Diagnosis of Pneumocystis carinii Pneumonia by Transbronchoscopic Lung Biopsy*

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A diagnosis of Pneumocystis carinii pneumonia was made in seven patients by the technique of transbronchoscopic lung biopsy. In this technique, flexible forceps are inserted through a rigid bronchoscope. No false negative results were obtained, that is, no other cases of pneumocystis pneumonia were discovered by any additional technique, including autopsy, among a group of 525 patients with diffuse pulmonary diseases who had transbronchoscopic lung biopsy. Transbronchoscopic lung biopsy is an effective and accurate method of obtaining pulmonary tissue that is suitable for the demonstration of P carinii, especially in patients who are too ill to withstand open lung biopsy.

Pneumonia caused by Pneumocystis carinii is becoming an increasingly frequent clinical problem. European physicians have known for a long time that this disease mainly affects premature and debilitated infants or children with congenital immunologic disorders. In the United States, during the last decade, P carinii pneumonia has been reported most frequently in patients with various immunologic disorders. Among patients who seem predisposed to develop this form of pneumonia are those with neoplasms of the hematopoietic, lymphoreticular, and other systems and who usually are receiving steroid or cytotoxic drugs, those with collagen diseases who are treated with steroids, those who have received kidney and heart transplants and who are treated with immunosuppressive drugs, and those with immunoglobin deficiencies, such as thymic alymphoplasia.

Since effective therapy for this once fatal disease is now available, it is important to make a diagnosis of P carinii pneumonia early. We report our experience with the technique of transbronchoscopic lung biopsy in obtaining material to make this diagnosis. The diagnosis of P carinii pneumonia was made in seven patients.

Patients and Methods

The technique of transbronchoscopic lung biopsy, a satisfactory method of obtaining pulmonary tissue from patients with diffuse pulmonary diseases, was used in 525 such patients. Among this group of 525, there were 7 patients in whom the diagnosis of P carinii pneumonia was made by this diagnostic procedure (Table 1). Two of these patients had Hodgkin's disease, two had received renal transplants, one had chronic lymphocytic leukemia, one had polycythemia rubra vera, and one had acute lymphocytic leukemia. Six of the seven patients had been on immunosuppressive therapy at the time pneumonia developed.

Transbronchoscopic lung biopsy is performed through a standard rigid bronchoscope. Topical anesthesia is preferred, because most patients suspected of having P carinii pneumonia are too ill to tolerate general anesthesia; indeed, our patients at the time biopsy was required generally were critically ill. A bronchoscopic examination is made in the usual manner. Then, flexible forceps having a rectangular cup approximately 2 by 4 mm or a circumference of approximately size 7 F (Fig 1) are carefully inserted into selected segmental bronchi. When the forceps become engaged in a peripheral bronchus, so that with respiratory motion the forceps are pulled downward and pushed outward, the jaws are opened during inhalation and closed during exhalation. Pulmonary tissue usually can be pulled away easily. We attempt to obtain at least three biopsy specimens, each from a different pulmonary segment; we have taken as many as five pieces of tissue.

In addition to the biopsies of pulmonary tissue, bronchial secretions were collected from all seven patients, and sputum was collected from two patients. Bronchial brushings were obtained in one patient.
Microscopic Findings

Transbronchoscopic lung biopsy provided a positive diagnosis of *P. carinii* in all seven patients. Moreover, no other case of pneumocystis pneumonia was discovered by any additional means, including autopsy, among the total 525 patients with diffuse pulmonary diseases who had transbronchoscopic lung biopsy. In other words, there were no false-negative biopsies.

The bronchial secretions contained demonstrable *P. carinii* organisms in two of the seven specimens examined. In one of the five specimens in which the bronchial secretions contained no demonstrable organisms, results of bronchial brushing were also negative.

The sputum in each of two cases was negative for *P. carinii*.

The patients subsequently were treated with pentamidine isethionate daily (dose, 4 mg/kg), by either intramuscular or intravenous injection. The periods of treatment are given in Table 1. Two patients are still living 15 and 20 months later; these two patients were treated for 7 and 14 days. A third patient received pentamidine for ten days, recovered from the infection, and, to date, has survived for eight months.

Patient 1 (Table 1) had pneumonia that persisted in spite of receiving pentamidine for 14 days. Bronchoscopy and lung biopsy, therefore, were repeated. The histologic diagnosis was "active interstitial pneumonitis and fibrosis," but the presence of *P. carinii* was not demonstrable in the second biopsy. She died after receiving pentamidine for 18 days; death was attributed to respiratory failure associated with cytomegalic inclusion disease. Autopsy confirmed the finding of the second biopsy that *P. carinii* had been eliminated after the course of pentamidine therapy.

Complications of Biopsy

In three of the seven patients pneumothorax developed after biopsy (Table 1). In two of the three patients the pneumothorax was small (less than 15 percent), but constant intrathoracic suction by catheter or S-needle was used for 24 to 48 hours in all three patients because of diminished pulmonary reserve. In none of the patients did the procedure appear to be a significant factor in the deterioration of the pulmonary status. It should be noted from Table 1 that two of the three pneumothoraces occurred in patients who ultimately became long-term survivors.

