Bronchoscopy in the Diagnosis of Pulmonary Histoplasmosis*

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Although histoplasmosis is the most common fungal infection of the lungs in the United States, there are no reports evaluating the efficacy of fiberoptic bronchoscopy in the diagnosis of this disease. We reviewed all cases of histoplasmosis diagnosed at our institution from 1972 to 1987. Of 469 patients, 71 underwent fiberoptic bronchoscopy and had culture/histologic proof of histoplasmosis established by fiberoptic bronchoscopy or other means. A diagnosis of pulmonary histoplasmosis could be made without thoracotomy in only 27. Among those not requiring thoracotomy, diagnosis of pulmonary histoplasmosis was confirmed by fiberoptic bronchoscopy and cultures of sputum, gastric washings, blood, bone marrow, and urine. In this subgroup, fiberoptic bronchoscopy was the only positive diagnostic method in eight of 27 patients. We conclude that fiberoptic bronchoscopy is a useful adjunct to other noninvasive measures yielding diagnostic material in most cases, except for solitary pulmonary nodule where it is rarely helpful.

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Pulmonary diseases caused by the pathogenic fungi are common. Histoplasmosis is numerically the most important, with the largest endemic area concentrated particularly in the Mississippi, Ohio, and Missouri river valley regions of the United States. Millions have been infected by this organism, with clinical illness appearing in an estimated 40 percent, and 10 percent ill enough to seek medical attention, although such cases may not be specifically recognized as histoplasmosis because of their generally benign and self-limited nature.

Fiberoptic bronchoscopy has been evaluated in many fungal diseases and is established as a useful aid in diagnosis, particularly in coccidioidomycosis and invasive aspergillosis in the immunocompromised host. Although Histoplasma capsulatum also has been found by bronchoscopy, the numbers reported are small and no conclusion can be drawn as to its efficacy. This study examines 71 cases of proven pulmonary histoplasmosis in which fiberoptic bronchoscopy and other noninvasive procedures were performed to assess their diagnostic yield.

METHODS

We retrospectively reviewed all cases of histoplasmosis diagnosed at our institution from 1972 to 1987. These cases were selected from a computer file of all inpatient and outpatient surgical, medical, and pathologic diagnoses. Of 469 such patients, there were 71 who had both fiberoptic bronchoscopy and culture or histopathologic proof of histoplasmosis.

All patients were evaluated with a complete history, physical examination, routine laboratory data, and chest roentgenogram.

RESULTS

Of the 71 patients proven to have pulmonary histoplasmosis there were 50 male and 21 female subjects (mean age, 54 years; range, 17 to 76 years). There were 24 patients living in the state of Minnesota and 47 from neighboring states at the time of their diagnosis. History of occupational exposure was elicited as a possible source for infection in 19 of 71 patients (27 percent). Absence of respiratory symptoms was specifically documented in 20 of 71 (28 percent) patients. Chest roentgenographic findings were varied, as listed in Table 1.

Diagnostic yields for the different procedures performed are presented in Table 2. Overall, fiberoptic bronchoscopy provided diagnostic material in 25 of 71...
(35 percent) patients. However, when SPNs were excluded, this yield increased to 24 of 44 (55 percent). Fiberoptic bronchoscopy was helpful in only one case of SPN and the other noninvasive tests were uniformly negative. Reviewing only those who did not ultimately have thoracotomy (Table 3), the yield for fiberoptic bronchoscopy was 22 of 27 (81 percent) patients. Of these 27 patients who did not require thoracotomy for diagnosis, eight (30 percent) were found to have cultures positive only from bronchoscopically obtained specimens. In this subgroup the yield for other noninvasive means was improved as well (Table 3).

