Diagnostic value of fiberoptic bronchoscopy in acquired immunodeficiency syndrome[1]

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Diagnostic results of flexible fiberoptic bronchoscopy done as the first invasive procedure were evaluated in 50 patients considered to have the acquired immunodeficiency syndrome (AIDS). Five patients (10%) had nondiagnostic bronchoscopic examinations and were thought to have the pre-AIDS form of the disease, since *Pneumocystis carinii* pneumonia (PCP) was diagnosed an average of 4.5 months later. Bronchoscopy revealed pathogens in 87% of the remaining 45 patients with AIDS and showed false-negative results in 13%. Thirty-eight patients (84%) had PCP diagnosed on their first bronchoscopic examination. Transbronchial lung biopsy and transbronchial lung biopsy with bronchoalveolar lavage had high yields for PCP (94% and 95% respectively). Lavage alone had a lower yield (63%). Although 69 different bronchoscopy specimens were sent for mycobacterial smear and culture, only two patients were found to have mycobacteriosis (one *M tuberculosis*, one *M avium-intracellulare*). Fiberoptic bronchoscopy was found to be a safe, high-yield first procedure in AIDS patients, especially for PCP. Mycobacterial infection did not appear to be a common infection in AIDS at presentation, and the authors recommend transbronchial lung biopsy and bronchoalveolar lavage be done earlier in the diagnostic evaluation of patients considered to have AIDS.

Index terms: Acquired immunodeficiency syndrome • Bronchoscopy

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The number of patients with the acquired immunodeficiency syndrome (AIDS) continues to increase and almost 7000 cases were reported in the USA by the end of 1984.[1] Pulmonary involvement, primarily with infection or Ka-

Table 1. Results of initial fiberoptic bronchoscopy in 45 AIDS patients

Results		Infections		
Outcome	No. patients (%)	Diagnosed	Missed	Confirmed by
Positive	39 (87%)	38 PCP 1 MAI	3 MAI*	sputum (1) open lung biopsy (1) autopsy (1)
Negative	6 (13%)	None	5 PCP	repeat BAL (1) repeat TBLB and BAL (2) open lung biopsy (2)
			1 cryptococcal pneumonia	autopsy (1)

PCP = *Pneumocystis carinii* pneumonia; *MAI* = *Mycobacterium avium-intracellulare*; *TBLB* = transbronchial lung biopsy; *BAL* = bronchoalveolar lavage

* 3 MAI infections missed in 3 patients with confirmed PCP

posi's sarcoma, is a major cause of morbidity and mortality in more than 50% of AIDS patients.[2] *Pneumocystis carinii* pneumonia (PCP), cytomegalovirus (CMV), and *Mycobacterium avium-intracellulare* (MAI) infection account for more than 90% of the lung infections in AIDS.[3] Fiberoptic bronchoscopy has been shown to be very useful to diagnose these infections in non-AIDS patients and recently fiberoptic bronchoscopy has also become an important diagnostic tool in AIDS patients.[4–8]

Since our report of the pulmonary manifestations in our first 15 patients with AIDS,[9] we have evaluated more than 70 patients with this syndrome. Fiberoptic bronchoscopy was the primary diagnostic procedure in only eight of our first fifteen patients. As our understanding of this syndrome grew, as well as our knowledge of the expected pulmonary infections, we increasingly applied bronchoscopy as the primary diagnostic measure in this patient group. Since bronchoscopy is an invasive procedure with rare but potentially life-threatening complications, the benefits of bronchoscopy must be known if we are to recommend its routine use in AIDS patients.[10,11] Therefore, to determine the expected value of bronchoscopy in AIDS, we evaluated the results of flexible bronchoscopy done as the first invasive procedure in the evaluation of 50 patients considered to have AIDS. In particular, we determined the relative contributions of bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) to the overall positive yield of fiberoptic bronchoscopy. Additionally, we evaluated the role of the second invasive procedure in patients in whom the first bronchoscopic examination was nondiagnostic.

