Utility of Fiberoptic Bronchoscopy in Nonresolving Pneumonia*

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Although fiberoptic bronchoscopy (FOB) has been traditionally used to evaluate nonresolving pneumonia, its efficacy is unknown. We, therefore, reviewed FOB in 35 consecutive patients who had (1) a roentgenographic infiltrate, (2) cough, (3) either temperature >38.1°C, leukocytosis, or sputum production, (4) symptoms present for at least ten days, and antibiotic therapy for at least one week. Known lung cancer and AIDS were excluded. Fiberoptic bronchoscopy was diagnostic in 86 percent (12/14) in whom a specific cause was found. No patient had endobronchial cancer. Two patients with nondiagnostic FOB and persistent systemic symptoms had open lung biopsy specimens showing Wegener's granulomatosis and bronchiolitis obliterans with organizing pneumonia (BOOP). Twenty-one patients with nondiagnostic FOB had no final diagnoses other than community-acquired pneumonia. We conclude that FOB is extremely useful in finding a specific diagnosis for a nonresolving pneumonia when a specific diagnosis can be made. Fiberoptic bronchoscopy was most likely to yield a specific diagnosis in nonsmoking patients with multilobar infiltrates of long duration and could have been avoided in older, smoking, or otherwise compromised patients with lobar or segmental infiltrates with no decrease in diagnostic yield in our series. *(Chest 1990; 98:1322-26)*

BOOP = bronchiolitis obliterans with organizing pneumonia; TBB = transbronchial biopsy

Nonresolving pneumonia is a commonly encountered problem and a common cause for pulmonary consultation and bronchoscopic evaluation. We have previously defined this syndrome as roentgenographic pulmonary infiltrate that begins in association with fever, sputum production, malaise, chest pain, or shortness of breath and does not resolve within an anticipated period of time based on the presumptive diagnosis.[1] Since the original characterization by Amberson[2] of "unresolved, organizing or protracted pneumonia" in 1943, other investigators have examined the problem.[3,4] They reported the frequent association of host defense impairments: either systemic (diabetes mellitus, heart failure, and old age) or local (endobronchial tumor) with impaired resolution of pneumonia. Endobronchial carcinoma was a surprisingly infrequent cause for nonresolving pneumonia, being found in from 0 to 8 percent of patients.

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Despite the ease and relative safety of fiberoptic bronchoscopy, its use in some clinical situations has recently come into question.[5,6] This procedure is frequently used to evaluate nonresolving pneumonia. However, there is surprisingly little support in the literature for this practice, nor are there guidelines to suggest the circumstances under which this procedure is likely to provide useful diagnostic information.[7,8] The purpose of this study was to evaluate the utility of fiberoptic bronchoscopy in the diagnosis of nonresolving pneumonia in patients in whom this was the only indication for this procedure.

Methods

The records of 35 consecutive patients who underwent fiberoptic bronchoscopy by the pulmonary service of Winthrop-University Hospital during a two-year period (1987 through 1988) were retrospectively examined. In each case, the patient's attending physician had requested pulmonary consultation for failure of a pneumonia to improve after what was considered adequate antibiotic therapy, and the pulmonary consultant agreed that improvement had not occurred in the expected time. The sole indication for the procedure was nonresolving pneumonia.

This group was drawn from a total of 437 patients who had fiberoptic bronchoscopy during this time period. Patients were excluded if they did not have a nonresolving roentgenographic infiltrate, cough, and either fever (>37.7°C), leukocytosis (greater than 10,000 cells/ml), or sputum production. Symptoms had to be present for at least ten days and antibiotic therapy given for at least one week. In all patients, infectious community-acquired pneumonia had been considered the leading diagnostic possibility at the time of initiation of antibiotic therapy by the referring attending physician. We excluded patients who at presentation had known lung

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Table 1—*Patient Characteristics (n = 35)*

Characteristic	
Age, yr	61 ± 15 (range, 44-90)
Sex	23 M, 12 F
Smokers	22
COPD	11
Immunocompromised	5
Symptom duration, days	30 ± 39 (range, 10-150)

cancer, acquired immunodeficiency syndrome (AIDS), or risk factors for AIDS (homosexuality, intravenous drug abuse).

Patient characteristics are summarized in Table 1. Patients were considered smokers if they had used at least one pack of cigarettes per day and ten pack years during their lifetime and had been smoking within the previous two years. Chronic obstructive pulmonary disease (COPD) was diagnosed on clinical grounds, including chronic cough with sputum production, obstructive changes on spirometry, or roentgenographic changes consistent with emphysema. Of the 35 patients, 11 had COPD, 19 were previously healthy (nine smokers, ten nonsmokers), and five were considered immunocompromised. In the immunocompromised group were one patient each with systemic lupus erythematosus, diabetes mellitus requiring insulin, myelodysplasia, chronic renal failure requiring dialysis, and chronic alcoholism. The ages ranged from 44 to 90 years (mean, 61 ± 15 years). Men predominated in the group (23 male and 12 female). Symptom duration ranged from ten to 150 days (mean, 30 ± 39 days).

