Role of Endoscopic Ultrasound-guided Fine-needle Aspiration in Lung and Mediastinal Lesions

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Background: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) was initially introduced for diagnosing gastrointestinal and pancreatic lesions, and later on for lung and mediastinal lesions. It can provide tissue diagnosis of lung cancer where bronchoscopy is non-diagnostic. It is a minimally invasive method for lymph node (N) and metastasis (M) staging of non-small cell lung cancer, and is helpful for tissue proof of mediastinal mass with unknown origin. Few data on this topic have been reported from Eastern countries. We report our experience of using EUS-FNA for tissue proof of lung and mediastinal lesions.

Methods: This was a retrospective analysis of prospectively collected data of 20 cases, with 21 EUS-FNAs of lung and mediastinal lesions (1 EUS-FNA performed on left adrenal gland) for tissue diagnosis and staging. With patients' informed written consent and fasting for 8 hours, EUS-FNA was performed with a linear echoendoscope using a 22- or 25-gauge needle and a syringe with 10–20 mL negative pressure. The cytology smear was fixed with 98% alcohol, while cell-block and tissue were sent for histology. There was no onsite cytopathologist. EUS-guided Tru-Cut biopsy was performed in 1 case. Malignancy was proven by FNA biopsy results, mediastinoscopy when performed, or by clinical course and follow-up.

Results: Of the 20 cases, 19 were male and 1 was female; mean age was 63.9 ± 12.6 years. Median tumor size was 2.6 cm (range, 1.8–5.0 cm), and median number of punctures was 3 (range, 2–7). Eighteen EUS-FNA punctures were performed at the mediastinum, and 2 directly on lung mass. The size of the left adrenal metastasis for extramediastinal EUS-FNA was 1.2 cm. Of the 16 EUS-FNA-positive cases, 12 were for tissue diagnosis, 3 were for both tissue diagnosis and staging (N2 and M1 staging), and 1 was for N2 staging. EUS-FNA provided a tissue diagnosis in 14 cases where bronchoscopy was negative. In 16 positive EUS-FNAs, all except 1 had adequate tissue for FNA biopsy. The sensitivity, specificity, and diagnostic accuracy of EUS-FNA were 84.2%, 100%, and 85%, respectively.

Conclusion: EUS-FNA can diagnose lung cancer by confirmation of mediastinal lymph node metastasis, by direct puncture of lung tumor close to the esophagus. It is useful for lymph node (N) stations 5, 7, 8 and metastasis (M) staging in non-small cell lung cancer, and for the diagnosis of mediastinal mass of unknown etiology. [*J Chin Med Assoc* 2010;73(10):523–529]

Key Words: endoscopic ultrasound-guided fine-needle aspiration, mediastinum, non-small cell lung cancer

Introduction

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) was introduced in 1991,[1] initially used in gastrointestinal lesions,[2–4] and then later extended for many other indications, including mediastinal lesions.[5] EUS-FNA can provide tissue diagnosis in lung cancer where bronchoscopic biopsy is non-diagnostic.[5] It is useful as a minimally invasive method for staging of non-small cell lung cancer (NSCLC).[6–21] EUS-FNA can also provide tissue diagnosis of mediastinal mass of unknown origin.[22,23] It is a minimally invasive procedure for obtaining tissue diagnosis 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 EUS-FNA for lung and mediastinal lesions (lung cancers, sarcoidosis, neurogenic tumors).

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E-mail: aucardla@yahoo.com.tw • Received: November 30, 2009 • Accepted: July 1, 2010

