The Usefulness of Step Sectioning of Transbronchial Lung Biopsy Specimen in Diagnosing Sarcoidosis*

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To evaluate the usefulness of step sectioning of the transbronchial lung biopsy (TBLB) specimens obtained from patients with suspected sarcoidosis, we examined all TBLB specimens obtained from 132 patients who were diagnosed clinically as having sarcoidosis at our institute. When routine sections of TBLB specimens did not show sarcoid granuloma, we prepared additional serial sections from each block and stained every fifth section with hematoxylin-eosin (step sectioning). All step sections were examined histologically. With the aid of step sectioning, the diagnostic yield of sarcoidosis increased from 38 percent (18/47) to 47 percent (22/47) in stage 1 patients, and from 57 percent (37/65) to 82 percent (53/65) in stage 2 patients. All of the newly detected granulomas were identified between the first and seventh sections. We conclude that step sectioning is useful method in diagnosing sarcoidosis.

(CHEST 1992; 102:1441-43)

TBLB = bilateral hilar lymphadenopathy; OLB = open lung biopsy; TBLB = transbronchial lung biopsy

Transbronchial lung biopsy (TBLB) specimens are useful in diagnosing such diffuse pulmonary diseases as sarcoidosis. With this procedure, the diagnostic yield of sarcoidosis is reported to be between 55 and 95 percent.1-3 The diagnostic yield of TBLB is lower than that of open lung biopsy (OLB) because the amount of lung tissue obtained is smaller. We previously described the utility of step-sectioning TBLB specimens in patients with migratory and diffuse lung disease, including a few with stage 2 sarcoidosis.4-7 However, the utility of step sectioning in diagnosing sarcoidosis in patients is still unclear. Also, it is not known how many sections are needed to detect a sarcoid granuloma. In this study, we investigated the usefulness of step sectioning of TBLB specimens in diagnosing sarcoidosis.

METHOD

We examined 132 patients who were diagnosed clinically at our institute as suffering from sarcoidosis between January 1979 and January 1990. The patients' clinical charts and TBLB sections were reviewed (Tables 1 and 2). Sarcoidosis was diagnosed on the basis of clinical features consistent with sarcoidosis, ie, bilateral hilar lymphadenopathy on chest roentgenograms, or extrapulmonary involvement, and/or biopsy findings, ie, the presence of noncaseating epithelioid granuloma. The clinical stage was defined as follows: stage 0, normal chest roentgenogram (20 patients); stage 1, bilateral hilar lymphadenopathy (BHL) alone (47 patients); and stage 2, both BHL and lung parenchymal infiltrates (65 patients).

TBLB was performed under fluoroscopic control. Specimens were obtained from the areas of greatest roentgenographic involvement in stage 2 patients, and from the right upper and lower lobe in stage 0 and 1 patients. From one to nine biopsy specimens were obtained by TBLB, with an average of 3.1 specimens per patient.

Biopsy specimens were stored in 10 percent buffered formalin. First, we prepared 3-μm-thick serial sections from all paraffin-embedded blocks and stained every fifth section with hematoxylin-eosin (step sectioning). When the first one or two sections (original section) did not show granuloma, we examined all step sections histologically.

A positive biopsy specimen was defined as that containing a noncaseating granuloma in the absence of an identifiable infectious process, foreign body, or allergic tissue reaction. Any specimen that showed interstitial pneumonitis, nonspecific fibrosis, or normal parenchyma without a granulomatous reaction was considered negative. If a specimen contained some alveolar tissue, it was considered to be an alveolar specimen. If it did not contain alveolar tissue, it was considered to be a nonalveolar specimen.

RESULTS

Of the 132 sarcoidosis patients, 112 had alveolar

Table 1—Characteristics of 132 Patients with Sarcoidosis

<table>
<thead>
<tr>
<th>No./Age, yr/ Sex, M:F</th>
<th>Clinical Stage (0:1:2)</th>
<th>No. of TBLB* Specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>132/17-73/58:74</td>
<td>20:47/65</td>
<td>1-9</td>
</tr>
<tr>
<td>(mean, 42.9)</td>
<td></td>
<td>(mean, 3.1)</td>
</tr>
</tbody>
</table>

*TBLB = transbronchial lung biopsy.

