Transbronchial Forceps Lung Biopsy through the Fiberoptic Bronchoscope
Diagnosis of Diffuse Pulmonary Disease

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Transbronchial forceps biopsy through the fiberoptic bronchoscope was performed in 37 patients. Tissue was technically inadequate for examination in two cases. A pathologic diagnosis was obtained in 26 (72 percent) and in five additional critically ill patients, direct histologic examination of lung tissue allowed exclusion of certain entities, thus significantly influencing therapy. Overall, the procedure was of value in 31 of 35 patients (90 percent). There was no significant hemorrhage and there was one 15 percent pneumothorax. The safety and high diagnostic yield of this technique in the diagnosis of diffuse lung disease is proved.

The diagnosis of diffuse lung disease, particularly in the acutely ill or debilitated patient, remains a major challenge. To obtain lung tissue, which is frequently required for definitive diagnosis, thoracotomy or one of various closed-blind techniques are used. Needle aspiration, cutting needle biopsies, trephine and punch biopsy methods, plus transbronchial lung biopsy through the rigid bronchoscope have all been employed. Recently, we reported the adaptation of the transbronchial biopsy technique of Andersen and Fontana1 for use with the fiberoptic bronchoscope in the diagnosis of Pneumocystis carinii pneumonia.2 The present study reports further use of this method in both acute and chronic diffuse lung disease in consecutive cases over an eight month period.

Material and Methods

Fourteen outpatients and 23 inpatients were studied. Patients were selected on the basis of a chest roentgenogram compatible with diffuse lung disease without prior tissue diagnosis. Patients with suspected sarcoidosis, with bilateral hilar adenopathy, were subjected to biopsy without visible parenchymal involvement on chest x-ray examination. Patients with congestive heart failure or valvular heart disease, whose interstitial pulmonary changes responded to diuretic therapy, were excluded. Laboratory tests prior to performance of the procedure were dictated by the clinical setting. These often included platelet counts, prothrombin times and arterial blood gases as well as spirometry, lung volumes and diffusion studies in those patients who were able to perform these tests.

Transnasal fiberoptic bronchoscopy with the Olympus BF 5B2 bronchofiberscope was performed once in each patient but was repeated if adequate tissue was not obtained. One percent topical lidocaine provided adequate anesthesia, without premedication in most cases, and fluoroscopy was not employed. Transbronchial forceps lung biopsy was obtained using the biopsy forceps supplied with the bronchoscope with the technique described by us previously.* Four to five specimens (each approximately 1.5 by 2.0 mm, Fig 1) were obtained from the lower lobe segments on the side of greatest involvement, if any, or from the right lower lobe if disease was distributed equally by roentgenogram. In this procedure, the upper lobes may also be biopsied, but middle lobe and lingula are avoided because, without parietal pleural pain as a warning, the major fissure may be trans-

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FIGURE 1A. Transbronchial lung biopsy (hematoxylin and eosin stain; × 56), representative in its size. The presence of non-caseating granulomata and intervening normal lung, with special stains and cultures negative, established the diagnosis of sarcoidosis in a patient with bilateral hilar adenopathy.
versed, with resultant pneumothorax. Specimens were then placed in saline solution for immediate frozen section and selective staining was done if an acute infectious process was suspected. Specimens were placed in 10 percent formaldehyde solution for routine histology, in saline solution for culture for tubercle bacilli and fungi, in 2 percent glutaraldehyde or Zamboni's fixative for electron microscopy, and in liquid nitrogen for subsequent immunofluorescent staining for globulins and complement.

Outpatients were told to call us immediately if pleuritic pain, shortness of breath, or significant amounts of hemoptysis occurred later. Patients received a chest x-ray examination immediately after the procedure and again 24 hours later. All histology was reviewed by the authors, the Pathology Department of Walter Reed Army Medical Center, and in some cases, the Lung Branch of the Armed Forces Institute of Pathology.