Materials and methods

Patients

During the two-year period from January 1982 to January 1984, 50 patients had fiberoptic bronchoscopy as their first invasive procedure to diagnose an opportunistic pulmonary infection to fulfill the Centers for Disease Control definition of AIDS.[2,12] Forty-one patients were men and nine were women; the mean age was 36 years. All patients had one or more risk factor(s) for AIDS including: intravenous drug abuse (35 patients), homosexuality (6 patients), and Haitian origin (6 patients). In addition, one patient had previous blood transfusions, three patients were heterosexual partners of persons at increased risk for AIDS, and in two patients no risk was identified.[1,13]

Bronchoscopy

Flexible fiberoptic bronchoscopy was performed in all patients with an Olympus BF-B2 bronchoscope (Olympus Corporation of America, New Hyde Park, NY). In all nonintubated patients, bronchoscopy was done transnasally with topical anesthesia and intramuscular atropine, with or without mild sedation as indicated in each case. Patients on ventilators underwent bronchoscopy through the endotracheal tube by means of a Portex Swivel adapter (Portex Inc., Wilmington, MA), which allowed continuous mechanical ventilation during the procedure. After visual inspection of the airways, BAL was done by wedging the bronchoscope in an involved segment, usually the right middle lobe or lingula. A total of 100 to 140 ml of normal saline was instilled in 20-ml aliquots and manually aspirated.

Table 2. Relative yield of TBLB *vs* BAL to diagnose PCP

Type of procedure	No. pos/total*	% Yield	Second procedure diagnostic of PCP (No.)
TBLB alone	15/16	94%	open lung (1)
BAL alone	5/8	63%	repeat BAL (1), open lung (1), repeat TBLB and BAL (1)
TBLB with BAL†	18/19	95%	repeat TBLB and BAL (1)

TBLB = transbronchial lung biopsy; *BAL* = bronchoalveolar lavage; *PCP* = *Pneumocystis carinii* pneumonia
* numerator = number of patients with PCP found by each procedure; denominator = total number of patients in whom PCP was diagnosed by initial bronchoscopy or repeat procedures
† both TBLB and BAL were positive for PCP in 14 patients and BAL alone was positive in 4 for a total of 18 positive bronchoscopic examinations

Transbronchial biopsy was then done in patients who did not have contraindications; a minimum of three biopsy specimens was obtained in standard manner using fluoroscopic control.[14] Since BAL was not a standard part of bronchoscopy in 1982, most patients in the first year of this study had TBLB without BAL. In the latter half of the study, both procedures were done in all patients without contraindications. Bronchial washings were obtained in standard manner by instilling 5-ml aliquots of normal saline randomly into central airways and suctioning it back through the bronchoscope.

Precautions and complications

Standard preoperative evaluation for bronchoscopy was done in all patients.[14] All patients had a PaO_2 of at least 70 mmHg while receiving supplemental oxygen. TBLB was not done in patients with severe thrombocytopenia (< 70,000 platelets per mm^3) with an uncorrectable coagulopathy or in patients on mechanical ventilators. No significant complications occurred with any bronchoscopy procedure. No pneumothorax developed in any patient and no procedure was terminated because of hemoptysis.

Specimen processing

BAL specimens were centrifuged and the sediment was examined by Gram Weigert, acid-fast, silver methenamine, and hematoxylin-eosin stains. The sediment was also routinely cultured for fungi, mycobacteria, and occasionally for viruses. TBLB specimens were examined by hematoxylin-eosin, acid-fast, and silver methenamine staining. If adequate tissue was available, TBLB specimens were cultured for mycobacteria. Bronchial washings were examined for acid-fast bacilli and cultured for mycobacteria.

Results

Sensitivity of bronchoscopy

Fifty patients underwent flexible fiberoptic bronchoscopy as their initial diagnostic procedure. Transbronchial lung biopsy was done as the only procedure in 18 patients, eight patients had BAL only, and both TBLB and BAL were done in 24 patients. In addition to TBLB or BAL, 30 patients had bronchial washings examined for mycobacterial smear and culture.

In five patients the results of bronchoscopy showed no pathogens (TBLB in two and TBLB with BAL in three). However, invasive procedures in these five patients were done an average of 18 weeks later when they presented with marked deterioration in their pulmonary status. *Pneumocystis carinii* pneumonia was found in these five patients by open-lung biopsy in two, BAL in one, and TBLB with BAL in two. These five patients, representing 10% of the study group, most likely had their initial bronchoscopy done during the pre-AIDS phase of their disease prior to development of the full syndrome 18 weeks later.[15–16]

In the remaining 45 patients, the bronchoscopy procedure can be evaluated for efficacy in diagnosing the active pulmonary complications of AIDS. *Table 1* summarizes the outcome of the 45 bronchoscopy procedures as a whole. Bronchoscopy resulted in a positive diagnosis in 87% of patients, although concomitant MAI infection was missed in three patients with PCP. Thirteen percent of the bronchoscopic examinations were completely nondiagnostic and are labelled false-negative since follow-up procedures done within days diagnosed infections missed by the initial bronchoscopy. These second procedures include repeat bronchoscopy in three and open-lung biopsy in two patients. All five patients had PCP diagnosed by the second procedure and one patient had MAI infection in addition.

