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Fiberoptic Bronchoscopy in Diagnosis of Opportunistic Lung Infections

Assessment of Sputa, Washings, Brushings and Biopsy Specimens

SAWTANTRA K. CHOPRA, MD, and ZAB MOHSENFAR, MD, Los Angeles

*Fiberoptic bronchoscopy (washings, brushings and biopsies) was done in 25 cases of proven opportunistic pulmonary infections in compromised hosts. Diagnostic yields of bronchoscopic procedures and expectorated sputum were compared. Sputum examination gave the lowest yield (14 percent). Bronchial washings and brushings were diagnostic in 30 percent and 38 percent of patients, respectively. On transbronchial biopsy of the lung (TBB) pathogens were identified in 75 percent of patients with *Pneumocystis carinii* infection and 67 percent of patients with other opportunistic infections. The overall TBB yield of 73 percent was superior ($P < 0.05$) to that of either washings or brushings. The yield from combining washings and brushings was greater than from either procedure alone, but combination with TBB did not result in any significant improvement. TBB is recommended as a useful diagnostic procedure in patients with suspected opportunistic pulmonary infections. Morbidity was minimal with this procedure, and the need for thoracotomy was reduced when it was used.*

FIBEROPTIC BRONCHOSCOPY (FOB) with brushing and biopsy technique has been used for more than ten years principally for evaluating potentially neoplastic pulmonary lesions.¹⁻³ Little is known about the diagnostic usefulness of FOB for identifying opportunistic pulmonary pathogens in compromised hosts.^{4,5} This report analyzes the usefulness of endobronchial brushings, washings and biopsies in evaluating this type of disease.

Patients and Methods

Case records of all immunocompromised patients who had FOB at the Center for the Health

Sciences at the University of California, Los Angeles, from July 1975 through February 1978 were studied. A diagnosis of pulmonary disease due to opportunistic pathogens was confirmed in 25 cases by cultures of either lung aspirates and material obtained by needle aspiration, or open lung biopsy or autopsy; or both.

Before bronchoscopy, two or three specimens of sputa were obtained. The presence of polymorphonuclear leukocytes and histiocytes in a specimen indicated that it was sputum and not saliva.

Fiberoptic bronchoscopy was done using local cocaine (3 percent) for anesthesia. Details of our technique of examination have been described elsewhere.^{1,6} Transbronchial biopsy was not done in patients in whom significant endobronchial

From the Division of Pulmonary Disease, Department of Medicine, UCLA School of Medicine (University of California, Los Angeles).

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Reprint requests to: Sawtantra K. Chopra, MD, Division of Pulmonary Disease, Department of Medicine, UCLA School of Medicine, Los Angeles, CA 90024.

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bleeding occurred after brushings, or in those with bleeding diathesis.

All diagnoses of *Pneumocystis carinii* pneumonia were made by examining material from bronchial secretions, from lung biopsy specimens or from autopsy specimens stained with Gomori silver methenamine nitrate. A diagnosis of cytomegalic viral infection was based on culture of lung tissue obtained by biopsy or at autopsy. A diagnosis of fungal infection was based on culture of organisms obtained by transtracheal aspiration, FOB, biopsy of the lung or autopsy. *Mycobacterium intracellulare* infection was diagnosed by growth of the organism from bronchial washings and brushings on Löwenstein-Jensen (plain or modified) medium.

Statistical analysis was done by the chi square method using the Yates correction factor ($P \leq 0.05$).

TABLE 1.—Types and Incidence of Infections

Infection	Number of Cases
<i>Pneumocystis carinii</i>	10
<i>Nocardia asteroides</i>	2
Cytomegalovirus	3
<i>Aspergillus fumigatus</i>	4
<i>Cryptococcus neoformans</i>	2
<i>Rhizopus oryzae</i>	1
Blastomycosis dermatitidis	1
<i>Mycobacterium intracellulare</i> ...	1
<i>Propionibacterium acne</i>	1
Total	25

Results

Table 1 lists the pathogens isolated from these patients. Table 2 lists the clinical diagnoses, radiographic findings and diagnostic yields of FOB of ten patients with proven *Pneumocystis carinii* infection of the lungs. All were immunocompromised following chemotherapy for leukemia or Hodgkin disease, or steroid treatment for aplastic anemia, vasculitis or bone marrow transplantation. They presented with either diffuse (n=8) or localized (n=2) infiltrates on radiographic examination of the chest. Prebronchoscopy sputa were not useful. The yield of bronchial washings was 12 percent, brushings yielded 60 percent and transbronchial biopsy of the lung (TBB) yielded 75 percent.

