Bronchoscopic Lung Biopsy With Fluoroscopy to Study 164 Localized Pulmonary Lesions

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OBJECTIVE: To assess the usefulness of bronchoscopic lung biopsy (BLB) in the diagnosis of localized pulmonary lesions.

METHODS: A prospective, descriptive study of consecutive patients with a suspected neoplastic nodule, mass, or infiltrate with nonspecific bronchoscopic findings after performing BLB with fluoroscopy. The lesions, clinical, and patient characteristics, and outcomes were evaluated.

RESULTS: One hundred sixty-four patients with a mean (SD) age of 65 (12) years and a total of 156 masses or nodules and 8 infiltrates (144 neoplasms and 20 nonneoplastic lesions) participated in the study. On average, the lesion was 4.3 (2) cm in diameter and 6 (2) BLBs were performed on each patient, with a rate of serious complications of less than 1%. BLB was diagnostic in 113 cases (69% of the neoplasms and 70% of the nonneoplastic). In cases diagnosed by BLB, the lesions were larger (4.6 [2] cm), more samples were obtained (6 [2] biopsies), nondiagnostic endoscopic alterations were found (30%), and the bronchus sign was present (22%). Moreover, bronchoscopy was better tolerated by those patients.

CONCLUSIONS: BLB with fluoroscopy increased the diagnostic yield of bronchoscopy for localized lesions with nonspecific findings, regardless of etiology. Larger neoplasms, the bronchus sign, good tolerance, and more tissue samples increased the number of diagnoses, with few complications.

Key words: Fiberoptic bronchoscopy. Bronchoscopic lung biopsy. Localized pulmonary lesions. Fluoroscopy.

Introduction

Bronchogenic carcinoma is among the most common neoplasms and is the leading cause of cancer death in men. Considering that the 5-year survival rate of 65% to 70% applies only to those patients diagnosed and treated at the earliest stages, new diagnostic techniques should be developed or the yield of current ones increased. In its early stages, a neoplasm usually presents as a nodule, mass, or localized infiltrate without lymph node or other involvement, making it necessary to first rule out other lesions with similar presentations.

Flexible bronchoscopy provides an excellent direct approach to the site and has a high diagnostic yield for endoscopically visible neoplasms. For nonvisible or
Figure. Computed tomography of the chest with neoplastic pulmonary nodule and positive bronchus sign (arrow).

Peripheral lesions, conventional techniques such as selective bronchial aspiration or bronchoalveolar lavage have a diagnostic yield of only 48%. The addition of other diagnostic procedures—such as transbronchial needle aspiration or bronchoscopic lung biopsy (BLB) —increases diagnostic yield to more than 70% when used in combination or when guided by fluoroscopy.

The aim of our study was to evaluate the contribution of BLB with fluoroscopy to the diagnosis of localized pulmonary lesions suspected to be neoplasms but with nonspecific bronchoscopic findings. Our focus was on those characteristics likely to affect diagnostic yield, such as size, location, histologic type, and presence of the bronchus sign.

Methods

A prospective, descriptive study was carried out between November 1994 and May 2001 with a total of 164 consecutive patients who met the following inclusion criteria: a) presence of a localized pulmonary lesion surrounded by healthy lung tissue and suspected of being a neoplasm classified as a pulmonary nodule (well-defined lesion whose largest diameter was ≤3 cm), a lung mass (localized lesion >3 cm in diameter), or a localized segmental or lobar pulmonary infiltrate; b) absence of an endoscopically visible lesion with a diagnostic biopsy; c) availability, prior to endoscopy, of a posteroanterior and lateral x-ray and a computed tomography (CT) chest scan with intravenous contrast; d) absence of contraindications for bronchoscopy or BLB; e) visualization of the lesion by fluoroscopy; f) final availability of a definitive cytological, histological, or microbiological diagnosis established by bronchoscopy, transbronchial needle aspiration, thoracotomy, or other techniques; or, if no definitive diagnosis was available, stability or radiographic resolution after at least 2 years follow up; and g) informed consent agreement signed by the patient.