Specimen yield for Pneumocystis carinii

Since 43 patients were diagnosed to have PCP by one or more invasive procedure(s), TBLB and BAL were comparatively assessed for their relative yield in establishing the presence of PCP. *Table 2* documents the yield of these techniques when done as sole procedures or jointly during bronchoscopy. BAL alone had a lower yield (63%) than TBLB (94%) or TBLB with BAL (95%). However, BAL alone was the only specimen showing PCP in four of the nineteen patients (21%) who had both TBLB and BAL. In addition, in no instance was TBLB positive and BAL negative for PCP in patients who had both procedures. Thus, BAL provided a major contribution to the diagnostic yield in this latter group of nineteen patients.

Specimen yield for other pathogens

The results of acid-fast smear and culture of various bronchoscopy specimens for MAI infection were available in 42 patients with AIDS; in three patients the mycobacterial cultures are pending. Sixty-nine different specimens were obtained from these 42 bronchoscopic examinations, including TBLB in 27, BAL in 19, and bronchial washings in 23 patients. All 69 specimens were negative on smear for acid-fast bacilli. The only positive specimens came from two patients: for one MAI grew on culture of both TBLB and BAL specimens and for the other *M tuberculosis* grew on culture of the BAL specimen (the TBLB specimen was culture-negative). False-negative smear and culture results were obtained from three bronchoscopy procedures (2 TBLB and 3 washes). In these three patients, presence of MAI infection was confirmed by culture of one each of the following: sputum, open lung biopsy specimen, and lung tissue from autopsy. In five patients, culture of open-lung biopsy or autopsy specimens confirmed the bronchoscopy results, showing absence of MAI infection. Thirty-one patients did not have other invasive tests that would confirm or refute the bronchoscopy results. Thus, acid-fast smear and mycobacterial culture of 69 bronchoscopy specimens produced only positive results in two patients and missed the diagnosis in a minimum of 10% (3/31).

BAL specimens were cultured for CMV in seven of our recent cases. CMV cultures were positive in two (29%) and negative in the remaining five (71%).

Discussion

In this study, fiberoptic bronchoscopy was a safe, effective diagnostic procedure in patients with AIDS. Our results indicate that the initial bronchoscopy procedure will reveal pathogens (usually PCP) in 87% of patients who actually have a pulmonary infection. Our results are similar to the composite data from six institutions reported by the National Heart, Lung, and Blood Institute workshop.[3] In this report, initial and repeat fiberoptic bronchoscopic studies enabled diagnosis of 91% of the pulmonary infections in 1552 AIDS patients. In this report and throughout the country, PCP appears to be the primary opportunistic infection in the AIDS patient with pulmonary infiltrates.[5–9] By initial bronchoscopy (38 patients) plus second invasive procedure (5 patients), we documented that PCP was the origin of the presenting pulmonary disease in 43 (95%) of our AIDS patients. TBLB and TBLB with BAL did not differ significantly in their high yield for PCP (94% and 95% respectively). However, the additive value of BAL is not apparent in these yields since BAL alone was positive in four of the nineteen patients who had both BAL and TBLB (*Table 2*). Thus, it is apparent that a patient can have a BAL specimen positive for PCP and a simultaneously negative TBLB specimen from the same bronchoscopy procedure. Thus, we recommend that both TBLB and BAL be done in all patients with AIDS in whom there are no contraindications, to assure maximum yield for PCP. Interestingly, BAL as a sole procedure was positive for PCP in only five of eight patients (63%). Other authors report a yield as high as 85% for PCP by BAL.[4] Although our number of false-negative BAL studies is too small to derive statistical inference, we can state some generalizations about BAL in AIDS. First, a negative BAL examination alone does not eliminate PCP as a possible infection. Second, a repeat BAL study, with a TBLB if possible, should be done in patients with a negative initial BAL examination if PCP is highly suspected. In all three of such patients in our series, repeat bronchoscopy revealed PCP (*Table 2*). Third, in one patient with a "negative" BAL result, airway collapse allowed the return of only 30 ml of the BAL volume. This volume is probably too small to insure adequate sampling of cells from peripheral spaces, and repeat BAL of 70 ml showed PCP. Thus, low-volume BAL should be considered a technically inadequate procedure.[4] We presently have altered our BAL procedure such that we