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

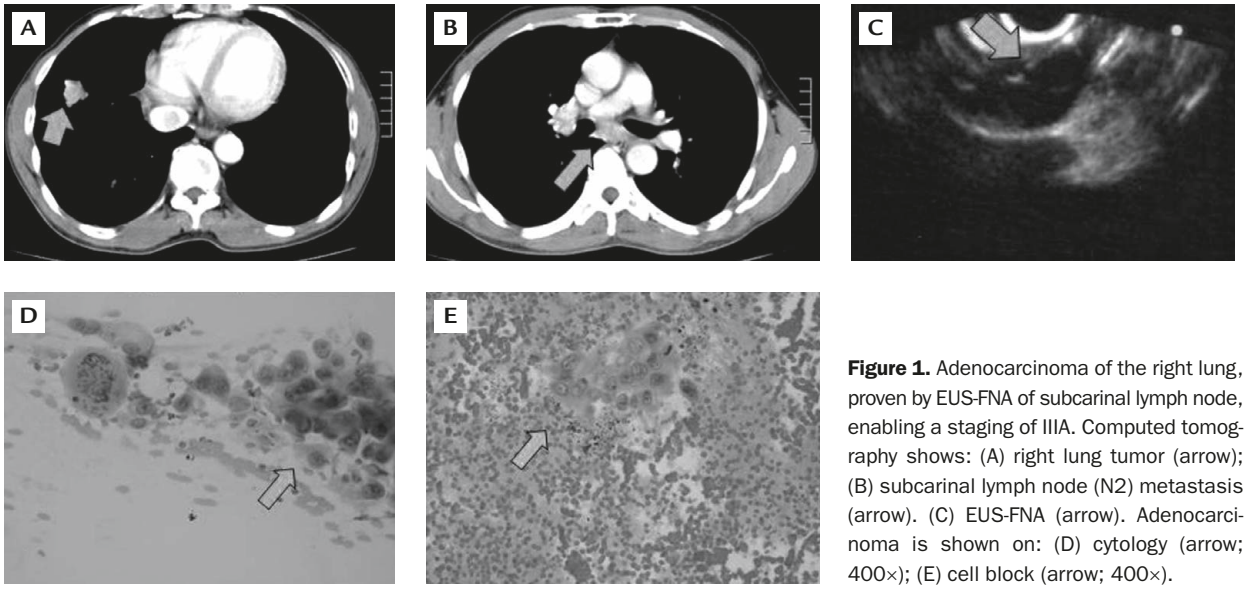

Figure 1. Adenocarcinoma of the right lung, proven by EUS-FNA of subcarinal lymph node, enabling a staging of IIIA. Computed tomography shows: (A) right lung tumor (arrow); (B) subcarinal lymph node (N2) metastasis (arrow). (C) EUS-FNA (arrow). Adenocarcinoma is shown on: (D) cytology (arrow; 400×);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

