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Endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of lung cancer

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ABSTRACT

Purpose: We performed this study to evaluate the role of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in the pathologic diagnosis of lung cancer including lung masses as well as lymph nodes as targets.
Methods: We retrospectively reviewed 126 patients who underwent EBUS-TBNA to diagnose radiologically suspected lung cancer. The patients had masses or lymph nodes that were highly suspicious for malignancy and accessible by EBUS-TBNA.
Results: EBUS-TBNA was performed on 195 lesions (lymph nodes, $n = 151$; lung masses, $n = 44$). In 61 cases, other diagnostic methods had failed previous to EBUS-TBNA. In 118 patients, no definite endobronchial mucosal tumor invasion was observed. In eight patients with endobronchial tumor invasion, EBUS-TBNA was chosen due to tumor bleeding, necrosis, or difficult location for endobronchial biopsy. EBUS-TBNA confirmed 105 lung cancers, five other malignancies and six specific benign cases, demonstrating a diagnostic yield of 92.1% (116/126). Nine cases were diagnosed by other methods (lung cancer, $n = 2$; other malignancies, $n = 2$; benign cases, $n = 5$). One case that was not confirmed by any diagnostic method was considered false negative. The sensitivity and diagnostic accuracy of EBUS-TBNA in the diagnosis of lung cancer were 97.2% (105/108) and 97.6% (123/126), respectively.
Conclusions: EBUS-TBNA targeting lymph nodes or masses highly suspicious for malignancy demonstrated high diagnostic value in the diagnosis of lung cancer. EBUS-TBNA is recommended for these cases, especially when other diagnostic methods have failed or are difficult.

1. Introduction

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), which enables real-time aspiration of peritracheal and peribronchial lesions, has broadened the diagnostic capability of bronchoscopy. EBUS-TBNA provides good access to mediastinal and hilar lymph nodes. Therefore, it has been widely used in the mediastinal staging of lung cancer and in the diagnosis of mediastinal disease, and has demonstrated high diagnostic value in mediastinal pathology [1–8].

In addition, EBUS-TBNA is able to access lung parenchymal lesions that are adjacent to the large bronchi [9,10]. Tournoy et al. reported that EBUS-TBNA achieved a sensitivity of 82% in the diagnosis of lung cancer in centrally located lung lesions that were not visible at routine bronchoscopy [9]. Nakajima et al. utilized EBUS-TBNA to diagnose central intrapulmonary lesions that were located near central airways within the reach of EBUS-TBNA bronchoscope, and achieved a high sensitivity rate (94.1%) [10].

Considering the accessibility of EBUS-TBNA, EBUS-TBNA can be a good method for establishing a diagnosis of lung cancer. However its role in the pathologic diagnosis of lung cancer, including lymph nodes as well as lung masses as targets, has not been well estimated. The aim of this retrospective study was to evaluate the role of EBUS-TBNA in the diagnosis of lung cancer. To show the specific conditions in which EBUS-TBNA may be indicated, we also analyzed the characteristics of patients who underwent EBUS-TBNA for diagnosing lung cancer.

2. Methods

2.1. Patients

We retrospectively reviewed the records of 710 patients who underwent EBUS-TBNA in the National Cancer Center, Korea from June 2006 to February 2009. Patients who underwent EBUS-TBNA to diagnose lung cancer were enrolled for this study. Cases of radi-

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ologically suspected lung cancer on chest CT scans were included. We excluded patients who had already received a diagnosis of lung cancer by other methods and underwent EBUS-TBNA for mediastinal staging or additional tissue samples. One hundred twenty-six patients met the inclusion criteria. The Ethical Committee of our institute approved this study.

2.2. EBUS-TBNA procedure

EBUS-TBNA was performed using an ultrasonic bronchoscope with a linear scanning transducer (convex probe-EBUS, BF-UC260F-OL8, Olympus, Tokyo, Japan). The outer diameter of the insertion tube of the bronchoscope is 6.7 mm and the distal end of the bronchoscope is 6.9 mm. A dedicated ultrasound processor (EU-C2000, Olympus) was used for image processing, and needle aspiration was performed with a dedicated 22-gauge needle (NA-201SX-4022, Olympus). EBUS-TBNA was performed by two bronchoscopists (B.H. and H.S.L.). The procedure was performed with the patient under conscious sedation (midazolam) and local anesthesia (lidocaine).

EBUS-TBNA was performed to obtain samples from lung parenchymal masses or mediastinal or hilar lymph nodes that were highly suspicious for malignancy. Samples of other lymph nodes were taken when the bronchoscopist decided to perform EBUS-TBNA for mediastinal staging in the same bronchoscopy session. Procedure time was calculated from the insertion of the bronchoscope through mouth to the retrieval of the bronchoscope after the procedure. The aspirate was expelled onto glass slides (2–3 pairs of slides), smeared and immediately fixed with 95% alcohol. Tissue cores were put into a solution of 10% neutral-buffered formalin. The remnants of each aspirate from the same lesion were collected for cell-block. Smeared cytology slides were stained with hematoxylin and eosin (HE) and Papanicolaou. Tissue cores and cell-blocks were stained with HE. A pathologist (G.K.L.) who was blinded to patient details performed the cytopathologic examinations. Rapid on-site cytopathologic examination was not performed.