Table 2—Pathologic Findings in TBLB Specimens Obtained from 132 Patients with Sarcoidosis

<table>
<thead>
<tr>
<th>Granuloma- Positive</th>
<th>Granuloma- Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original Section</td>
<td>56</td>
</tr>
<tr>
<td>Step Section</td>
<td>20</td>
</tr>
<tr>
<td>Lymphangitic</td>
<td>15</td>
</tr>
</tbody>
</table>


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tissue in their TBLB specimens and the remaining 20 patients had only bronchial mucosa without alveolar tissue. Fifty-six patients showed noncaseating epithelioid granuloma in the original sections. Considering the clinical stage of disease, the diagnostic yield in the original sections was as follows: stage 0, 1/20 (5 percent); stage 1, 18/47 (38 percent); and stage 2, 37/65 (57 percent). The remaining 76 patients were not diagnosed as having sarcoidosis histologically by the original sections. However, with step sectioning, 20 of the 76 patients showed noncaseating epithelioid granuloma. Of the 20 patients, four had stage 1 disease and 16 had stage 2 disease. The incidence of granuloma in the original sections vs the step sections is shown in Figure 1. The diagnostic yield in the three clinical stages was as follows: stage 0, 1/20 (5 percent); stage 1, 22/47 (47 percent); and stage 2, 53/65 (82 percent). Step sectioning did not reveal sarcoid granuloma in any patient with stage 0 disease. To standardize the extent of improved diagnostic yield, we also analyzed the diagnostic yield of 28 patients having four biopsy specimens. Of the 28 patients, 14 patients showed the sarcoid granuloma in original section. The diagnostic yield in the three clinical stages was as follows: stage 0, 0/5 (0 percent); stage 1, 5/10 (50 percent); and stage 2, 9/13 (69 percent). With step sectioning, the diagnostic yield improved to 6/10 (60 percent) in patients with stage 1 and 12/13 (92 percent) in patients with stage 2, respectively. This result is similar to the total one. Secondly, to determine the optimal number of step sections required for a positive diagnosis in patients with a negative result in the original biopsy sections, we examined the relationship between diagnostic yield and the number of step sections until the first granuloma-positive section was obtained. As shown in Figure 2, the diagnostic yield increased rapidly to about 40 percent in the first step section and about 70 percent in the second step section, then increased gradually to approach a 100 percent diagnostic yield between the fourth and seventh sections. We concluded that a total of seven step sections were required to obtain a granuloma-positive section in patients showing a negative result in the original biopsy section.

**DISCUSSION**

The relationship between diagnostic yield and number of TBLB specimens has been discussed in studies of patients with sarcoidosis. Gilman and Wang reported that in diffuse pulmonary sarcoidosis, the likelihood of obtaining a positive biopsy specimen using the TBLB technique is related directly to the number of biopsy specimens per patient. They concluded that in stage 2 sarcoidosis, only four biopsy specimens are necessary for a diagnostic yield of approximately 90 percent, and that obtaining more than four biopsy specimens added little to the outcome. However, we did not know of any reports concerning the relationship between diagnostic yield and the number of sections obtained from a TBLB specimen. We therefore examined the step sections obtained from TBLB specimens histologically. Since sarcoid granuloma is known to be located in the lung with lymphangitic distribution, the granuloma is considered to be present around the bronchioles. Therefore, when a sarcoid granuloma is not present in the original section of the TBLB specimen, it can be predicted that some granulomas are newly detected; therefore, the diagnostic yield can be improved by step sectioning. This study demonstrated that the diagnostic yield is related directly to the number of sections obtained from TBLB specimens with step sectioning in patients with sarcoidosis. The use of step sectioning presents two problems determining the optimal interval between step sections and the optimal
number of step sections to be obtained. In this study, the diameter of noncaseating epithelioid granuloma exceeded 50 μm; the 15-μm interval we applied in step sectioning was sufficient to detect the granuloma. Concerning the optimal number of step sections to be obtained, all granulomas were found by the seventh section, as shown in Figure 2. Therefore, seven step sections were optimal in this study. However, this may change with the interval between sections.

Our results lead us to conclude that step sectioning is useful for diagnosing pulmonary sarcoidosis.

REFERENCES
1 Gilman JM, Wang PK. Transbronchial lung biopsy in sarcoidosis.
2 Roethe RA, Fuller PB, Byrd RB, Hafermann DR. Transbronchial lung biopsy in sarcoidosis. Chest 1980; 77:400-02