Lesions fulfilling the inclusion criteria were divided into 2 groups for later analysis: neoplasms and nonneoplasms. In all cases, the most significant data from the patient records were assessed, including the following: age; sex; smoking history; Karnofsky rating; body mass index; diagnosis of chronic obstructive pulmonary disease; main symptoms (cough, hemoptysis, dyspnea, and wasting syndrome); findings from the x-ray, CT scan, bronchoscopy, and fluoroscopy; histological type; and definitive diagnosis. The CT chest scan was used to assess the characteristics of the lesions: 3 different CT views (posteroanterior, lateral, and craniocaudal) were used to measure the lesion and the largest of the 3 diameters was used as the reference size. This diameter was used to classify the lesion; limits were set at 3 cm—to distinguish a lung mass from a pulmonary nodule—and 2 cm, which is considered a critical size in most reported studies.

Based on the CT scan, the hemithorax around the pulmonary hilum was divided into 3 equal, elliptical parts, to categorize the lesion as central (inner third), intermediate (middle third) or peripheral (outer third). The scan was also used to determine in which lobe the lesion was located and to identify the presence of the bronchus sign (presence of an obstructed bronchus or one which leads to the lesion until contact is made) in conventional images of the lung window (Figure). When the lesion overlapped 2 areas, it was assigned to the one containing the greater part of the lesion and which was most proximal to the pulmonary hilum.

All endoscopies were performed by a single endoscopist using an Olympus BF P30 and P40 fiberoptic bronchoscope (Medical Europa S.A.; Barcelona, Spain) using the conventional method: the transnasal approach with 2% to 4% lidocaine for local anesthesia. The patient was monitored throughout the procedure. In each case, the tracheobronchial tree up to the subsegmental bronchi was thoroughly inspected, with particular attention on the area where the lesion was seen on the x-ray. Given the possible presence of visible alterations in this area, tissue samples were taken for cytology and histology analysis. Once this phase was complete, but before fluoroscopy was used to locate the lesion, biopsy forceps were inserted until contact with the lesion was made. If no contact was achieved, the multiplanar vision provided by C-arm fluoroscopy was used to guide the forceps to the lesion. The intention was to perform at least 6 BLBs for evaluation by a single pathologist. No biopsy samples were taken until the forceps made contact with the lesion and then tissue samples were taken from different entry points whenever possible. All patients were examined by fluoroscopy and an x-ray was taken 4 to 6 hours after the bronchoscopy to rule out complications. Both the bronchoscopist and the nurse assessed each patient’s tolerance for the exploration. Tolerance was considered very good (the patient cooperated well by controlling coughing, performing appropriate breathing maneuvers during the biopsies, and permitting repeated access to the lesion so that at least 6 samples were taken), good (tolerance between very good and limited), and limited (patient had difficulty controlling cough, understanding instructions, coordinating breathing during the procedure, and permitting repeated access to the lesion; as a result, fewer than 6 biopsies were performed). Radiation monitoring systems to monitor the hospital staff performing the procedures were checked monthly.

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A descriptive analysis of the lesions, clinical, and patient characteristics, and outcomes was performed. This data was compared in terms of the results of the BLB and the distribution of these results according to the following variables: size, location, and histological type of lesion; presence or absence of the bronchus sign on the CT scan; and toleration for the exploration. The t test was used to compare quantitative variables and the χ² or Fisher exact test for qualitative variables. The odds ratio (OR), the presence of a linear association, and the likelihood ratio of these comparisons were analyzed to check for correlations. Results were considered statistically significant when the P value was less than or equal to .05.

