did not add to the diagnostic yield of any of these procedures.

As many of the studies of bronchoscopy in AIDS patients have dealt exclusively with PCP or included few patients with other types of opportunistic infections, there is little information available concerning the efficacy of BB in the diagnosis of opportunistic infections such as cryptococcosis or tuberculosis. A theoretic argument can be made for the use of BB on HIV-infected patients with possible tuberculosis as the disease is frequently interstitial or miliary, while cavitory disease is unusual.23 Thus, performing only BAL, which samples mainly alveolar fluid, might result in a significant number of false-negative results. Indeed, in a large study of tuberculosis in HIV-infected patients, acid-fast smears of BAL samples were positive in only nine of 44 (20 percent) cases.24 This contrasts with the results of a study of non HIV-infected patients with smear-negative miliary tuberculosis in which six of nine (67 percent) BBs had positive acid-fast smears.24

In the present study, BB did not add to the diagnostic yield for patients with opportunistic infections other than PCP. Positive acid-fast smears were obtained from zero of seven BBs performed on patients who were diagnosed with mycobacterial disease, while BAL was positive for four of seven by either culture or smear. Nor was BB helpful in diagnosing fungal diseases. In five bronchoscopies on patients with cryptococcosis, both BAL and BB were positive for three; in one patient each, BAL and transbronchial needle alone were positive. The one patient with coccidioidomycosis was diagnosed by serologic methods, as BAL, BB, and transbronchial biopsy were all negative.

Although we found that BB did not add to the diagnostic yield in these 84 bronchoscopies, the literature does disclose some cases in which BB has detected pathogens missed by BAL.1,8 The question then becomes, "Is the risk and expense of doing BB routinely on HIV-infected patients justified by the few cases in which it would be useful?" Brush biopsy is thought to be a procedure with minimal risks; however, pneumothoraces and severe bleeding25,26 are known complications of BB. Also, four instances of brushes breaking off within the tracheobronchial tree have been reported with one patient requiring a thoracotomy for brush removal.25 In addition, peripheral BB is usually done under fluoroscopic guidance necessitating radiation exposure to the patient.

The use of BB adds considerable expense to the bronchoscopy. The additional cost resulting from BB, including the professional charges, charges for fluor-
oscopy, and charges by the cytology laboratory amounts to approximately $400 at our institution. Thus, during 1989, the use of routine BB on HIV-infected patients at our institution cost approximately $33,200 and yielded no diagnoses.

In summary, the results of this study demonstrate that bronchoscopy with the use of BAL is extremely useful for diagnosing a wide variety of pulmonary pathogens in HIV-infected patients. However, the routine use of BB does not appear to be indicated because it adds risk and cost to the procedure while rarely adding to the diagnostic yield from BAL alone.

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