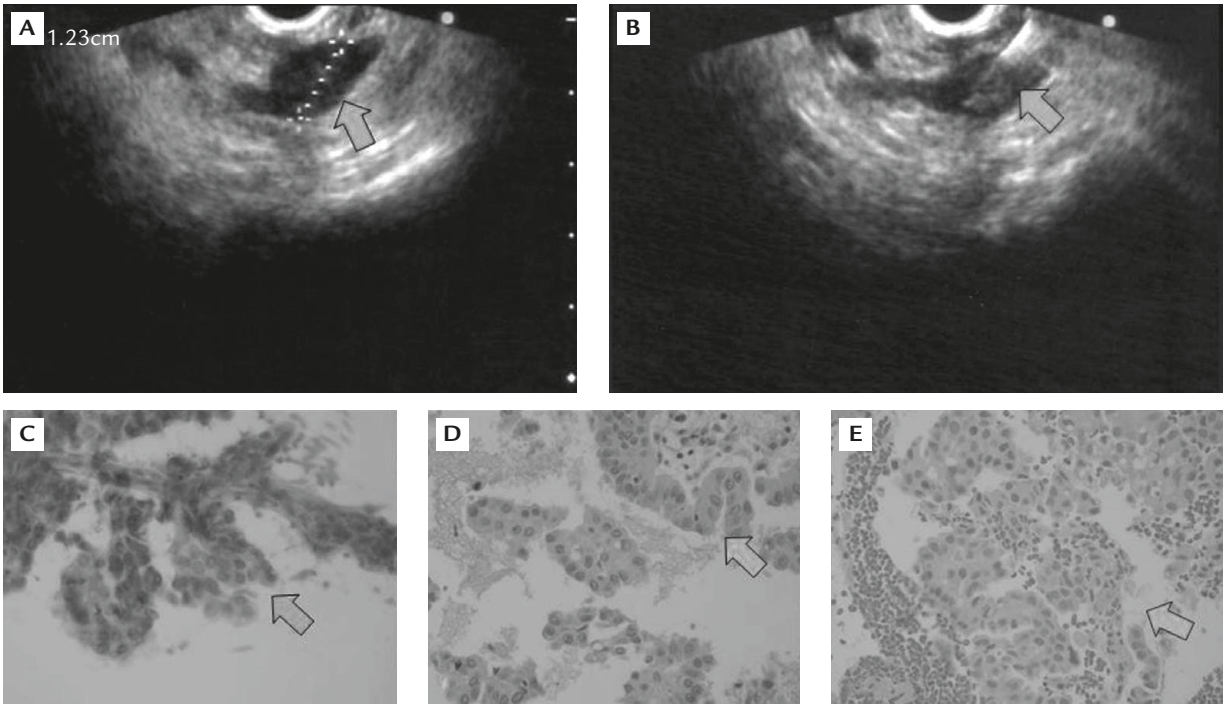

Figure 2. Left lung adenocarcinoma with left adrenal gland metastasis, proven by EUS-FNA, enabling a staging of M1. (A) Metastatic left adrenal gland, 1.2 cm in size (arrow). (B) EUS-FNA of the left adrenal gland (arrow). Adenocarcinoma is shown on: (C) cytology (arrow; 400×); (D, E) EUS-FNA biopsy histology (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.[24] 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 paraesophageal 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;

Table 1. Result of endoscopic ultrasound-guided fine-needle aspiration of lung and mediastinal lesions

Case	Sex	Age (yr)	Lesion location	EUS-FNA site	Size (cm)	Punctures (*n*)	FNA	FNAB	Cell block	Diagnosis
1	M	67	RUL	Media station 7	2.6	2	–ve	No tissue	–ve	Squamous cell carcinoma of lung, post CCRT
2	M	51	RUL	Media station 5	2	3	+ve	+ve	+ve	Small cell carcinoma of lung (bronchoscopic cytology suspicious)
3	M	74	RML	Media station 7	3.8	2	+ve	+ve	+ve	Extensive small cell carcinoma of lung
4	M	79	RML	Media region 8	4.5	2	+ve	+ve	+ve	Squamous cell carcinoma of lung*
5	M	55	Media	Media station 8	2.2	3	–ve	–ve	–ve	Sarcoidosis
6	M	58	LUL	Media station 8	2.3	3	–ve	–ve	–ve	Adenocarcinoma of lung
7	M	54	LUL	Media station 7	2	3	+ve	+ve	+ve	Small cell carcinoma of lung
8	M	55	LLL	Media station 8	2	3	+ve	+ve	+ve	Adenocarcinoma of lung*
9	M	69	RLL	Media station 7	3.2	2	+ve	+ve	+ve	Small cell carcinoma of lung
10	M	69	RLL	Media station 8	2.8	4	+ve	+ve	+ve	Small cell carcinoma of lung
11	M	81	Media	Media station 5†	3.5	3	+ve	+ve	+ve	Schwannoma
12	F	76	LLL	Media station 7‡	2	3	+ve	+ve	+ve	Adenocarcinoma of lung, left adrenal metastasis
13	M	76	RUL	RUL tumor	5	5	+ve	+ve	+ve	Giant cell tumor
14	M	49	RUL	Media station 7	1.8	4	+ve	–ve	+ve	Adenocarcinoma of lung
15	M	34	RLL	RLL tumor	3.7	4	–ve	–ve	–ve	Organized pneumonia
16	M	63	LLL	Media station 5	2.4	5	+ve	+ve	+ve	Adenocarcinoma of lung§
17	M	76	LLL	Media station 7	2	7	+ve	+ve	+ve	Squamous cell carcinoma of lung
18	M	74	RLL	Media station 7‖	2.7	3	+ve	+ve	+ve	Small cell carcinoma of lung
19	M	50	Media	Media station 7	2.5	6	+ve	+ve	+ve	Sarcoidosis
20	M	68	LUL	Media station 7	3.2	4	+ve	+ve	+ve	Squamous cell carcinoma of lung

**For both tissue diagnosis and N2 staging; †second EUS-FNA positive for malignancy; ‡EUS-FNA for M1 staging (left adrenal gland, 1.2 cm in size); §for N2 staging; ‖negative computed tomography-guided FNAB. EUS-FNA = endoscopic ultrasound-guided fine-needle aspiration; FNAB = FNA biopsy; RUL = right upper lung; Media = mediastinum; CCRT = combined chemoradiation therapy; RML = right middle lobe; LUL = left upper lung; LLL = left lower lung; RLL = right lower lung.*

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.

