Endobronchial Needle Aspiration in the Diagnosis of Small-Cell Carcinoma

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Endobronchial biopsy specimens of small-cell carcinoma often exhibit extensive crush artifact that precludes definitive diagnosis. Occasionally, cytoplogic study from the brushings and washings is also nondiagnostic, contributing to the frustration of the bronchoscopist. We reviewed our experience with this problem over the past 4 years. We identified five cases in which an endobronchial needle aspiration proved critical in establishing the diagnosis of small-cell carcinoma. We believe endobronchial needle aspiration is a valuable adjunct in the diagnosis of endobronchial small-cell carcinoma.

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Since its introduction by Wang et al1 in the early 1980s, transbronchial needle aspiration (TBNA) via the fiberoptic bronchoscope has become a valuable adjunct in the evaluation of patients with lung cancer. The utility of TBNA in assessing mediastinal adenopathy and in staging lung cancer has been well documented.1-6 Additionally, TBNA has been shown to increase diagnostic yield in patients with submucosal or peribronchial tumors, and it can be used to sample peripheral masses with the help of fluoroscopy.7-9 By contrast, the role of endobronchial needle aspiration (EBNA) in the diagnosis of endobronchial masses is less well defined; forceps biopsy remains the preferred method of pathologic evaluation of these lesions. It has been suggested that needle aspiration of endobronchial masses is useful primarily in avoiding bleeding from friable lesions.10 However, we have recently noted several instances in which EBNA of exophytic masses played a definitive role in establishing a diagnosis of small-cell carcinoma. We describe five patients who had obstructing endobronchial masses in whom forceps biopsy specimens were nondiagnostic due to crush artifact (four cases) or sampling error (one case). In three cases, all other cytoplogic specimens were nondiagnostic; in one, a transtracheal needle aspirate was also positive; and in a fifth case, a concurrent bronchial wash of borderline adequacy was interpreted as positive after comparison with the EBNA material.

METHODS

A review of a computerized list of specimens obtained

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CASE REPORTS

CASE 1

A 49-year-old man presented with a 3-month history of cough and intermittent fever. The chest radiograph revealed left hilar fullness and left upper lobe opacification. Computed tomography scan confirmed a 6.5x7.0-cm hilar mass with associated volume loss of the left lung. Bronchoscopy demonstrated an exophytic endobronchial tumor in the apical posterior segment of the left upper lobe.

Endobronchial washing, brushing, biopsy specimens, and paratracheal TBNA were all nondiagnostic. The forceps biopsy specimen exhibited a mechanically distorted cellular infiltrate, ie, "crush artifact." Because of the high clinical suspicion of carcinoma, bronchoscopy was repeated and EBNA of the left upper lobe endobronchial lesion was performed. The EBNA specimens were diagnostic for small-cell undifferentiated carcinoma. The concurrent bronchial washing and brushing as well as multiple endobronchial forceps biopsy specimens were again nondiagnostic. A repeated transtracheal needle aspirate was also positive.

CASE 2

A 65-year-old woman presented with dyspnea, right-sided chest pain, an exudative right pleural effusion, and a right hilar mass. Pleural fluid cytologic study was negative. Subsequent bronchoscopy showed occlusion of the right lower lobe bronchus by an endobronchial lesion. A TBNA of the mediastinum was not performed. Bronchial brushing and washing were nondiagnostic. Forceps biopsy specimens were suspicious for
carcinoma, but definitive diagnosis was precluded by crush artifact. Repeated bronchial washings, brushings, and forceps biopsy specimens were again nondiagnostic. An EBNA provided material that was diagnostic of small-cell undifferentiated carcinoma.

CASE 3

An 83-year-old woman was found to have mediastinal enlargement on a chest radiograph. Computed tomography of the chest revealed a subcarinal mediastinal mass. Bronchoscopy revealed an endobronchial mass arising from the posterior wall of the bronchus intermedius. Bronchial washings, TBNA of the carina, and endobronchial forceps biopsy specimens were all nondiagnostic. Needle aspirates of the endobronchial lesion were consistent with small-cell carcinoma.

CASE 4

A 65-year-old man with a history of multiple myeloma presented with dyspnea, cough, and mild hemoptysis. Serial chest radiographs revealed progressive infiltrates on the right side despite a course of empiric antibiotic therapy. Subsequent computed tomography of the chest additionally demonstrated a large right mediastinal hilar mass. Bronchoscopy revealed narrowing of the bronchus intermedius and complete occlusion of the right middle lobe orifice by an endobronchial mass. Forceps biopsy specimens demonstrated crush artifact (Fig 1). A TBNA of the main carina and bronchial washings were negative for tumor. Repeated bronchoscopy was performed and EBNA of the endobronchial mass was positive for small-cell carcinoma (Fig 2). A bronchial wash from the second bronchoscopy was of questionable adequacy but was interpreted as positive after comparison to the EBNA material.

CASE 5

A 77-year-old man presented with a history of increasing dyspnea, malaise, weight loss, and dry cough over the preceding months. Chest radiograph and computed tomography demonstrated a large peripheral right lower lobe mass with hilar and mediastinal adenopathy. Bronchoscopy revealed extensive submucosal involvement of the right middle and lower lobe bronchi with tumor nodules protruding through the mucosa. Bronchial washings, brushings, and transcruinal needle aspirate were negative for tumor. The forceps biopsy specimen showed crush artifact. A diagnosis of small-cell carcinoma, intermediate variant, was rendered on the EBNA specimen.

