

EUS-guided fine needle tissue acquisition for the diagnosis of pleural metastases from endometrial cancer

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Abstract. – Transesophageal EUS-FNA have become a useful tool in the evaluation of the mediastinum, especially during the staging work-up examination of patients with non-small-cell lung cancer (NSCLC) or other malignancies. We report a challenging case of a 53 years-old woman with an endometrial adenocarcinoma who subsequently presented with right pleural effusion, diffuse pleural thickening with few pleural lesions. The patient referred a long history of exposure to amiantum, this posing a differential diagnosis between primary pleural tumour (mesothelioma) and neoplastic pleural localization of the endometrial cancer. The cytological examination of the pleural effusion (sampled via thoracentesis) was not adequate to reach a diagnosis. Although a right-video-assisted thoracoscopy was considered the gold standard in this clinical setting to achieve a tissue acquisition of the pleura, an EUS (as the least invasive procedure) was attempted to reach a definitive diagnosis. EUS-FNTA of the pleura was done using a 19-Gauge needle and the pathological and immunophenotypic features were diagnostic for a pleural metastasis of high-grade endometrial serous carcinoma. The patient received adjuvant chemotherapy with a complete regression of the pleural lesions. We take the opportunity of this challenging case to discuss the efficacy and safety of EUS-FNAT to sample the pleural lesions with the use of a large calibre needle if the lesion lies just under the EUS cursor. We may assume that, in selected patients, this technique could be presented as a viable option to the more invasive surgical procedure, which has been previously the gold standard for the pleural tissue acquisition.

Key Words:

Pleural metastases, EUS-FNA, Endometrial adenocarcinoma.

Introduction

Endoscopic Ultrasound-Guided Fine Needle Aspiration (EUS-FNA) has become an indispensable diagnostic modality for non-small cell lung cancer (NSCLC) diagnosis and staging and tissue diagnosis of mediastinal masses and/or lymphadenopathy of unknown origin¹⁻³. EUS detection and sampling of small pleural effusions are additional procedures described in the mediastinum⁴⁻⁶ and recently there have been reports of the feasibility of a EUS-guided biopsy and FNA of the pleura for suspicious tuberculosis and metastases from pancreatic cancer, respectively^{7,8}. We present an additional patient with an endometrial cancer who subsequently presented with pleural lesions that were diagnoses as metastases by EUS-fine needle tissue acquisition (EUS-FNTA).

Case Report

The patient is a 53 year-old woman who underwent laparotomic radical hysterectomy (Piver types III-IV) with bilateral salpingo-oophorectomy, pelvic and paraortic lymphadenectomy for a stage IIIC endometrial adenocarcinoma. Adjuvant chemotherapy based on the combination of Paclitaxel and Carboplatin was subsequently administered without major toxicity.

Follow-up imaging studies were negative until February 2011 when a CT-scan revealed right pleural effusion, diffuse pleural thickening with few pleural lesions (the largest in size measuring 40 mm of diameter) (Figure 1A). The patient referred a 20-yrs history of exposure to amiantum, thus, posing a differential diagnosis between primary pleural tumour (mesothelioma) and neoplastic pleural localization of the endometrial

cancer. A Pet-scan assessment detected a pathological metabolic uptake of the pleural lesions (Figure 1B). Thoracentesis was performed and cytological examination of the fluid was negative for neoplastic cells. EUS was then scheduled as the least invasive procedure to attempt to reach a definitive diagnosis. EUS was performed using a conventional linear echo-endoscope and confirmed the presence of several solid lesions in the pleural space that appeared located just under the EUS probe. EUS-FNTA of the pleura was done using a 19-Gauge needle as previously described⁹, and the collected specimen was placed in formalin. Histological examination revealed examination, pleomorphic neoplastic cells with marked nuclear atypia and frequent mitotic figures, organized in solid sheets and papillae with necrosis. Tumor cells stained markedly positive for p53, cytokeratin 7, vimentin, estrogen receptor and focally for progesteron receptor. Immunostaining for WT1, cytokeratin 20, calretinin, thrombomodulin and CEA monoclonal were all negative. These morphological and immunophenotypic features were diagnostic for a pleural metastasis of high-grade endometrial serous carcinoma. The patient received 8 cycles of chemotherapy based on Carboplatin (5 AUC) and Caelyx (30 mg/mq) every 28 days with complete regression of the pleural lesions. At the time of the present report, the patient is alive with no evidence of disease recurrence.

Discussion

We reported a patient in whom a diagnosis of pleural metastases from a previously diagnosed and treated endometrial neoplasm was achieved by EUS-FNTA, a technique developed to acquire tissue samples under EUS guidance⁹. The pleural lesions were located just under the EUS probe without any intervening tissue or structure, rendering EUS-FNTA easily feasible. We chose this technique because considering mesothelioma in the differential diagnosis the availability of a tissue specimen instead of a cytological one would have allowed for a qualitative examination of the tissue architecture and an easier performance of immunostaining, which can be critical to diagnose and fully characterize certain neoplasms.