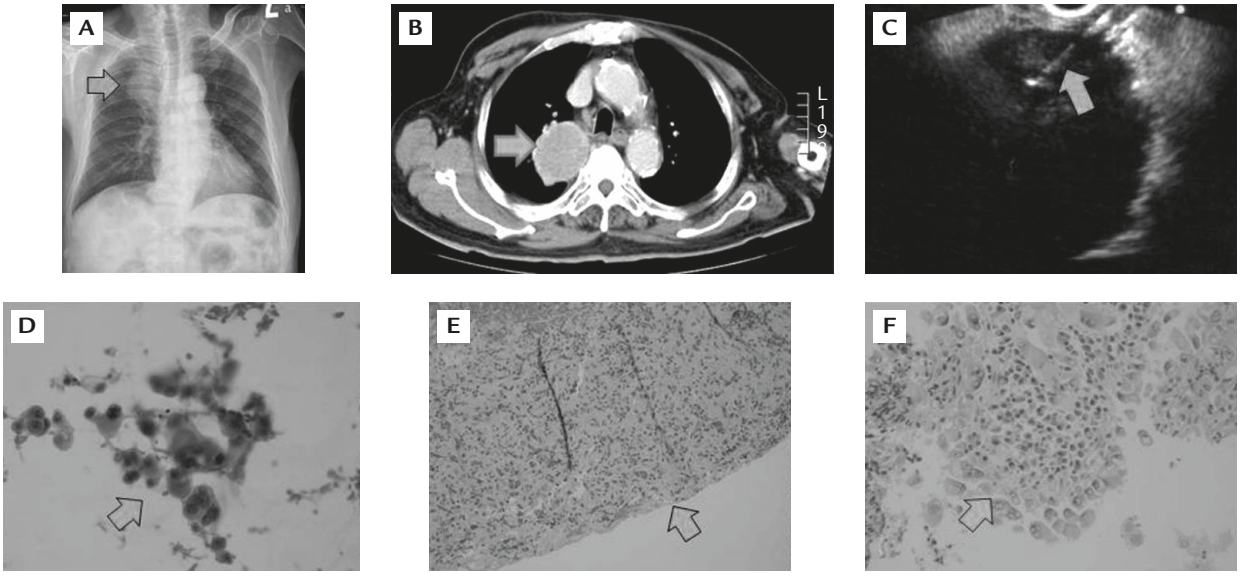

Figure 3. Right lung tumor close to the esophagus, proven by EUS-FNA to be giant cell carcinoma. Right lung tumor is seen on: (A) chest X-ray (arrow); (B) computed tomography (arrow). (C) EUS-FNA directly on the lung tumor (arrow). (D) Cytology reveals malignant cells (arrow; 400×). (E, F) Giant cell carcinoma is diagnosed by EUS-FNA biopsy histology (arrows).