When comparing the roentgenographic findings with positive diagnostic procedures (Table 4), we found that histoplasmosis presenting as SPN was rarely diagnosed prior to thoracotomy (one of 27 patients, 4 percent). The results from fiberoptic bronchoscopy were improved when nodules were multiple (three of eight patients, 38 percent). However, the best results occur in the diagnostic evaluation of local or diffuse infiltrates or cavitated lesions. Fiberoptic bronchoscopy provided diagnostic material in 14 of 22 (64 percent) patients of infiltrative lesions and in seven of eight (88 percent) patients with cavities. Fiberoptic bronchoscopy was unsuccessful in demonstrating H *capsulatum* when manifested as hilar adenopathy, chronic pleural effusion, or bronchopleural fistula.

Table 2—Diagnostic Yield for Procedures Performed in 71 Patients with Pulmonary Histoplasmosis

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. (%)</th>
<th>SPN* No. (%)</th>
<th>Non-SPN† No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchoscopy</td>
<td>25/71</td>
<td>3/27</td>
<td>22/44 55</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>44/45</td>
<td>9/26 100</td>
<td>35/19 95</td>
</tr>
<tr>
<td>Sputum</td>
<td>13/28</td>
<td>0/9 0</td>
<td>13/29 45</td>
</tr>
<tr>
<td>Gastric washings</td>
<td>10/22</td>
<td>0/3 0</td>
<td>10/19 53</td>
</tr>
<tr>
<td>Blood</td>
<td>5/22</td>
<td>0/1 0</td>
<td>5/21 24</td>
</tr>
<tr>
<td>Urine</td>
<td>1/14</td>
<td>0/2 0</td>
<td>1/12 8</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>3/12</td>
<td>. . . 3/12 25</td>
<td></td>
</tr>
<tr>
<td>Pleural fluid or biopsy</td>
<td>3/6 50</td>
<td>. . . 3/6 50</td>
<td></td>
</tr>
</tbody>
</table>

* Those with SPN only.
† All cases other than those with SPN.

Of the 27 SPN, chest roentgenograms were available for review by the authors in 16 patients (59 percent). The average nodule size was 1.9 cm (1.0 to 4.0 cm) in diameter and they were located in all lobes of the lung. Most (75 percent) were in peripheral lung zones and none was calcified on plain films or tomograms.

The description of endobronchial findings was available for all patients. The airways were normal in 41 (58 percent) patients and evidence of acute or chronic bronchitis was noted in 23 (32 percent). Bronchial narrowing was seen in three (4 percent), and friable mucosa, endobronchial nodularity, bronchopleural fistula, and a widened carina in one each.

Serologic testing in 52 cases, using complement fixation to the mycelial phase, produced the following titer results: in 33 of 52 (63 percent), negative; in ten of 52 (19 percent), <1:32; and in nine of 52 (17 percent), ≥1:32. Complement fixation to the yeast phase documented 14 of 52 (27 percent), negative; 12 of 52 (23 percent), <1:32; and 26 of 52 (50 percent), ≥1:32. Findings for the immunodiffusion technique showed 33 of 52 (63 percent), negative; 12 of 52 (23 percent), positive M bands alone; 7 of 52 (13 percent), positive M and H bands, and no isolated positive H bands.

**DISCUSSION**

Histoplasmosis is a frequently encountered disease in the midwestern United States. Infection and reinfection are known to occur regularly in heavily endemic regions; however, persistent chest roentgenographic changes or progressive pulmonary disease is the exception. When such findings come to the attention of the physician, the diagnostic possibilities are numerous, and the roentgenographic presentation may need to be reviewed extensively to confirm the diagnosis. The procedure of choice is fiberoptic bronchoscopy with culture or histologic proof of histoplasmosis, and the subject of this report.