Table 3 lists clinical presentations, radiographic findings and diagnostic yields from FOB of 15 patients with other opportunistic lung infections. The radiographic presentation again varied from localized to diffuse pulmonary involvement. Sputa obtained before bronchoscopy were diagnostic in 20 percent (*Nocardia asteroides* in two patients and *Cryptococcus neoformans* in one patient), bronchial washings in 6 of 15 (40 percent), brushings in 3 of 14 (21 percent) and TBB in 2 of 3 (67 percent) patients.

Table 4 lists the diagnostic yield from various types of specimens alone and in combination from all 25 patients with proven opportunistic pulmonary infections. The yield from sputa was

TABLE 2.—*Pneumocystis carinii* Infection: Diagnoses and Role of Fiberoptic Bronchoscopy in Diagnosis

No.	Age	Sex	Clinical Diagnosis	Findings on X-ray Studies of Chest	Bronchoscopic Modalities				Other Diagnostic Techniques
					Sputa	Washings	Brushings	Trans-bronchial Biopsy	
1	32	M	Stem cell leukemia on ct	Diffuse infiltrates	-	-	-	-	Open lung biopsy (+)
2	19	M	ALL on ct	Diffuse infiltrates	-	N.D.	+	+
3	43	M	Hodgkin disease on ct	Bilat. perihilar infiltrates	-	-	-	+	Autopsy (+)
4	46	M	Ankylosing Spondylitis on ct	Bilat. interstitial reticular nodular infiltrates	-	-	+	N.D.
5	35	F	Hodgkin disease on ct	Consolidation right lung	-	-	+	+	Needle aspirate(+)
6	26	F	ALL on ct	Bilat. nodular infiltrates	-	-	-	-	Open lung biopsy (+)
7	34	F	Aplastic anemia on steroids	Bilat. diffuse reticular infiltrates	-	-	+	+
8	78	M	Vasculitis on steroids	Right upper lobe consolidation	N.D.	-	+	N.D.
9	30	F	S/P bone marrow transplant	Diffuse infiltrates	N.D.	+	+	+
10	17	M	ALL on ct	Diffuse infiltrates	N.D.	N.D.	-	+
					0/7 =0%	1/8 =12%	6/10 =60%	6/8 =75%	

+ = Diagnostic of *Pneumocystis carinii*
- = nondiagnostic

ALL = acute lymphocytic leukemia
ct = chemotherapy

N.D. = not done
S/P = status post

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not greatly different from that of washings or brushings ($P > 0.05$). However, the yield from a combination of washings and brushings was better ($P < 0.05$) than the from sputa. The yield from TBB was much greater ($P < 0.05$) than that from sputa, washings or brushings. The yield from combining washings or brushings with TBB was not notably greater than that from TBB alone. The yield from FOB was 57 percent in patients in whom TBB was *not* done, and 73 percent in patients in whom TBB was done.

Discussion

Pulmonary infection in immunocompromised patients is a difficult problem. To plan an appropriate antimicrobial regimen the etiological agent usually must be isolated as soon as possible. Many techniques have been used to diagnose pulmonary infiltrates in immunocompromised hosts, includ-

ing percutaneous biopsy of the lung, transtracheal aspiration and fiberoptic bronchoscopic techniques.^{4,7-9} However, to our knowledge no study comparing examinations of pulmonary secretions and lung biopsy specimens obtained during FOB for identifying opportunistic pulmonary secretions has been reported previously. We, therefore, analyzed the usefulness of sputa examination, bronchial washings, brushings and biopsies for diagnosis in this situation.

The pulmonary infections in our patients were similar to those reported in a comparable population surveyed at the National Institutes of Health,¹⁰ where the most common cause of diffuse pulmonary infiltrates was *Pneumocystis carinii*. In one patient with lymphoma and hypogammaglobulinemia, *Propionibacterium acne* infection developed, causing necrotizing pneumonia with multiple pulmonary microabscesses. TBB

TABLE 3.—Other Opportunistic Infections: Clinical Diagnoses and Role of Fiberoptic Bronchoscopy In Diagnosis