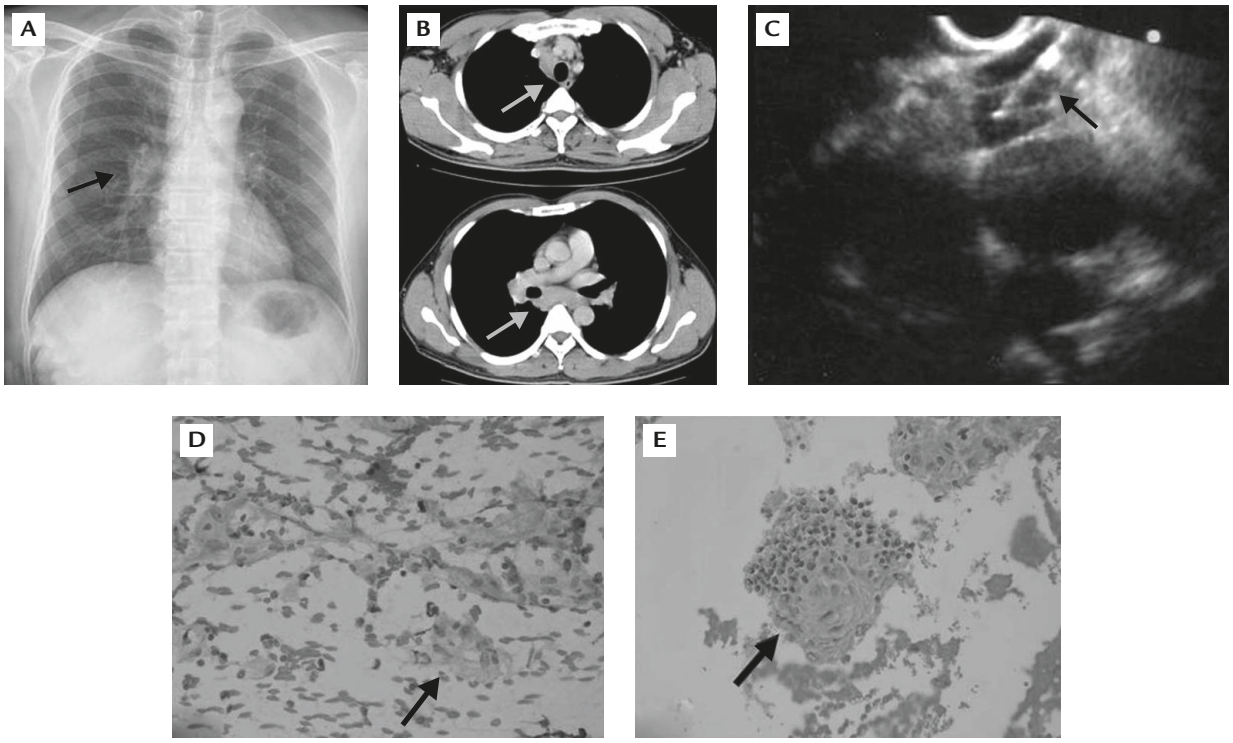

Figure 4. Sarcoidosis diagnosed by EUS-FNA. (A) Chest X-ray shows enlarged hilar lymph node (arrow). (B) Computed tomography shows enlarged mediastinal lymph nodes (arrows). (C) EUS-FNA of mediastinal lymph node, station 7 (arrow). Non-caseating granuloma is shown on: (D) cytology (arrow; 400×); (E) EUS-FNA biopsy (arrow; 400×).

A classification for lung cancer staging has been described by the American Joint Committee on Cancer[24] 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.[5,7,23] 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%.[25–27] 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.[28] 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).[29] 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.[30] In contrast, EUS-FNA is safe and effective, and can easily approach lymph nodes in stations 5, 7 and 8.[10] 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%.[21] 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

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 bronchoscopic 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