DISCUSSION

Forceps biopsy is generally considered to be the method of choice in the diagnosis of exophytic endobronchial tumors because it offers the advantages of a high diagnostic yield and results in procurement of a histologic, rather than a cytologic, specimen. The yield exceeds 90 percent and approaches 100 percent when multiple biopsy specimens are obtained.11-13 Several studies have shown that in the evaluation of visible endobronchial tumors, forceps biopsies result in an equivalent or higher diagnostic yield than EBNA. Buirski et al14 studied 60 consecutive patients with proximal endobronchial tumors and reported the diagnostic yield from endobronchial forceps biopsies to be 67 percent compared with 80 percent for needle aspirates.14 This difference was not statistically significant. Lundgren et al15 found that in individuals with visible tumors, the yield of needle aspiration was 65 percent, while that of forceps biopsies was 85 percent. Conversely, Shure and Fedullo7 studied 31 patients with endoscopic abnormalities suggestive of submucosal or peribronchial tumor (without frank endobronchial lesions) and found that needle aspiration significantly increased the yield over forceps biopsy alone. Pearse and Wang16 investigated the utility of endobronchial needle aspiration using an 18-gauge needle and noted that, compared with forceps biopsy, there was less bleeding and crush artifact. Therefore, the use of EBNA in the evaluation of exophytic endobronchial lesions has been relegated mainly to friable or bleeding lesions and, in particular, to endobronchial carcinoid tumors.17 However, we report five cases that suggest that EBNA may serve as an important adjunct in the diagnosis of endobronchial small-cell carcinoma.

In all five of our patients (Table 1), the forceps

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21693/ on 06/26/2017)

**Figure 1.** Endobronchial forceps biopsy specimen. The biopsy specimen exhibits extensive crush artifact resulting in a loss of nuclear detail (hematoxylin-eosin, original magnification X300).

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21693/ on 06/26/2017)

**Figure 2.** Endobronchial needle aspirate. The aspirate smear exhibits the typical cytologic features of small-cell carcinoma, including a very high nuclear-to-cytoplasmic ratio, nuclear molding, stippled chromatin, absence of nucleoli, and single cell necrosis (Papanicolaou, original magnification X500).
Table 1—Summary of Results*

<table>
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<th>Patient</th>
<th>Biopsy</th>
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<th>Brush</th>
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*Minus sign=nondiagnostic; plus sign=diagnostic; plus/minus sign-equivocal; and NP=not performed.

biopsy specimens of an endobronchial small-cell carcinoma were nondiagnostic due to either extensive mechanical crush artifact (cases 1, 2, 4, and 5) or to sampling error (case 3). The concurrently obtained cytologic specimens were all nondiagnostic, with the exception of a transtracheal needle aspirate (case 1) and a bronchial wash of borderline adequacy (case 4). The tendency of small-cell carcinoma to undergo crush artifact when sampled by the forceps biopsy technique is well recognized in the surgical pathology literature.18-20 While the presence of crush artifact in an endobronchial forceps biopsy is strongly suggestive of small-cell carcinoma, other entities, such as benign lymphoid infiltrates and lymphoma, may exhibit similar distortion.19,21 Hence, a definitive diagnosis of small-cell carcinoma cannot be rendered on crush artifact alone. The propensity of small-cell carcinoma to show crush artifact may be related to a number of factors, including increased cell fragility, scanty cytoplasm, poorly developed desmoplastic response to tumor, altered cellular attachments, and possibly, myofibroblast contraction.20,22 The alteration in cellular attachments, as reflected in decreased cellular cohesion, may actually contribute to an increased yield by EBNA sampling. In this regard, Schenk et al23 have previously noted a significantly higher yield of TBNA in patients with small-cell carcinoma. This finding could not be accounted for solely by the propensity of this neoplasm for bulky mediastinal nodal involvement, and seemed to reflect an increased amenability of this tumor type to diagnosis by this technique.

In a recent survey of bronchoscopy performed in North America, Prakash et al24 reported that only 12 percent of practicing bronchoscopists routinely use the TBNA procedure. Inexperience with the technique, nonacceptance of specimens by pathologists, and the potential damage to the bronchoscope were cited as reasons for its low use despite the remarkably high yields, safety, and cost savings reported in the literature. Moreover, there is a limit to the number and type of specimens that can be obtained during a routine bronchoscopic procedure. The presence of bulky mediastinal adenopathy or of a paraneoplastic syndrome associated with small-cell carcinoma as well as the more extensive involvement of the bronchial tree (both endobronchial and submucosal) should suggest the possibility of small-cell carcinoma and the need for an EBNA and/or TBNA procedure. Certainly, if the initial bronchoscopic procedure is not definitive and the presence of crush artifact is found in the endobronchial biopsy specimen (as in three of our patients), the use of the EBNA procedure at repeated bronchoscopy may obviate the need for another more invasive and costly diagnostic procedure.

Needle aspiration has proven utility in staging lung cancer and in diagnosing submucosal endobronchial tumors. In addition, our cases suggest that needle aspiration can serve as a valuable diagnostic tool in evaluating exophytic intraluminal lesions, especially when small-cell carcinoma is a diagnostic consideration.

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