Conventional transesophageal EUS-FNA and the more recently introduced endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) have become key players in the evaluation of the mediastinum. Complete endoscopic evaluation of the mediastinum is now possible with approach of the posterior and the anterior mediastinum through the esophagus and the trachea, respectively. This is clearly of major value in the diagnosis, but more importantly, in the staging of NSCLC where a staging strategy that combines endosonography and surgical staging has been

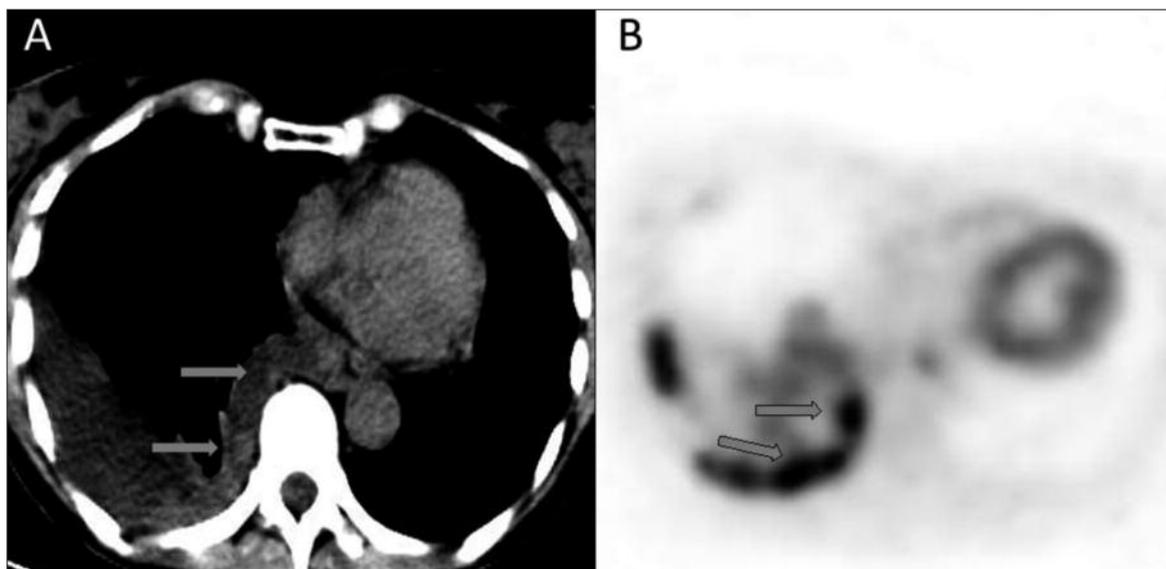


Figure 1. Radiological evaluation: CT-scan (A) showed an abundant right pleural effusion and diffuse pleural thickening with few pleural lesions (the largest in size measuring 40 mm of diameter) just in the azygosoesophageal recess; PET-scan assessment confirmed the metabolic uptake of these lesions (B).

