Introduction

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) was introduced in 1991, initially used in gastrointestinal lesions, and later extended for many other indications, including mediastinal lesions. EUS-FNA can provide tissue diagnosis in lung cancer where bronchoscopy is non-diagnostic. It is useful as a minimally invasive method for staging of non-small cell lung cancer (NSCLC). EUS-FNA can also provide tissue diagnosis of mediastinal mass of unknown origin. It is a minimally invasive procedure compared with invasive procedures such as mediastinoscopy and thoracotomy. However, very few data have been reported from Eastern countries. We hereby report our experience of using EUS-FNA for tissue proof of lung and mediastinal lesions.
Methods

From June 2005 to June 2009, a retrospective analysis of prospectively collected data of 20 cases of lung and mediastinal lesions was performed. Twenty patients with 21 EUS-FNAs of lung and mediastinal lesions after bronchoscopy and computed tomography (CT)-guided (Case 18) FNA biopsy were enrolled for tissue diagnosis and staging of NSCLC, both N staging (Figure 1) and M staging (Figure 2).

After informed written consent was obtained and patients had fasted for 8 hours, EUS-FNA was performed with a linear echoendoscope (GF-UCT2000, EUC2000 unit; Olympus, Tokyo, Japan). The FNA needle set was fixed at the working channel of the endoscope. With no intervening vascular structure

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Figure 1. Adenocarcinoma of the right lung, proven by EUS-FNA of subcarinal lymph node, enabling a staging of IIIA. Computed tomography shows: (A) right lung tumor (arrow); (B) subcarinal lymph node (N2) metastasis (arrow). (C) EUS-FNA (arrow). Adenocarcinoma is shown on: (D) cytology (arrow; 400×); (E) cell block (arrow; 400×).

Figure 2. Left lung adenocarcinoma with left adrenal gland metastasis, proven by EUS-FNA, enabling a staging of M1. (A) Metastatic left adrenal gland, 1.2 cm in size (arrow). (B) EUS-FNA of the left adrenal gland (arrow). Adenocarcinoma is shown on: (C) cytology (arrow; 400×); (D, E) EUS-FNA biopsy histology (arrows; 400×).
between the lesion and the scope after turning on the color Doppler, the needle was pushed into the lesion with a thrust. The stylet was removed, and the needle was connected with a 10–20-mL syringe using negative pressure for aspiration. The 22- or 25-gauge needle (Echotip; Cook Endoscopy, Winston Salem, NC, USA) was moved back and forth for 10–20 seconds, withdrawn into the catheter, and then the whole needle set was removed from the endoscope. The aspirated material was obtained by pushing the stylet into the needle, and the tissue was sent for cytology and histology.

The cytology smear was fixed with 98% alcohol. EUS-guided Tru-Cut biopsy with a 19-gauge Quick Core needle (Cook Endoscopy) was performed in addition to EUS-FNA (Case 19). There was no onsite cytopathologist. The sites of EUS-FNA are listed in Table 1. All EUS-FNA procedures were done from the esophagus (posterior mediastinum), where the locations of the lymph nodes are stations 5, 7 and 8, and direct lung puncture of EUS-FNA were also undertaken from the esophagus, where the lesions were close to the esophagus.

Pathology and malignancy were proven by FNA biopsy results, mediastinoscopy when performed, or by clinical outcome and follow-up for more than 6 months. Mediastinal lymph node location was classified according to the American Thoracic Society system. N2 is the ipsilateral mediastinal lymph node metastasis, and N3 is the contralateral mediastinal lymph node metastasis. Station 5 is the aortopulmonary window, station 7 the subcarinal region, and station 8 the paracardiac region below the subcarina.

**Results**

Table 1 shows the results of EUS-FNA for the lung and mediastinal lesions. There were 20 cases (19 males;
1 female); mean age was 63.9 ± 12.6 years. Median lung and mediastinum tumor size was 2.6 cm (range, 1.8–5.0 cm), and median number of punctures was 3 (range, 2–7).

There were 21 EUS-FNA punctures in the 20 cases: 18 EUS-FNA punctures (3 cases at station 5, 10 cases at station 7, and 5 cases at station 8) were performed at the mediastinum; 2 were performed directly on lung masses (Cases 13 and 15, Figure 3); and 1 was performed for metastasis (M) in the left adrenal gland. A second EUS-FNA was done in 1 patient (Case 11) with a negative initial result. The final diagnoses of the cases were: 6 small cell carcinoma of the lung, 5 adenocarcinoma of the lung, 4 squamous cell carcinoma of the lung, 1 giant cell carcinoma (poorly differentiated carcinoma) of the lung, 2 sarcoidosis (Figure 4), 1 schwannoma, and 1 organized pneumonia.

Of the 16 EUS-FNA-positive cases (including the second EUS-FNA in Case 11), 12 were for diagnosis, 3 were for both diagnosis and staging (N2 lymph node staging and M1 staging for left adrenal gland metastasis), and 1 was for N2 lymph node staging. In the 16 EUS-FNA cases positive for malignancy, 1 had a positive bronchoscopic biopsy result (Case 16), and another had pleural effusion cytology suspicious for small cell carcinoma (Case 2), and EUS-FNA was able to diagnose the remaining 14 cases of tumors, making a tissue diagnosis of 87.5% (14/16 cases). In the 16 EUS-FNA punctures, all had adequate tissue for FNA biopsy except for Case 14. Twelve cases had immunohistochemical staining done (including 1 with Tru-Cut biopsy). Four cases were EUS-FNA-negative for malignancy: 1 true negative (organized pneumonia), and 3 false negatives (1 sarcoidosis, 1 lung cancer, and 1 lung cancer post chemoradiation therapy).