Demographic information available on these patients discloses the fact that the age distribution is...
considerably shifted to a higher range than that expected for first-time exposure to *H capsulatum*. The mean age is 54 years and in part denotes the degree to which these roentgenographic abnormalities are assessed when malignancy is suspected. It is not clear how many patients were evaluated simply because of an abnormal chest roentgenogram, but a significant minority (28 percent) were specifically noted in their medical records to have no respiratory symptoms at presentation. Many of these asymptomatic individuals had SPN as their only roentgenographic abnormality (55 percent), and in these an evaluation was pursued to exclude malignancy. In patients with respiratory symptoms the degree to which we could relate symptomatology to roentgenographic abnormalities ascribed to histoplasmosis was not always discernible because some patients had other pulmonary problems, particularly chronic obstructive lung disease. However, regardless of symptomatology each of the 71 cases appeared to adequately document the relationship of the roentgenographic abnormality in question to the culture or histologic presence of *H capsulatum* in appropriate specimens.

Although most cases of histoplasmosis occur without a clear history of exposure, 27 percent of our patients had occupations which could place them at greater risk, eg, farming. The male-to-female ratio was 2.4:1, which also may reflect an increased exposure profile. Of the 71 patients, 24 resided in Minnesota, 15 in Iowa, and 13 in Illinois, states which are recognized areas of endemic histoplasmosis.

In an earlier roentgenographic review from our institution, the incidence of nodules on chest x-ray film was nearly twice that found in this study; however, serologic evidence alone of histoplasmosis was permitted as proof of disease, allowing the positive diagnosis of an unbiopsied SPN. Additionally, the greater incidence of all other roentgenographic patterns in the present report most likely represents the tendency for symptomatic patients to come to definitive diagnostic procedures, since there were only 24 percent with symptoms in the earlier article, compared to 72 percent in this review.

It is established that the etiology of a SPN is not easily diagnosed prior to thoracotomy or other invasive procedure. Although transthoracic needle aspiration has been successful in the positive identification of benign granulomatous disease presenting as SPN, this technique, which is utilized at our institution, was not part of the evaluation of this patient population. When excluding SPN, we found the yield for fiberoptic bronchoscopy, sputum and gastric sampling encouraging at 55, 45, and 53 percent, respectively. Limiting analysis to those 27 patients who did not require thoracotomy for diagnosis, fiberoptic bronchoscopy, sputum and gastric sampling produced 81, 71, and 69 percent positive results. In this subgroup, 30 percent were diagnosed by fiberoptic bronchoscopy alone, the most significant single diagnostic procedure. This compares similarly with the bronchoscopic evaluation of coccidioidomycosis, where 20 of 29 non-SPN cases (69 percent) were documented by fiberoptic bronchoscopy and ten of 29 (35 percent) were found exclusively by fiberoptic bronchoscopy.

Viewing the results of fiberoptic bronchoscopy with respect to various chest roentgenographic presentations indicates that the highest yield is found in those with cavitated lesions (88 percent). This has not been previously documented, but is not surprising, since these lesions are typically sources of significant fungal production and sputum commonly reveals positive cultures. We found this to be true to a lesser extent when assessing local or diffuse infiltrates.

The endobronchial description offers little diagnostic information and was normal or showed only evidence of acute or chronic bronchitis in 90 percent of these cases. Even if these findings were due to histoplasmosis, the nonspecificity of the bronchoscopic appearance could not assist in differentiating similar changes due to other respiratory diseases.

Using serologic methods for the initial diagnosis of histoplasmosis is controversial and there are no data concerning the institution of therapy based on these tests alone. However, they are often utilized by the
clinician in an integrative manner, raising the suspicion of this diagnosis and prompting the pursuit of a diagnostic evaluation. In our patients, completely negative mycelial, yeast, and immunodiffusion testing was found in 25 percent, while significantly elevated titers for mycelial or yeast phase serologic findings (≥ 1:32) or M or H band positivity by immunodiffusion was seen in 63 percent of those tested.

In summary, we found that fiberoptic bronchoscopy in the evaluation of pulmonary histoplasmosis, although dependent on the roentgenographic presentation, is a significantly valuable adjunct to other noninvasive measures which yield the diagnosis of histoplasmosis in the majority of cases. However, when pulmonary histoplasmosis presents as a solitary nodule, bronchoscopy and noninvasive testing rarely are productive.

REFERENCES
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