Records were reviewed to determine what the leading prebronchoscopy diagnoses were in each case. Presumptive diagnoses prior to antibiotic treatment included pneumococcal pneumonia in 13 patients, atypical pneumonia in ten patients, Gram-negative infection in four patients, anaerobic pneumonia in four patients, and viral pneumonia in four patients. No patient had diagnostic sputum cytologic study or culture prior to bronchoscopy. Bronchoscopy was performed because of the failure of the pneumonia to resolve, both roentgenographically and clinically.

Each chest roentgenogram was reviewed by a single radiologist without knowledge of the diagnosis and infiltrates were classified as segmental, lobar, or multilobar. All patients underwent fiberoptic bronchoscopy by one of the investigators and findings were tabulated. Cytologic evaluation and culture for mycobacteria were done in all cases. Either direct vision biopsy or transbronchial biopsy and stains for fungi, parasites, and viral cultures were done at the bronchoscopist's discretion when clinically indicated. Six patients underwent transbronchial lung biopsy at the time of bronchoscopy. Patients were followed up for at least six months (mean, 10 ± 6 months) and examined for clinical and radiologic resolution as well as development of additional chest abnormalities.

Results

Chest roentgenograms taken just prior to bronchoscopy were independently reviewed without knowledge of the final diagnosis. Of the 35 patients who presented with presumed infectious pneumonia that did not resolve, the infiltrate was multilobar in 14 patients (40 percent), lobar in 11 patients (31 percent), and segmental in ten patients (29 percent).

Fourteen patients had a specific diagnosis made that would account for a prolonged course (Table 2). In these cases, fiberoptic bronchoscopy was diagnostic in 12 (86 percent) of 14 patients. Diagnoses made at bronchoscopy were most commonly infectious (7/12). Cytologic evaluation alone was diagnostic in the case of cytomegalovirus pneumonia (one case) and *Pneumocystis carinii* pneumonia (three cases). In two cases, the diagnosis of tuberculosis was made by culture of lavage fluid. Culture also provided the diagnosis of actinomycosis. Carcinoma was found in four patients; (alveolar cell in two patients and adenocarcinoma in two patients); all were diagnosed cytologically and one also had a diagnostic transbronchial biopsy. In no case was an endobronchial lesion found causing obstructive pneumonia. Eosinophilic pneumonia was diagnosed in one patient by transbronchial biopsy specimen. In this patient, the diagnosis was supported by the high peripheral eosinophil count (35 to 43 percent) as well as a dramatic clinical response to corticosteroid therapy within seven days.

Two patients remained persistently ill, with fever, malaise, anorexia, arthralgias, and mildly abnormal results of liver function tests. Progression of radiologic infiltrates beyond two weeks led to open lung biopsy. Pathologic examination revealed typical Wegener's granulomatosis in one patient and bronchiolitis obliterans with organizing pneumonia (BOOP) in another.

Transbronchial biopsy (TBB) was done in six patients and was diagnostic in four patients: two with bronchoalveolar carcinoma, one with adenocarcinoma, and one with eosinophilic pneumonia. The two patients in whom this was not definitively diagnostic were the patients who proceeded to open lung biopsy. The three patients with TBB showing cancer also had positive bronchoscopic cytologic findings. Thus, TBB provided additional useful information in only one patient.

Overall, fiberoptic bronchoscopy was highy sensitive for patients in whom a specific diagnosis could be made. Twelve of 14 patients in whom a specific cause other than community-acquired pneumonia was made had this diagnosis established by fiberoptic bronchoscopy.

Twenty-one patients had no specific diagnosis other than infectious pneumonia. None of these was blood culture positive and in all the presumptive cause was

Table 2—*Specific Diagnoses Established*

Diagnosis	No.	Established by*
Pneumocystis	3	BAL cytology
Tuberculosis	2	BAL cytology
Bronchoalvolear carcinoma	2	BAL cytology
Adenocarcinoma	2	Transbronchial bx and BAL cytology
Cytomegalovirus	1	BAL cytology
Actinomycosis	1	BAL culture
Eosinophilic pneumonia	1	Transbronchial bx
Wegener's granulomatosis	1	Open lung bx
Bronchiolitis obliterans organizing pneumonia	1	Open lung bx

*BAL = bronchoalveolar lavage; bx = biopsy.

either pneumococcus, *Hemophilus influenza, Legionella,* or *Mycoplasma pneumoniae*. Eighteen of 21 patients were followed up for at least six months (mean, 10±6 months). All patients had completely cleared roentgenographic infiltrates and demonstrated clinical improvement in their initial symptoms over this period of time. No patient in this group had a malignant disease develop over the period of observation. Three patients were followed up for less than six months. One was unavailable for follow-up, one died at two months after bronchoscopy from sudden cardiac death, the other died at three months from the complications of uremia. In the two latter patients, no evidence of other causes for their persistent pneumonia was found.