RESULTS

In this series of 37 cases of diffuse lung disease, a pathologic diagnosis compatible with the clinical course and roentgenographic appearance was achieved in 26 cases (72 percent) with transbronchial biopsy. The results are summarized in Table 1. Alveolar tissue adequate for histopathologic diagnosis by usually accepted criteria was obtained in 31 cases. In two cases inadequate tissue was obtained, and in four cases results were nondiagnostic in spite of what was considered to be adequate tissue.

There were five suspected cases of *Pneumocystis carinii* pneumonia, with transbronchial biopsies showing nonspecific inflammatory changes and no organisms on silver staining. None of these was a "false negative" biopsy, as none of these patients subsequently was shown to have this infection by additional procedures or postmortem examination.

Pentamidine was not given to any patients with negative transbronchial biopsies. Two of these five cases were later judged to have cytomegalovirus infection by rise in titer of specific antibody, another to have diffuse pulmonary lymphosarcoma (dramatic response to bleomycin therapy) and one to have uremic lung (clearing with dialysis as the only treatment). The final patient recovered spontaneously. There was a single pneumothorax with no other complications.

**DISCUSSION**

Transbronchial lung biopsy through the fiberoptic bronchoscope has been shown to be an extremely safe and effective method for obtaining lung tissue for diagnostic purposes. The low incidence of complications is not surprising in light of the results of Andersen and colleagues; in over 550 cases, the incidence of pneumothorax was 11 percent and the incidence of significant bleeding less than 1 percent. The technique employed with the fiberoptic bronchoscope is very similar, and the biopsy forceps smaller.

Levin et al have reported no significant complications in 33 patients using a technique similar to ours. While fluoroscopic control, used by those authors, is obviously needed for biopsy of localized lesions, we have shown that it is not necessary in patients with diffuse disease. This makes the procedure more "portable" and valuable as a bedside diagnostic tool in an acutely ill patient. In spite of the fact that four to five separate samples were taken.
in each patient at fiberoptic bronchoscopy, in our series only one 15 percent pneumothorax occurred. It was managed by needle aspiration of air. This patient had been sedated with diazepam (Valium) and meperidine because of excessive anxiety, and the patient's inability to indicate pleural pain during the procedure was probably significant.

While blood streaking of the sputum occurred transiently in most cases, there was no significant hemorrhage. Two patients coughed up approximately 200 ml of blood immediately following the procedure, then produced only blood streaked sputum for a few hours. One patient receiving chemotherapy for acute leukemia with a pre-biopsy platelet count of 6000, was biopsied following six units of platelet infusion. There was slightly more bleeding in this case than with the "routine" biopsy. It is probably advisable to obtain a platelet count and pro-thrombin time in all patients before biopsy. The military setting of this study allowed close follow-up of outpatients who were biopsied. Reasonable caution should be exercised in selection of outpatients for study; if a patient is very debilitated or lives alone, it would be advisable to admit him overnight following the procedure.

The 72 percent diagnostic yield in this series is similar to that reported by Levin and colleagues in the 22 patients (from the total they had studied) who had diffuse lung disease. These authors, in addition, noted a high correlation (73 percent) between results of transbronchial lung biopsy and open lung biopsy in 15 cases subjected to thoracotomy, thus helping to establish the validity of pathologic diagnosis made with the small pieces of tissue obtained by means of this procedure.

In the eight-month period of our own study, it was only necessary to resort to open lung biopsy in one case to establish the correct diagnosis. The indication for proceeding with thoracotomy was simply that the negative transbronchial biopsy did not fit the patient's downhill clinical and roentgenographic course. Alveolar cell carcinoma was discovered. This patient (the patient of probable diffuse lymphosarcoma in whom Pneumocystis carinii was ruled out) along with the patients with sarcoidosis and Hodgkin's disease (listed in the lower half of Table 1), represent the only "false negative" biopsies in the series (15 percent).