The sensitivity, specificity, and diagnostic accuracy of mediastinum and lung EUS-FNA were 84.2%, 100%, and 85%, respectively. Excluding EUS-FNA performed directly on lung masses (right upper lung and right lower lung), the median mediastinal tumor size was 2.5 cm (range, 1.8–4.5 cm), and the median number of mediastinal mass punctures was 3 (range, 2–7), with a sensitivity, specificity, and diagnostic accuracy of 83.3%, 100%, and 83.3%, respectively.

In the EUS-FNA-negative cases, Case 1 was a documented case of squamous cell carcinoma by bronchoscopy before combined chemoradiation therapy, who was shown to have residual tumor by follow-up after negative EUS-FNA. Sarcoidosis was diagnosed by mediastinoscopy in Case 5, by surgery in Case 6, and by clinical course in Case 15. Case 12 was the patient who had EUS-FNA done in 2 regions, 1 in region 7 and the other in the left adrenal gland; both EUS-FNAs were positive for malignancy. There were no complications in our series.

**Discussion**

Treatment strategies for lung cancers are dependent on histology (small cell vs. non-small cell) and the presence of mediastinal or distant spread of the tumor.

![Figure 3](image-url)
A classification for lung cancer staging has been described by the American Joint Committee on Cancer for NSCLC. Metastases to ipsilateral and subcarinal nodes (N2) is classified as stage IIIA disease, the management of which is controversial (presurgical chemotherapy followed by surgery), whereas treatment of stage IIIB (metastasis to contralateral mediastinal nodes, N3) is usually chemoradiation without surgery. EUS-FNA can obtain a tissue diagnosis in suspected NSCLC with mediastinal lymph node seen on CT when transbronchial biopsy is non-diagnostic. In our series, EUS-FNA obtained a tissue diagnosis in 14 of 16 cases where bronchoscopic results were non-diagnostic.

CT is a noninvasive and widely used staging method for mediastinal lymph node in NSCLC, with a sensitivity and specificity of 70%. Positron emission tomography with fluorodeoxyglucose has an accuracy of 85% and is noninvasive as well, but gives false-negative results in lymph nodes with low metabolic activity or when the size is < 1 cm. Positron emission tomography can also give false-positive results when lymph nodes have high metabolic activity, such as in cases of pneumonia and granulomatous diseases. Bronchoscopy and transbronchial biopsy has a sensitivity of 53–70%, but it is not accessible to aortopulmonary window lymph nodes (station 5) and the inferior mediastinal region (station 8). Mediastinoscopy and thoracoscopy are invasive, costly, and require general anesthesia. Mediastinoscopy cannot access lymph nodes in stations 5 and 8, and had a higher morbidity of 16% and 1 mortality. In contrast, EUS-FNA is safe and effective, and can easily approach lymph nodes in stations 5, 7 and 8. In our series, the most common stations of mediastinal lymph nodes that underwent EUS-FNA, in order of frequency, were stations 7, 8, and then 5 (Table 1). In our 16 positive EUS-FNA cases (including the second EUS-FNA in Case 11), 12 were for diagnosis, 3 were for both diagnosis and staging (2 cases of N2 lymph node establishing a stage of IIIA in Cases 4 and 8, and 1 M1 staging in the left adrenal gland metastasis in Case 12), and 1 was for N2 lymph node staging in Case 16. The smallest size of positive EUS-FNA was the left adrenal gland metastasis, which was 1.2 cm in size. In a meta-analysis of 18 studies of EUS-FNA staging of mediastinal lymph nodes in NSCLC, the pooled sensitivity and specificity were 83% and 97%, respectively, with a minor complication rate of only 0.8%. In our series, the sensitivity and specificity of EUS-FNA of mediastinal lymph nodes were 83.3% and 100%, respectively (excluding 2 cases of direct

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**Figure 4.** Sarcoidosis diagnosed by EUS-FNA. (A) Chest X-ray shows enlarged hilar lymph node (arrow). (B) Computed tomography shows enlarged mediastinal lymph nodes (arrows). (C) EUS-FNA of mediastinal lymph node, station 7 (arrow). Non-caseating granuloma is shown on: (D) cytology (arrow; 400×); (E) EUS-FNA biopsy (arrow; 400×).
lung punctures), with no complications. EUS-FNA can also detect malignant mediastinal lymph nodes in CT-negative patients, ranging from 22% to 44%.10,31

EUS-FNA can obtain a tissue diagnosis by directly puncturing the lung tumor close to the esophagus;25,32 we had 2 cases in which EUS-FNA was performed directly through the lung mass from the esophagus, which presented as right upper and right lower lung masses located close to the esophagus. CT-guided lung tumor biopsy is invasive and can be complicated by pneumothorax and hemoptysis.33 A case of transaortic EUS-FNA of lung tumor using a 25-gauge needle without complications has been reported.34

Wallace et al reported a complete mediastinoscopy by combining EUS-FNA and endobronchial ultrasound-guided FNA (EBUS-FNA), which could achieve 93% sensitivity in staging mediastinal lymph nodes, instead of 69% sensitivity for each procedure alone.35

EUS-FNA is also useful for diagnosis in mediastinal lymph nodes of unknown etiology.22 We had a case of sarcoidosis (Case 19) that was diagnosed by EUS-FNA; in that case, we also performed EUS-guided Tru-Cut biopsy, which could be helpful in cases missed by EUS-FNA.36

Not being a prospective study and the relatively small number of cases in this series are the study’s limitations.

In conclusion, EUS-FNA, a minimally invasive endoscopic procedure, is safe and effective for tissue diagnosis when bronchoscopy results are non-diagnostic, for mediastinal lymph node (N) and metastasis (M) staging in NSCLC, and for diagnosis in mediastinal lymph nodes with unknown etiology.

References