To establish when fiberoptic bronchoscopy might be most useful in the diagnosis of nonresolving pneumonia, we compared the 12 patients in whom bronchoscopy led to a specific diagnosis with the 23 in whom it did not (Table 3). We found that when these two groups were compared, the presence of a multilobar infiltrate on chest roentgenogram ($p<.005$) and age younger than 55 years ($p<.01$) were strongly associated with a specific diagnosis at fiberoptic bronchoscopy. Other predictors of a diagnostic bronchoscopy were longer symptom duration (43±14 days compared with 24±2 days, $p=.05$) and a normal, nonsmoking patient ($p=.01$). Smoking history in pack years, the patient's sex, the presence of COPD or compromised host defenses, duration of antibiotic therapy, and maximum temperature did not influence the likelihood of positive bronchoscopic yield.

Bronchoscopy was less useful in patients older than age 55 years; with a history of smoking, COPD, or immunocompromised state; or roentgenogram showing lobar or segmental infiltrate. We reviewed our series to determine whether bronchoscopy could have been avoided in any subset of these patients. Table 4 shows the yield of bronchoscopy in patients with zero, one, or more of these factors. There was a decreased yield in patients with one or more factor, with only one patient with a positive bronchoscopy result who had all three factors. In this patient, the diagnosis of tuberculosis was made at bronchoscopy, but it could have been made at a slightly later time by sputum culture if bronchoscopy had not been performed.

Table 3—*Features of Patients with Diagnostic Bronchoscopy*

	Diagnostic (n=12)	Nondiagnostic (n=23)	p
Multilobar infiltrate	9	6	.004*
Age <55 yr	7	3	.007*
Normal host (nonsmoker)	8	4	.01*
Symptom duration, days	43±43	24±19	.05†
Maximum temperature, °C	38.8±0.8	39±0.9	NS†
Antibiotic duration, days	13±4	13±5	NS†
Sex, M/F	6/6	15/8	NS*

*By χ^2 analysis. NS = not significant.
†By Student's *t* test.

Discussion

Nonresolving pneumonia is a common clinical problem.[1] We recenty examined our own experience and found that approximately 15 percent of consultations and 8 percent of bronchoscopies over a one-year period were done specifically to evaluate conditions in patients who presented with a roentgenographic infiltrate and symptoms and signs suggesting an acute lower respiratory tract infection but in whom radiologic resolution was beyond what would usually be expected for the common community-acquired pneumonias. Several studies in the past reported that failure to resolve a community-acquired pneumonia occurs in from 13 to 26 percent of patients.[3,4] In these studies, increasing age, systemic host defense impairments like diabetes and alcoholism, and specific reductions in pulmonary clearance as in COPD accounted for the majority of prolonged pneumonias. In most instances, pneumonia had resolved by eight weeks and malignancy as a cause for nonresolution was seen in a total of only four (1.2 percent) of 337 patients. While unusual infections,[9-11] immunologic disorders,[12,13] metastatic or primary neoplasms,[14,15] and thromboembolism[16] may lead to a prolonged course, these are, in general, uncommon. In fact, most pneumonias will resolve over two to three months.[17,18]

With the development of fiberoptic bronchoscopy in the 1970s, this technique has become a commonly employed tool in the evaluation of nonresolving pneumonia. Despite the frequency of its use, there are few data that address the indications for the procedure or the expected yield. Jay et al[17] examined a group of patients with bacteremic pneumococcal pneumonia. In this group, 37 percent had residual consolidation at one month. In those older than age 50 years with both COPD and alcoholism, 60 percent had abnormal chest

Table 4—*Diagnostic Yield for Bronchoscopy in Patients with Negative Predictive Factors**

No. of Factors	Positive	Negative	Yield (%)
0	4	0	100
1	2	6	25
2	5	7	42
Total <3	11	13	46
3	1	10	9

*Factors predictive of negative results of bronchoscopy: age older than 55 years; history of smoking, COPD, or immune defect; and lobar or segmental infiltrate.

roentgenograms at 14 weeks. They, therefore, recommended that in pneumococcal pneumonia, bronchoscopy be delayed for at least eight weeks pending resolution.