Even so, the occurrence of pneumothorax in three of the seven patients is disconcerting. On the other hand, they were gravely ill and it was essential to make a diagnosis. Among the total group of 525 cases in which transbronchoscopic lung biopsy had been performed for various pulmonary diseases, the incidence of pneumothorax was 14 percent. In the most recent 375 of the 525 cases, the incidence has been only 11 percent. The present sample of seven patients is too small to permit one to conclude that this method of biopsy is more hazardous in patients with *P. carinii* pneumonia than it is in those with other diffuse pulmonary diseases.

Bleeding has been no problem in any of these seven cases and has not been a serious problem in any of the total group of patients with transbronchoscopic lung biopsy. If the endoscopist observes more than a very small amount of blood, he can insert narrow surgical gauze tape through the bronchoscope into the segmental bronchus from which the biopsy was taken. This can be left for two or three minutes, then removed. This maneuver has been successful in stopping bleeding in every instance in which it has been used. The ability to control bleeding so simply is a distinct advantage of the transbronchoscopic biopsy as compared with the percutaneous needle biopsy.

Discussion

In 1909, Chagas observed pneumocystis organisms in the lungs of guinea pigs that were infected with *Trypanosoma cruzi*, and in 1910, Carini reported the presence of these organisms in lungs of rats that were infected with *Trypanosoma lewisi*. In 1912, the Delanoes gave the name *Pneumocystis*...
# Diagnosis of Pneumocystis carinii Pneumonia

Table 1.—Clinical and Diagnostic Data in Seven Cases of P carinii Pneumonia

<table>
<thead>
<tr>
<th>Patient, Sex and Age (Yr)</th>
<th>Underlying Disease</th>
<th>Clinical Data</th>
<th>Diagnostic Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>F, 37</td>
<td>chr. glomerulonephritis, renal transplant</td>
<td>azathioprine, prednisone</td>
<td>TBLB, bronchial secretions: positive</td>
</tr>
<tr>
<td>M, 60</td>
<td>chr. lymphocytic leukemia, secondary hypogammaglobulinemia</td>
<td>none</td>
<td>TBLB: positive; bronchial secretions: negative</td>
</tr>
<tr>
<td>M, 67</td>
<td>Hodgkin's disease</td>
<td>cyclophosphamide 7 days</td>
<td>TBLB, bronchial secretions: positive</td>
</tr>
<tr>
<td>F, 37</td>
<td>chr. pyelonephritis, renal transplant</td>
<td>azathioprine, prednisone</td>
<td>TBLB: positive; bronchial secretions: negative</td>
</tr>
<tr>
<td>M, 26</td>
<td>Hodgkin's disease</td>
<td>procarbazine HCl, 10 days prednisone, vinblastine sulfate, irradiation</td>
<td>TBLB: positive; bronchial secretions: negative</td>
</tr>
<tr>
<td>M, 58</td>
<td>polycythemia rubra vera</td>
<td>chlorambucil</td>
<td>TBLB: positive; bronchial secretions: negative</td>
</tr>
<tr>
<td>F, 22</td>
<td>ac. lymphocytic leukemia</td>
<td>prednisone, vincristine sulfate, methotrexate</td>
<td>TBLB: positive; bronchial secretions and brushing, negative</td>
</tr>
</tbody>
</table>

P carinii to these organisms. Since then there have been many reports of pneumonia due to P carinii.

Various methods have been used in attempts to demonstrate this organism, but it is not always easy to obtain material safely for diagnosis in a sick patient. P carinii has been detected in sputum, and, in certain cases, as aspirates from the nasopharynx, hypopharynx, trachea, and bronchi. In the experience of most groups, however, attempts to diagnose P carinii pneumonia by the above methods have been unsuccessful.

Open lung biopsy is a good method of obtaining tissue for demonstration of P carinii, but patients with the disease are frequently too ill to withstand this procedure. Transthoracic lung biopsy and transthoracic lung aspiration also have been used. Needle aspiration and needle biopsy have been used to obtain P carinii cysts but attempts to identify them occasionally have failed in those patients later proved by other methods to have P carinii pneumonia.

A complement-fixation test is reportedly helpful in identifying patients who have been infected with P carinii, but this serologic test has been used infrequently in this country. Results have been disappointing, probably because of the severe suppression of the immune response in most of these patients.

Rarely the organism has been found in other tissues. Zandanell reported several cases in which P carinii was found in the peripheral blood. A skin test for the infection has been used, but its reliability has not been adequately evaluated. P carinii has been found in the peripheral blood, and study of posterior iliac crest bone marrow aspirate (taken antemortem) revealed P carinii in a case of systemic dissemination of this organism.
removed by thoracentesis.31

The use of an immunofluorescent technique for
identification of specific immunofluorescent bodies
in the sputum from patients suspected of having P
carinii pneumonia has been reported.32 This method
might provide a means of diagnosis that would not
require lung biopsy, but it needs further evaluation.

Bronchial brushing has been used as a method for
making a diagnosis of P. carinii pneumonia. A re-
port33 published in 1969 described poor results, but
a recent report34 is more encouraging.

Various methods for the detection of P. carinii in
the lung thus have been reported. Apart from trans-
bronchoscopic or open lung biopsy, none of these
has been uniformly successful. We have encountered
no case in which transbronchoscopic lung biopsy
was falsely negative for P. carinii pneumonia, where-
as aspum examination was negative for pneumo-
cystis in each of two patients whose sputum was
studied, and bronchial secretions obtained at bron-
choscopy were negative for Pneumocystis in five of
the seven patients. Bronchial brushings were nega-
tive in the one case in which they were obtained.

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