Although our experience with transbronchial lung biopsy includes only 37 patients up to the date this report was submitted, a definite role has evolved for the use of this procedure on our clinical service. It has become the procedure of choice in all adult cases of suspected Pneumocystis carinii infection. It proved an accurate guide to therapy in all nine such patients, four with the infection, and five without. As noted by Walzer et al., methods for antemortem diagnosis of Pneumocystis carinii are currently unsatisfactory, despite the fact that all procedures which provide lung tissue (aspiration biopsy, closed needle biopsy, open biopsy) have a high degree of diagnostic accuracy. It is the attendant morbidity and mortality with all available procedures (with the exception of bronchial brush biopsy) in the acutely ill, hypoxemic patient that limits their usefulness. This results in delay in performing diagnostic procedures in a disease in which mortality is adversely affected by delay in treatment. In 194 cases of Pneumocystis carinii reported by Walzer, the mean duration of symptoms prior to diagnosis was 19.7 days. It is not surprising that Walzer and colleagues concluded that an aggressive diagnostic approach should be instituted early in cases of suspected Pneumocystis carinii pneumonia.

Thus it has been our policy to biopsy all such cases as soon as cough, fever, minimal x-ray changes, and mild hypoxemia make the diagnosis a realistic consideration. In three of the four cases of confirmed Pneumocystis carinii pneumonia, symptoms had been present for less than one week. All four patients recovered with pentamidine isethionate therapy.

Sarcoidosis was the clinical diagnosis in nine of the 37 cases. Diagnosis was established by transbronchial biopsy in five of the seven cases in which adequate tissue was obtained (71 percent). Lung parenchyma has been known to be a fruitful source of sarcoid granulomata even in the absence of radiographic infiltrates. The availability of procedures with less morbidity, such as liver biopsy or mediastinal node biopsy, has limited the general use of lung biopsy in establishing the diagnosis of intrathoracic sarcoidosis. Because of the low morbidity with transbronchial lung biopsy through the fiberoptic bronchoscope, it has become our policy to use this procedure before liver biopsy or mediastinal lymph node biopsy at mediastinoscopy. The diagnostic yield we have just cited compares favorably with liver biopsy results (75 percent), and recovery of granulomata from lung tissue may be more specific. In addition, the multiple biopsy technique allows one to perform special stains and cultures for acid-fast bacilli and fungi on lung parenchyma. Though the diagnostic yield in this small series is less than mediastinal node biopsy, there is the attractive advantage of avoiding general anesthesia and of sparing the patient a suprasternal scar.

Goodpasture's syndrome was diagnosed in two patients. Both had recurrent episodes of hemoptysis, with transient and persistent pulmonary infiltrates, and had undergone renal biopsies demonstrating...
characteristic immunofluorescence. Because of the attendant morbidity, lung biopsies had not been performed. Hematoxylin and eosin stain of the specimen obtained transbronchially, showed normal lung in both cases, with scattered hemosiderin-laden macrophages in the alveolar spaces. However, immunofluorescent deposits in the lung parenchyma were demonstrated with anticomplement and anti-immunoglobulin G stains. In the large group of chronic interstitial fibroses, represented in this series by the eight usual interstitial pneumonias, application of special techniques such as this, as well as electron microscopy, may provide information regarding etiology and pathogenesis. Such studies are being conducted. Further, transbronchial biopsy allows infectious agents and special types of interstitial disease (such as desquamative interstitial pneumonia) to be ruled out, and attempted treatment may be more rational. Serial biopsies may be performed in a given patient.

In summary, the major application of this promising biopsy procedure lies in its use in the hypoxemic patient with diffuse lung disease in whom procedures with higher morbidity are not indicated. This broadened availability of the lung biopsy in clinical medicine will be particularly helpful in medical centers where chemotherapy and organ transplantation are common and acute diffuse lung disease of unknown etiology is frequently encountered. The differential diagnosis of acute infectious agent, drug reaction, radiation pneumonitis, or diffuse tumor infiltration is more easily resolved when lung tissue is obtained. Fifteen of our patients (Table 1) presented this type of diagnostic dilemma, and in every case but one, the alveolar cell carcinoma case, transbronchial biopsy was helpful. When the five patients of this type in whom Pneumocystis carinii was excluded are added to the 26 patients in whom diagnostic tissue was obtained, we find that either a definitive diagnosis was established or a valuable exclusion of a specific entity was accomplished in 31 of 35 patients (90 percent).

REFERENCES