Results

BLB with fluoroscopy established the diagnosis in 113 of the 164 patients studied (69%), while an additional method was needed for a definitive diagnosis in 51 (31%). Table 1 shows the main characteristics of the patients studied and the differences according to the results of the BLB with fluoroscopy. Patients diagnosed by BLB had larger lesions (P=.002), a lower forced expiratory volume in 1 second (P=.01), more BLBs (P=.01), and more endoscopic findings—in large part due to the presence of stenosis, hyperemia, or localized extrinsic compression that was visible but nondiagnostic (P=.001). Patients grouped according to the BLB diagnosis presented no differences with regards to clinical characteristics, prior history of chronic obstructive pulmonary disease, lung function, or arterial blood gases. The linear relation between diagnosis by BLB and the diameter of the lesion as measured by the CT scan tended to increase, such that the relation was good between a positive result and large diameters (analysis of variance; F ratio=10.4, P=.002). The rate of serious complications was less than 1%, with no cases of pneumothorax and only 1 case of hemoptysis caused by a peripheral carcinoid mass that forced us to abandon the procedure. Radiation markers of staff exposed to the fluoroscopy during the study were not significant. Included in the study were 144 cases (88%) with neoplasms and 20 (12%) with nonneoplastic lesions. Table 2 shows the etiology and distribution of both in relation to the results of the BLB. A total of 49 CT-guided transthoracic fine-needle aspirations were performed to confirm diagnosis in cases with a nondiagnostic BLB. Results of the needle aspiration were diagnostic in 34 cases (70%) with a negative BLB and nonspecific for the remaining patients, including 10 cases in which the BLB was later diagnostic. Transthoracic fine-needle aspiration was associated with 10 cases (20%) of pneumothorax, 4 of which required a chest tube. The other diagnostic methods in patients with a negative BLB included sputum cytology.
(1 case), bronchial aspirate (2 cases), thoracotomy (8 cases), mediastinoscopy (1 case), needle aspiration of a bronchus (1 case), bronchial aspirate (2 cases), thoracotomy (8 cases). The overall OR for a diagnostic BLB between patients with very good tolerance and those with good or limited tolerance was 2.6 (95% CI, 1.1-5.5; \( P=0.008 \)). The degree of tolerance had a positive linear relation to the BLB diagnosis \((P=0.01)\), with a likelihood ratio of 8.8 \((P=0.01)\). In patients with a positive bronchus sign, the OR for a positive result with BLB was 6.9 (95% CI, 1.5-44; \( P=0.007 \)) for neoplasms 5.8 (95% CI, 1.2-38; \( P=0.02 \)) and for nonneoplasms 2.4 (95% CI, 0.2-71; \( P=4.0 \)).

Table 4 presents the results of the BLB with fluoroscopy according to the proximity of the lesion to the pulmonary hilum and the lobe where it was located. Although most lesions were peripheral (81 cases; 49%), BLB was more effective in diagnosing intermediate or central lesions, with an OR of 3.6 (95% CI, 1.7-8; \( P=0.005 \)) and an OR of 3.5 (95% CI, 1.6-8; \( P=0.001 \)) for the neoplasms and 1.5 (95% CI, 0.3-7.5; \( P=8.0 \)) for the nonneoplasms. The number of diagnostic BLB results had a positive linear correlation to the lesion’s proximity to the pulmonary hilum \((P=0.005)\), with a likelihood ratio of 15.3 \((P<0.0001)\). Most lesions (101; 61.5%) were located in the right hemithorax, primarily in the 2 upper lobes (90 cases, 55%). These lesions mainly involved the left apicoposterior segment and the

### Table 3

Results of Bronchoscopic Lung Biopsies (BLB) with Fluoroscopy According to the Largest Diameter Size as Measured by Computed Tomography, Tolerance for the Exploration, and the Bronchus Sign

<table>
<thead>
<tr>
<th>Largest Diameter</th>
<th>Cases, No. (%)</th>
<th>Diagnostic BLBs, No. (%)</th>
<th>Neoplasms, %</th>
<th>Nonneoplasms, %</th>
<th>Diagnostic BLBs, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3 cm</td>
<td>54 (33)</td>
<td>29 (54)</td>
<td>48</td>
<td>26 (54)</td>
<td>6</td>
</tr>
<tr>
<td>&gt;3 cm</td>
<td>110 (67)</td>
<td>84 (76)</td>
<td>96</td>
<td>73 (76)</td>
<td>14</td>
</tr>
<tr>
<td>≤2 cm</td>
<td>25 (15)</td>
<td>12 (48)</td>
<td>22</td>
<td>10 (45)</td>
<td>3</td>
</tr>
<tr>
<td>&gt;2 cm</td>
<td>139 (85)</td>
<td>101 (73)</td>
<td>122</td>
<td>89 (73)</td>
<td>17</td>
</tr>
<tr>
<td>Tolerance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limited</td>
<td>36 (22)</td>
<td>18 (50)</td>
<td>33</td>
<td>18 (54)</td>
<td>3</td>
</tr>
<tr>
<td>Good</td>
<td>22 (13)</td>
<td>14 (64)</td>
<td>19</td>
<td>13 (68)</td>
<td>3</td>
</tr>
<tr>
<td>Very good</td>
<td>106 (65)</td>
<td>81 (77)</td>
<td>64</td>
<td>68 (74)</td>
<td>14</td>
</tr>
<tr>
<td>Bronchus sign</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>27 (17)</td>
<td>25 (93)</td>
<td>23</td>
<td>21 (91)</td>
<td>4</td>
</tr>
<tr>
<td>Negative</td>
<td>137 (83)</td>
<td>88 (64)</td>
<td>121</td>
<td>78 (64)</td>
<td>16</td>
</tr>
</tbody>
</table>