No.	Age	Sex	Clinical Diagnosis	Findings on X-ray Studies of Chest	Sputa	Bronchoscopic Modalities				Final Pulmonary Diagnosis
						Washings	Brushings	Trans-bronchial Biopsy	Other Diagnostic Techniques	
11	36	M	Chronic renal failure Consolidation	Rt. lower lobe	+	-	-	N.D.	Needle aspiration	Nocardiosis
12	42	F	Chronic renal failure	Lt. lower lobe consolidation	-	-	-	+	Phycomycosis
13	41	F	S/P mastectomy on ct and steroids	Unilateral infiltrates	+	+	-	N.D.	Nocardiosis
14	24	M	AML on ct	Bilat. basal infiltrates	-	-	-	N.D.	Open lung biopsy	Cytomegalovirus (CMV) infection
15	19	M	AML on ct	Bilat. diffuse infiltrates	-	+	+	N.D.	Autopsy	CMV infection
16	25	M	AML on ct	Bilat. diffuse infiltrates	-	-	-	N.D.	Open lung biopsy	CMV infection
17	39	M	Chronic alcoholism	Perihilar infiltrates	-	-	-	+	Cryptococcosis
18	37	M	Aplastic anemia	Unilateral infiltrates	-	-	-	N.D.	Open lung biopsy	Invasive aspergillosis and mycetoma
19	30	M	Pneumonia	Unilateral infiltrates	-	+	N.D.	N.D.	Aspergillosis
20	50	M	Lung tumor	Lingular infiltrates	+	+	+	N.D.	Cryptococcosis
21	72	F	Chronic granulomatous lung disease	Bilat. diffuse infiltrates	-	+	+	N.D.	Mycobacterium intracellulare infection
22	36	M	Aplastic anemia	Perihilar infiltrates	-	+	-	N.D.	North American blastomycosis
23	34	M	S/P bone marrow transplant	Perihilar infiltrates	-	-	-	N.D.	Autopsy	Disseminated aspergillosis
24	65	M	Lymphocytic lymphoma	Bilat. basilar infiltrates	-	-	-	-	Open lung biopsy	Propionibacterium acne
25	39	M	AML on ct	Bilat. diffuse infiltrates	-	-	-	N.D.	Autopsy	Diffuse aspergillosis

3/15 = 20% 6/15 = 40% 3/14 = 21% 2/3 = 67%

+ = Diagnostic
- = nondiagnostic

AML = acute myelocytic leukemia
ct = chemotherapy

N.D. = not done
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was not diagnostic in this case and the diagnosis was made by open lung biopsy. Organisms were seen on Gram stain and anaerobic culture yielded pure isolates of *Propionibacterium acne*. This pathogen had not been isolated in previous studies^{4,5} and incidence of this infection in lungs of immunocompromised patients is not known. Cases in which *Candida albicans* was grown on culture of material obtained during FOB were excluded from analyses of the data. This was done because previous studies reported the isolation of *Candida* organisms from 20 percent of lung tissue specimens obtained at biopsy or surgical operation in patients with chronic lung disease that was not due to *Candida* organisms.¹¹ Also, *Candida* organisms have been grown on culture of lung tissue specimens obtained at autopsy in cases without antecedent clinical disease or histologic evidence of tissue invasion.¹² Reliable information about possible *Candida* infection of the lung, therefore, cannot be obtained by FOB.

It has been reported that expectorated sputum yields *Pneumocystis carinii* organisms occasionally in cases of interstitial pneumonitis.¹³ In our study sputum examination was not useful. However, *Nocardia asteroides* were isolated from sputum in two cases and *Cryptococcus neoformans* were found in one case. These organisms were also isolated from secretions obtained at FOB. The overall diagnostic yield of sputum examination was low (14 percent) and not cost-effective.

Most authors favor the use of open lung biopsy to diagnose *Pneumocystis carinii* infection. With this procedure sufficient material can usually be obtained to assess the relative contributions of two or more concomitant disease processes. However, the yield is nearly as high with TBB, a much less invasive procedure, which established the diagnosis of *Pneumocystis carinii* infection in six of eight patients (75 percent) in our series. Others have found similar results with TBB in immunocompromised hosts.¹⁴⁻¹⁶ Among all infections, the yield from TBB alone was 73 percent and with TBB along with brushings or washings, the yield was 65 percent to 75 percent. However, TBB was done in only three of 15 patients with infections from organisms other than *Pneumocystis carinii*. More data are needed to confirm the value of this procedure in diagnosing these infections. When TBB was not done the yield of FOB was 57 percent (Table 4). Therefore, TBB is the most important single bronchoscopic procedure for diagnosing these infections. However,

TABLE 4.—Diagnostic Yield of Sputum Examination and Fiberoptic Bronchoscopy in 25 Patients

Specimen	Number of Cases	Diagnosis Established	Percent Yield
Sputum	22	3	14
Washings	23	7	30
Brushings	24	9	38
Biopsy	11	8	73
Washing and brushings	22	10	45
Brushings and biopsy	11	8	73
Washings and biopsy	9	6	67
Washings and brushings and biopsy	9	6	67
Washings or brushings or biopsy	25	16	64

a possibility of associated second or third infections in these persons should be kept in mind and these may be missed in the tissue specimens obtained by TBB. Compared with brushings or washings, there were no false negative findings from TBB.

Major complications of TBB occurred only rarely in this group of patients. Significant endobronchial blood loss occurred in one. Pneumothorax requiring chest tube placement did not occur in this series. We conclude that FOB combined with TBB is a useful diagnostic procedure for determining the cause of opportunistic pulmonary infections in immunocompromised hosts, and that the need for thoracotomy is diminished when this procedure is available.

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