will continue to instill enough saline, up to a volume of 150 ml, to insure at least 60 ml return. Other authors report that CMV is a common infection found in 17% to 29% of AIDS patients and that CMV frequently accompanies PCP.[7,8] Since we only recently have been culturing specimens for CMV, we have data only on our most recent BAL examinations, showing two of seven (29%) positive for CMV. Thus, with continued culturing of BAL specimens it is possible that we will be able to document that CMV is a common copathogen with PCP in the initial phase of AIDS pulmonary disease.

Our experience with mycobacterial disease in AIDS differs from earlier reports, which indicate that MAI infection will be found in at least 17% of AIDS patients, and that bronchoscopy in this setting will yield MAI in 62 to 78% of patients who have this disease[3,7,8] We have culture data from 69 different bronchoscopy specimens in 42 AIDS patients. These bronchoscopy specimens showed MAI and *M tuberculosis* infection in only one patient each, and missed the diagnosis of MAI in at least three patients in whom we had other positive cultures of lung specimens. In addition, we confirmed our earlier observation that acid-fast smears and histologic studies of bronchoscopy specimens are poor indicators of the presence of mycobacterial infection in AIDS.[17] In this present series of patients, none of the 69 acid-fast smears were positive and none of the 27 TBLB specimens showed granulomas, including the specimens from the patients with confirmed mycobacterial infection. Thus we believe pulmonary mycobacterial infection is rarely a presenting infection in AIDS and bronchoscopy is unreliable to diagnose MAI when it is present. It is unclear if patients should be treated who have MAI found only in pulmonary secretions. Since therapy is frequently ineffective and usually requires multiple drugs, we recommend that organ sites other than lung be investigated to document MAI dissemination.[8,18,19]

Finally, we believe that the role of bronchoscopy in AIDS is not fully defined at this moment. As noted above, 10% of the 50 patients in this study who were thought to have AIDS did not have opportunistic pulmonary infections until an average of 4.5 months after their initial bronchoscopy. These patients possibly represent the pre-AIDS form of this disease.[15,16,20] It is presently estimated that at least 400,000 people in the USA have antibodies to the human T-cell lymphotropic virus (HTLV-III) that may be the cause of AIDS.[20–22] At least 25% of these HTLV-III antibody-positive patients will be sick with nonspecific, debilitating symptoms that hallmark pre-AIDS. How many patients from this group will eventually have full-blown AIDS is not known, but Quinn has estimated that there will be 40,000 new cases of AIDS in the next two years.[23] Since it is exceedingly difficult to determine the moment when a sick pre-AIDS patient has full-blown AIDS, it is likely that the number of bronchoscopic procedures done for HTLV-III-related disease will markedly increase in the next two years. We can expect a large increase in two categories of fiberoptic bronchoscopy: multiple nondiagnostic bronchoscopic procedures in the pre-AIDS period; and diagnostic, multiple follow-up bronchoscopic procedures in the AIDS phase. It is not unreasonable to expect that an individual high-risk AIDS patient might have four or more bronchoscopic examinations in the course of illness. Thus, it is difficult to estimate how much this large increase in the number of pre-AIDS and AIDS patients will change our understanding of the expected diagnostic yield as well as the indications and timing of bronchoscopy in AIDS.

In summary, we evaluated the diagnostic utility of fiberoptic bronchoscopy in 50 patients thought to have AIDS. Five patients had pre-AIDS, and the results of bronchoscopy in the 45 AIDS patients indicated that this procedure is safe and effective in this patient population. In 87% of our AIDS patients, bronchoscopy resulted in a diagnosis, usually PCP. We found that both TBLB and TBLB with BAL have high yields for PCP but that BAL alone was more likely to have false-negative results. We did not document a high incidence of MAI infection by initial bronchoscopy and we found a tendency for bronchoscopy specimens to be falsely negative for MAI when other lung specimens had positive cultures. Finally, we recommend fiberoptic bronchoscopy with TBLB and BAL be done as the initial invasive diagnostic test in the AIDS patient, and if the clinical suspicion of PCP is high, we suggest that repeat bronchoscopy be done if the initial procedure is nondiagnostic.

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