1. Caletti GC, Brocchi E, Ferrari A, Bonora G, Santini D, Mazzoleni G, Barbara L. Guillotine needle biopsy as a supplement to endosonography in the diagnosis of gastric submucosal tumors. *Endoscopy* 1991;23:251–4.
2. Vilmann P, Jacobsen GK, Henriksen FW, Hancke S. Endoscopic ultrasonography with guided fine-needle aspiration biopsy in pancreatic disease. *Gastrointest Endosc* 1992;38:172–3.
3. Grimm H, Binmoeller KF, Soehendra N. Endosonography-guided drainage of a pancreatic pseudocyst. *Gastrointest Endosc* 1992;38:170–1.
4. Wiersema MJ, Wiersema LM. Endosonography-guided celiac plexus neurolysis. *Gastrointest Endosc* 1996;44:656–62.
5. Fickling W, Wallace MB. EUS in lung cancer. *Gastrointest Endosc* 2002;56:S18–21.
6. Silvestri GA, Hoffman BJ, Bhutani MS, Hawes RH, Coppage L, Sanders-Cliette A, Reed CE. Endoscopic ultrasound with fine-needle aspiration in the diagnosis and staging of lung cancer. *Ann Thorac Surg* 1996;61:1441–5.
7. Gress FG, Savides TJ, Sandler A, Kesler K, Conces D, Cummings O, Mathur P, et al. Endoscopic ultrasonography, fine-needle aspiration biopsy guided by endoscopic ultrasonography, and computed tomography in the preoperative staging of non-small-cell lung cancer: a comparison study. *Ann Intern Med* 1997;127:604–12.
8. Wiersema MJ, Vazquez-Sequeiros E, Wiersema LM. Evaluation of mediastinal lymphadenopathy with endoscopic US-guided fine-needle aspiration biopsy. *Radiology* 2001;219:252–7.
9. Larsen SS, Krasnik M, Vilmann P, Jacobsen GK, Pedersen JH, Faurschou P, Folke K. Endoscopic ultrasound-guided biopsy of mediastinal lesions has a major impact on patient management. *Thorax* 2002;57:98–103.
10. Fritscher-Ravens A, Bohuslavizki KH, Brandt L, Bobrowski C, Lund C, Knöfel WT, Pforte A. Mediastinal lymph node involvement in potentially resectable lung cancer: comparison of CT, positron emission tomography, and endoscopic ultrasonography with and without fine-needle aspiration. *Chest* 2003;123:442–51.
11. Kramer H, van Putten JW, Post WJ, van Dullemen HM, Bongaerts AH, Pruim J, Suurmeijer AJ, et al. Oesophageal endoscopic ultrasound with fine-needle aspiration improves and simplifies the staging of lung cancer. *Thorax* 2004;59:596–601.
12. Wallace MB, Ravenel J, Block MI, Fraig M, Silvestri G, Wildi S, Schmulewitz N, et al. Endoscopic ultrasound in lung cancer patients with a normal mediastinum on computed tomography. *Ann Thorac Surg* 2004;77:1763–8.
13. Savides TJ, Perricone A. Impact of EUS-guided FNA of enlarged mediastinal lymph nodes on subsequent thoracic surgery rates. *Gastrointest Endosc* 2004;60:340–6.
14. Larsen SS, Vilmann P, Krasnik M, Dirksen A, Clementsen P, Skov BG, Jacobsen GK. Endoscopic ultrasound-guided biopsy versus mediastinoscopy for analysis of paratracheal and subcarinal lymph nodes in lung cancer staging. *Lung Cancer* 2005;48:85–92.
15. LeBlanc JK, Devereaux BM, Imperiale TF, Kesler K, DeWitt JM, Cummings O, Ciaccia D, et al. Endoscopic ultrasound in non-small cell lung cancer and negative mediastinum on computed tomography. *Am J Respir Crit Care Med* 2005;171:177–82.
16. Tournoy KG, Praet MM, Van Maele G, Van Meerbeeck JP. Esophageal endoscopic ultrasound with fine-needle aspiration with an on-site cytopathologist: high accuracy for the diagnosis of mediastinal lymphadenopathy. *Chest* 2005;128:3004–9.
17. Eloubeidi MA, Cerfolio RJ, Chen VK, Desmond R, Syed S, Ojha B. Endoscopic ultrasound-guided fine-needle aspiration of mediastinal lymph node in patients with suspected lung cancer after positron emission tomography and computed tomography scans. *Ann Thorac Surg* 2005;79:263–8.
18. Annema JT, Versteegh MI, Veseliç M, Voigt P, Rabe KF. Endoscopic ultrasound-guided fine-needle aspiration in the diagnosis and staging of lung cancer and its impact on surgical staging. *J Clin Oncol* 2005;23:8357–61.
19. Caddy G, Conron M, Wright G, Desmond P, Hart D, Chen RY. The accuracy of EUS-FNA in assessing mediastinal lymphadenopathy and staging patients with NSCLC. *Eur Respir J* 2005;25:410–5.
20. Vilmann P, Herth F, Krasnik M. State of the art lecture: mediastinal EUS. *Endoscopy* 2006;38:S84–7.
21. Micames CG, McCrory DC, Pavey DA, Jowell PS, Gress FG. Endoscopic ultrasound-guided fine-needle aspiration for non-small cell lung cancer staging: a systematic review and meta-analysis. *Chest* 2007;131:539–48.
22. Catalano MF, Nayar R, Gress F, Scheiman J, Wassef W, Rosenblatt ML, Kochman M. EUS-guided fine-needle aspiration in mediastinal lymphadenopathy of unknown etiology. *Gastrointest Endosc* 2002;55:863–9.
23. Savides TJ. EUS for mediastinal disease. *Gastrointest Endosc* 2009;69:S97–9.
24. Mountain CF, Dresler CM. Regional lymph node classification for lung cancer staging. *Chest* 1997;111:1718–23.