\(^{1}\text{P}<.05\) between patients with a diagnostic and nondiagnostic BLB
\(^{2}\text{P}<.05\) within-group comparison of the 2 diameters of the biopsied lesions
\(^{3}\text{P}<.05\) according to tolerance type
\(^{4}\text{P}<.05\) according to the presence of a positive or negative bronchus sign.

### Table 4

Results of the Bronchoscopic Lung Biopsy (BLB) With Fluoroscopy According to Location of the Lesion Relative to the Pulmonary Hilum (Central, Intermediate, and Peripheral) and the Pulmonary Lobe Involved

<table>
<thead>
<tr>
<th>Cases, No. (%)</th>
<th>Diagnostic BLBs, No. (%)</th>
<th>Neoplasms, %</th>
<th>Nonneoplasms, %</th>
<th>Diagnostic BLBs, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>37 (23)</td>
<td>28 (76)(^{+})</td>
<td>34</td>
<td>26 (76)(^{+})</td>
</tr>
<tr>
<td>Intermediate</td>
<td>46 (28)</td>
<td>40 (87)(^{+})</td>
<td>41</td>
<td>35 (85)(^{+})</td>
</tr>
<tr>
<td>Peripheral</td>
<td>81 (49)(^{+})</td>
<td>45 (55)(^{+})</td>
<td>69</td>
<td>38 (55)(^{+})</td>
</tr>
<tr>
<td>RUL</td>
<td>51 (31)(^{+})</td>
<td>33 (65)(^{+})</td>
<td>47</td>
<td>32 (68)(^{+})</td>
</tr>
<tr>
<td>ML</td>
<td>14 (7)</td>
<td>5 (45)(^{+})</td>
<td>8</td>
<td>5 (62)(^{+})</td>
</tr>
<tr>
<td>RLL</td>
<td>36 (22)(^{+})</td>
<td>28 (78)(^{+})</td>
<td>31</td>
<td>23 (74)(^{+})</td>
</tr>
<tr>
<td>LUL</td>
<td>39 (24)(^{+})</td>
<td>31 (79)(^{+})</td>
<td>36</td>
<td>28 (78)(^{+})</td>
</tr>
<tr>
<td>Lingula</td>
<td>6 (4)</td>
<td>4 (67)(^{+})</td>
<td>6</td>
<td>4 (67)(^{+})</td>
</tr>
<tr>
<td>LLL</td>
<td>21 (13)</td>
<td>12 (57)</td>
<td>16</td>
<td>7 (44)(^{+})</td>
</tr>
</tbody>
</table>

\(^{+}\text{RUL indicates right upper lobe; ML, middle lobe; RLL, right lower lobe; LUL, left upper lobe; and LLL, left lower lobe.}
\(^{1}\text{P}<.05\) between patients with a diagnostic and nondiagnostic BLB
\(^{2}\text{P}<.05\) according to the location relative to the pulmonary hilum
\(^{3}\text{P}<.05\) according to the location relative to the pulmonary hilum

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anterior and posterior segments of the right upper lobe. No differences were found in diagnosis by BLB between the 2 hemithoraces (OR=1.2; 95% CI, 0.6-2.5; \( P=7 \)), the upper and lower lobes (OR=1; 95% CI, 0.5-2; \( P=9 \)), or the upper and middle lobes (OR=2.2; 95% CI, 0.7-7; \( P=.2 \)).