To evaluate the role of fiberoptic bronchoscopy in the diagnosis of nonresolving pneumonia, we reviewed our experience with this problem over a one-year period. Our 35 patients represented a heterogeneous group and were not evaluated and treated in a uniform fashion. However, all patients met our criteria for nonresolution and underwent bronchoscopy for that purpose alone. Bronchoscopy was performed only when it was clear that resolution was delayed beyond the expected time and thus the mean duration of abnormality was 30 days prior to bronchoscopy. This was not a prospective trial, and no attempt was made for all patients with delayed resolution of pneumonia to undergo bronchoscopy, and our data suggest that only certain patients with nonresolving pneumonia need bronchoscopy. Nevertheless, bronchoscopy proved to be an extremely useful tool for determining a specific cause for nonresolution of pneumonia. Of the 14 patients in whom a diagnosis other than community-acquired pneumonia was established, 12 diagnoses were made using fiberoptic bronchoscopy. Infection by nonbacterial organisms accounted for most of these diagnoses, and included patients with tuberculosis, actinomycosis, and cytomegalovirus (CMV). *Pneumocystis carinii* pneumonia was found in three patients in whom there were no known risk factors for AIDS at the time of presentation. All had multilobar infiltrates and were subsequently found to have positive serologic findings for the human immunodeficiency virus. This diagnosis must be considered in all patients, regardless of history for risk factors, presenting with a nonresolving multilobar infiltrate.

Malignancy was found as a specific cause for nonresolution in four of 35 patients. However, none of our patients had evidence of an endobronchial carcinoma. This is consistent with previous studies that have found malignancy to be unusual as a cause for nonresolution of acute pulmonary infection.[3,4,17]

Only two of 23 patients with nondiagnostic bronchoscopy results subsequently had a specific diagnosis other than community-acquired pneumonia established. These two, who had open lung biopsy, differed from the others with normal findings from bronchoscopic examinations in that they had persistent systemic illness, including temperature greater than 38.3°C, arthralgias, persisting abnormalities of liver function (elevated transaminase values), and no resolution of their infiltrates two weeks after the bronchoscopic examination. The diagnoses made, Wegener's granulomatosis and BOOP, require larger volumes of tissue than can generally be obtained by transbronchial biopsy.

Twenty-one of 23 patients with nondiagnostic bronchoscopic findings had no specific diagnosis ever made. This suggests there is a high negative predictive value of a nondiagnostic bronchoscopy in this patient group. These patients were believed to have delayed resolution of ordinary pneumonia. Interestingly, of this group, only two were immunocompromised, four had COPD, and four were current smokers, factors that might have contributed to delayed resolution.

The value of TBB in our experience was very limited. Six of 35 patients had this procedure performed. While it was diagnostic in four patients, in only one patient was this additional information useful. In the two patients who had an additional diagnosis made after bronchoscopy, TBB had been negative. Thus TBB, if more widely applied to this group, would not have been of value.

We found that a specific bronchoscopic diagnosis was significantly more likely in patients younger than 55 years of age, in those with multilobar infiltrates, and in normal nonsmokers. These data support previous studies that suggest that prolonged course of a community-acquired pneumonia is more likely in the elderly patient with compromised host defenses.[19,20] In our patients, other diagnoses were more likely to be present in those who did not have systemic or local reasons for failure to resolve. We found symptoms to have been present nearly twice as long in those with positive results of bronchoscopic examinations as those with nondiagnostic bronchoscopic findings. Thus, the longer a bronchoscopy is delayed after an acute infection, the more likely it is that an unnecessary procedure can be avoided.

Our study also suggests that a significant number of procedures can easily be avoided without significantly reducing diagnostic yield. In our study, if no patient older than age 55 years, with a history of smoking, COPD, or immunocompromised state, and with a segmental or lobar infiltrate had undergone bronchoscopy, we could have avoided 11 procedures (31 percent of the total) with no significant reduction in diagnostic yield. This would have caused a substantial decrease in costs and patient discomfort.

Summary and Recommendations

We found fiberoptic bronchoscopy to be useful in establishing a cause for failure of resolution of what appeared on presentation to be a community-acquired pneumonia. The yield is especially high in younger, nonsmoking patients who present with multilobar findings on roentgenogram and who have symptoms prior to bronchoscopy for at least four to six weeks. We recommend that patients who present with pneumonia that fails to resolve in the expected time be examined for host defense impairments. When these are present, the infection may be expected to take

longer than usual to clear. Particularly common associations are COPD, advanced age, alcoholism, and diabetes. When infection is not resolving appropriately and host defenses are presumed to be normal, an unusual infection, immunologic disease, or malignant neoplasm is to be suspected. Our data suggest that negative results of a bronchoscopic examination are very useful in this setting. Patients with negative results of bronchoscopy who are not clinically ill should be observed without further procedures; those with persistent clinical findings should have open lung biopsy.

We suggest that patients with ages older than 55 years, history of smoking, COPD, or immune defect, and lobar or segmental infiltrates should be observed without bronchoscopy, as the yield of bronchoscopy in this group appears minimal. This represented a fairly large subset of our procedures, and eliminating this group might yield significant savings in cost and morbidity.

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