2.3. Data collection and outcome measures

Collected data included complications, prior diagnostic methods, location of primary tumors and target lesions, and endobronchial puncture site for target lung masses. Cytopathologic diagnosis by EBUS-TBNA and the final diagnosis were also reviewed. To evaluate the reasons for selecting EBUS-TBNA, we also reviewed findings by white-light bronchoscopy and anticipated difficulties of transthoracic needle aspiration (TTNA) for peripheral primary tumors.

Serious complications, such as mediastinitis, bleeding requiring intervention, pneumothorax, or any complications requiring hospital admission were noted. We reviewed all cytopathologic methods prior to EBUS-TBNA. Lymph node location was classified according to the Mountain and Dresler lymph node map [11]. Lobar location of parenchymal tumors was recorded. Tumors in contact with the main stem bronchi, bronchus intermedius, lobar bronchi, or segmental bronchi on chest CT scans were considered to be central tumors, otherwise tumors were considered peripheral. Findings by white-light bronchoscopy were divided into four categories: (1) no endobronchial lesions; (2) extrinsic compression without mucosal change; (3) submucosal lesions (erythema, edema, mucosal thickening, bronchial narrowing, disappearance of mucosal signs, and/or marked vascular structure) [12] without definite mucosal tumor invasion; and (4) definite mucosal tumor invasion. In cases of definite mucosal tumor invasion, the reasons for choosing EBUS-TBNA were reviewed. In cases of peripheral tumors, reasons for difficulty of TTNA were reviewed. By agreement of three interventional radiologists (H.Y.K., K.Y.L., and S.H.L.) with 5–13 years of experience in pulmonary interventional radiology, cases with severe chronic obstructive pulmonary disease (COPD) (FEV1 < 50% predicted), severe emphysema, very small tumors (long diameter < 1 cm on axial CT scans), thin cavitary nodules, or tumors in technically difficult locations (e.g., small nodules abutting the trachea) were considered to be difficult cases for TTNA.

Cytopathologic diagnoses by EBUS-TBNA were categorized as lung cancer, other malignancy, suspicious for malignancy (not confirmative), specific benign disease (e.g., sarcoidosis, tuberculosis), or non-specific benign lesions. In cases with lesions suspicious for malignancy or non-specific benign lesions, EBUS-TBNA was considered to be nondiagnostic. Those cases were subsequently confirmed by other diagnostic methods or clinical follow-up (>6 months). Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated according to the standard definitions in the diagnosis of lung cancer and in the diagnosis of malignancy.

3. Results

3.1. Patient characteristics, target lesions, and EBUS-TBNA procedures

We performed EBUS-TBNA on 195 lesions in 126 patients (Table 1, Fig. 1). No procedure-related complications were observed. Patient characteristics, target lesions, and EBUS-TBNA procedures are displayed in Tables 1 and 2. In 61 patients (48.4%), at least one cytopathologic technique ($n = 104$) was performed prior to the EBUS-TBNA bronchoscopy session, and all were nondiagnostic. The most common technique was sputum cytology ($n = 37$), which was followed by TTNA ($n = 22$), pleural effusion cytology ($n = 18$), endobronchial biopsy (EBBx, $n = 9$), bronchoscopic washing ($n = 8$), conventional transbronchial needle aspiration (TBNA, $n = 3$), transbronchial lung biopsy ($n = 3$), supraclavicular lymph node aspiration ($n = 2$), pleural biopsy ($n = 1$), and pericardial effusion cytology ($n = 1$).

Seventy-six patients had primary tumors located centrally and 39 patients had peripheral tumors. We performed EBUS-TBNA

Table 1
Patient characteristics, target lesions, and EBUS-TBNA procedures.

Characteristic	Data
No. of patients	126
Male/female, no. of patients	98/28
Age, median (range)	65.0 (27–82)
Prior diagnostic methods	
Not performed, no. of patients (%)	65 (51.6)
Performed, but nondiagnostic, no. of patients (%)	61 (48.4)
Location of target lesions, no. of lesions (%)	195
Mediastinal nodes	127 (65.1)
Hilar nodes	24 (12.3)
Masses	44 (22.6)
Target lesions, no. of patients (%)	
Mediastinal or hilar nodes only	82 (65.1)
Lymph nodes and mass	12 (9.5)
Lung mass only	32 (25.4)
Location of primary tumors and target lesions sampled by EBUS-TBNA	
Central tumor, no. of patients (%)	76 (60.3)
Targeting lung mass	41
Targeting lymph nodes only	35
Peripheral tumor, no. of patients (%)	39 (31.0)
Targeting lung mass	3
Targeting lymph nodes only	36
Lymph nodes only, no. of patients (%)	11 (8.7)
Targeting lymph nodes	11
Procedure time, mean min (range)	14.3 (4–48)
Aspirations per lesion, mean (range)	2.4 (1–6)