25. McKenna RJ Jr, Libshitz HI, Mountain CE, McMurtrey MJ. Roentgenographic evaluation of mediastinal nodes for preoperative assessment in lung cancer. *Chest* 1985;88:206–10.
26. McLoud TC, Bourgouin PM, Greenberg RW, Kosiuk JP, Templeton PA, Shepard JA, Moore EH, et al. Bronchogenic carcinoma: analysis of staging in the mediastinum with CT by correlative lymph node mapping and sampling. *Radiology* 1992; 182:319–23.
27. Arita T, Kuramitsu T, Kawamura M, Matsumoto T, Matsunaga N, Sugi K, Esato K. Bronchogenic carcinoma: incidence of metastases to normal sized lymph nodes. *Thorax* 1995;50:1267–9.
28. Vansteenkiste JF, Mortelmans LA. FDG-PET in the locoregional lymph node staging of non-small cell lung cancer: a comprehensive review of the Leuven Lung Cancer Group experience. *Clin Pos Imaging* 1999;2:223–31.
29. Harrow EM, Abi-Saleh W, Blum J, Harkin T, Gasparini S, Addrizzo-Harris DJ, Arroliga AC, et al. The utility of transbronchial needle aspiration in the staging of bronchogenic carcinoma. *Am J Respir Crit Care Med* 2000;161:601–7.
30. Best LA, Munichor M, Ben-Shakhar M, Lemer J, Lichtig C, Peleg H. The contribution of anterior mediastinotomy in the diagnosis and evaluation of diseases of the mediastinum and lung. *Ann Thorac Surg* 1987;43:78–81.
31. Wallace MB, Silvestri GA, Sahai AV, Hawes RH, Hoffman BJ, Durkalski V, Hennesey WS, et al. Endoscopic ultrasound-guided fine-needle aspiration for staging patients with carcinoma of the lung. *Ann Thorac Surg* 2001;72:1861–7.
32. Sawhney MS, Kratzke RA, Lederle FA, Holmstrom AM, Nelson DB, Kelly RF. EUS-guided FNA for the diagnosis of advanced lung cancer. *Gastrointest Endosc* 2006;63:959–65.
33. Cheung YC, Chang JW, Hsieh JJ, Lin G, Tsai YH. Adequacy and complications of computed tomography-guided core needle biopsy on non-small cell lung cancers for epidermal growth factor receptor mutations demonstration: 18-gauge or 20-gauge biopsy needle. *Lung Cancer* 2010;67:166–9.
34. Wallace MB, Woodward TA, Raimondo M, Al-Haddad M, Odell JA. Transaortic fine-needle aspiration of centrally located lung cancer under endoscopic ultrasound guidance: the final frontier. *Ann Thorac Surg* 2007;84:1019–21.
35. Wallace MB, Silvestri GA, Sahai AV, Hawes RH, Hoffman BJ, Durkalski V, Hennesey WS, et al. Endoscopic ultrasound-guided fine-needle aspiration for staging patients with carcinoma of the lung. *Ann Thorac Surg* 2001;72:1861–7.
36. Eloubeidi MA, Mehra M, Bean SM. EUS-guided 19-gauge Tru-Cut needle biopsy for diagnosis of lymphoma missed by EUS-guided FNA. *Gastrointest Endosc* 2007;65:937–9.