Discussion

Our study showed that BLB with fluoroscopy is a useful technique in the diagnosis of localized pulmonary lesions that are not endoscopically visible because it increased the diagnostic yield of conventional bronchoscopy, such that diagnosis was achieved in 69% of the cases, regardless of etiology. The use of fluoroscopy allowed us to locate the lesions and assure sampling when neoplasia was suspected, with acceptable tolerance in most cases and a rate of serious complications under 1%. The diagnostic yield of this technique was better than the reported yields for bronchial aspirate (4%-43%; 9% in our study), bronchial brushing (12%-40%), and bronchoalveolar lavage (20%-65%). However, the yield was only equivalent or inferior to transbronchial needle aspiration (40%-80%) and sligher better than the reported results of studies using the same technique to examine peripheral neoplasms (20%-65%).

Our findings are of particular interest given that most studies that have assessed the factors influencing the bronchoscopic yield in these patients have only evaluated those etiologies they considered to be fundamental and studies of nodular lesions are scarce. We have observed an increase in the yield of BLB when pulmonary nonneoplasms are included. This increase is due to the presence of pulmonary tuberculosis—which has a greater prevalence in our practice—and localized forms of cryptogenic organizing pneumonia. The overall results of BLB reported in our country are similar though limited, confirming that the use of fluoroscopy is not widespread but rather limited to certain hospitals.

The analysis of the characteristics of the groups studied confirmed that BLB with fluoroscopy had a higher diagnostic yield for lesions that are larger, closer to the pulmonary hilum (central or intermediate), and that have airway involvement—as evidenced by the presence of the bronchus sign on the CT scan. BLB was also more effective in patients who had better tolerance, more BLBs, a lesion located in the left upper or right lower lobe, and even when endoscopy was not diagnostic, it identified areas that could be accessed for biopsy. The relation between the size of the lesion and a diagnostic BLB can be found in most studies; analyses of resected tissue samples have shown that in 60% of cases tumors less than 3 cm in diameter can only be accessed through a single bronchus while larger lesions can be reached through 3 or more bronchi. Nonetheless, in our study, diagnosis was established in 54% of cases with lesions smaller than 3 cm and in up to 48% for lesions smaller than 2 cm. These percentages are high when compared to other techniques—such as bronchial aspirate, brushing, or bronchoalveolar lavage—for similar lesions. The presence of the bronchus sign was quite important, although this should be distinguished from displacement of the bronchus as a result of external compression, submucosal growth of the tumor, or related lesions such as diseased lymph nodes, which limit access of the biopsy forceps.

Although the bronchus sign was observed in only 17% of cases, its presence is associated with diagnosis by BLB with fluoroscopy in more than 90% of cases (91% for neoplasms and 100% for nonneoplasms), which would support the use of BLB when the bronchus sign is present, regardless of etiology.

Given that no consensus exists regarding the initial approach to the solitary pulmonary nodule and several complementary endoscopic or transthoracic techniques are available, our results support the inclusion of BLB with fluoroscopy among these diagnostic approaches because it has a high diagnostic yield for both malign and benign lesions and offers the additional advantages of allowing airway exploration and better tumor staging. Nevertheless, this technique should be used in addition to transbronchial or transthoracic needle aspiration because better samples can be obtained by penetrating the lesion, especially in cases without infiltration or in which bronchial access is difficult.

Although we did not use transbronchial needle aspiration in this study, our data confirm the importance of having both BLB and transthoracic needle aspiration available. Most diagnoses were established by these 2 techniques, even when they were used as complementary tests, as shown by cases in which findings were positive even after the other was negative. The importance of BLB is also supported by an observation of fewer complications with that technique. In our study, up to 20% of lesions with a negative finding from transthoracic needle aspiration were later found to be positive by BLB with fluoroscopy, in contrast to results reported by other studies. These findings confirm the variability of diagnostic yield with all these techniques according to local factors, perhaps related to the accumulated experience and skill of the bronchoscopist, radiologist, and pathologist at each hospital. It was the demonstrated ability to obtain histologic tissue samples with few complications, even for lesions with nonneoplastic etiologies, that increased our interest in BLB. Indeed, regardless of etiology, we recommend BLB to maximize the number of diagnoses, minimize risk, and avoid more invasive procedures in which diagnosis involves greater morbidity and higher economic costs.

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