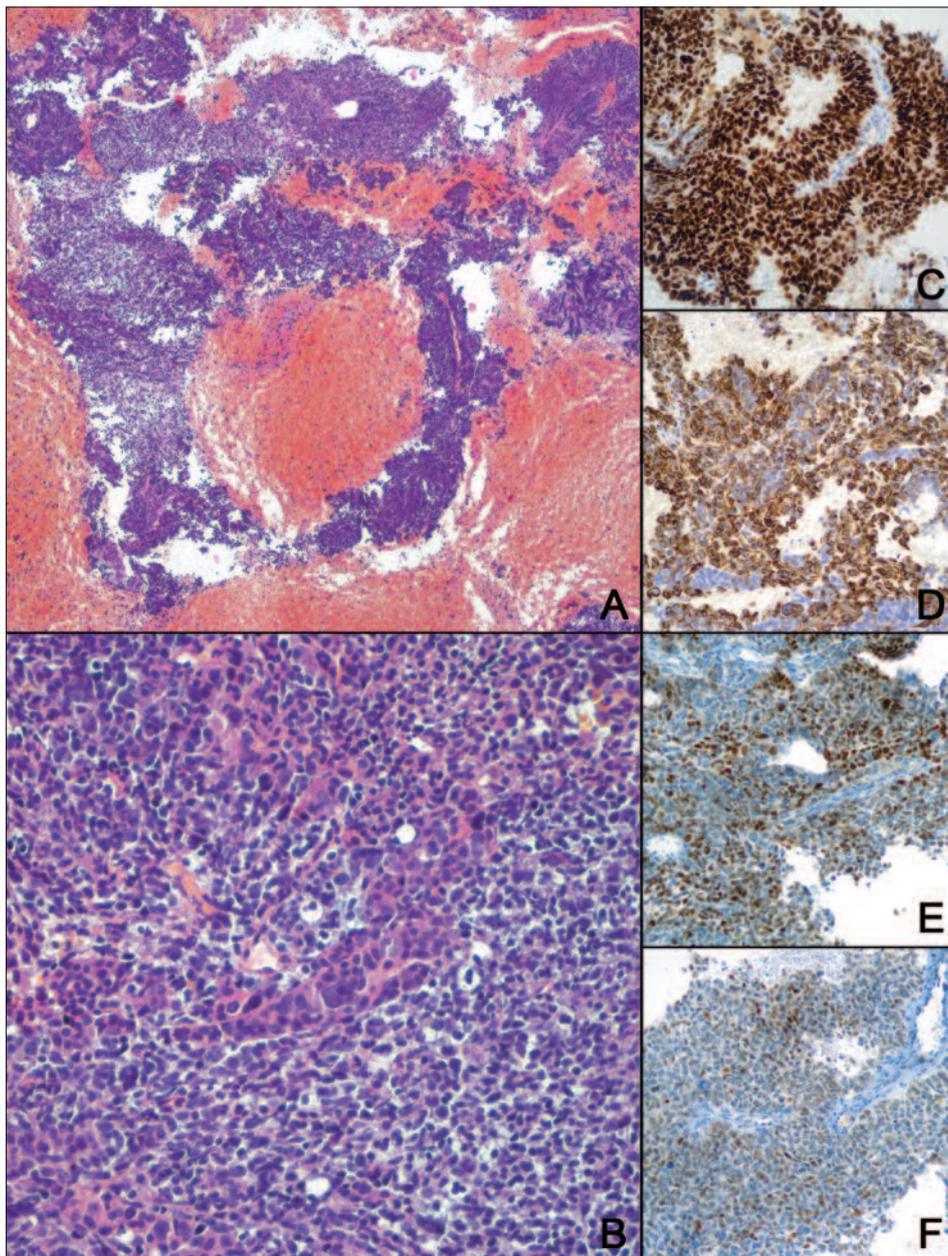


Figure 2. The morphological and immunophenotypic features of the pleural sample (Panel **A**). Low power view of the fine needle biopsy of pleura composed of blood and neoplastic tissue organized in solid sheets and papillae with necrosis. (Haematoxylin and Eosin, magnification $\times 40$). **B**, A solid tumor area with highly pleomorphic neoplastic cells showing marked nuclear atypia, with evident nucleoli and frequent mitosis. (Haematoxylin and Eosin, magnification $\times 200$). **C**, Tumor cells exhibiting diffuse immunoreactivity for p53, for vimentin (**D**), and estrogen receptor (**E**), and focal for progesterone receptor (**F**) at Haematoxylin counterstaining (magnification $\times 200$).

found to be more effective and less expensive with fewer unnecessary thoracotomies as compared with surgical staging alone^{10,11}.

Centrally located pulmonary lesions and mediastinal masses/lymphadenopathy of unknown origin are other well-established indications to perform EUS-FNA^{2,3,12,13}. In cases of unknown

lymphadenopathy the value of tissue acquisition using a large caliber needle has first been described by Yasuda et al¹⁴, who were able to reach a definitive diagnosis in 98% of patients, with the capability of lymphoma subtyping in 88% of those with this diagnosis. Moreover, additional EUS-guided procedures in the mediastinum that

have been reported include: (1) FNA of lymph nodes metastase from extrathoracic tumors¹⁵; (2) aspiration of small pleural effusions with the fluid that can be sent for cytological evaluation and may be able to diagnosed advanced cancer⁴⁻⁶; (3) biopsy of a thickened pleura to confirm the clinical suspicious of pleural tuberculosis⁷; (4) FNA of a pleural metastasis from pancreatic cancer⁸. We reported the second case of pleural metastases in which EUS was able to sample the lesions and to determine the definitive diagnosis. In both the reported cases, EUS spared the patients a more invasive surgical procedure such as a video-assisted thoracoscopy, which has been previously the gold standard for the tissue acquisition in this clinical setting. Furthermore, we proved for the second time that the use of a large calibre needle in sampling of the pleura is safe and can be easily accomplished if the lesion lies just under the EUS cursor.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

- 1) TOURNOY KG, KELLER SM, ANNEMA JT. Mediastinal staging of lung cancer: novel concepts. *Lancet Oncol* 2012; 13: e221-229.
- 2) SAVIDES TJ. EUS for mediastinal disease. *Gastrointest Endosc* 2009; 69(2 Suppl): S97-S99.
- 3) SAVIDES TJ, BEHLING CM. EUS for unexplained mediastinal lesions. *Endoscopy* 2006; 38(Suppl 1): S73-76.
- 4) TWINE CP, BARRY JD, BLACKSHAW GR, CROSBY TD, ROBERTS SA, LEWIS WG. Prognostic significance of endoscopic ultrasound-defined pleural, pericardial or peritoneal fluid in oesophageal cancer. *Surg Endosc* 2009; 23: 2229-2236.
- 5) VANDERVELDT HS, GANJEI-AZAR P, SHANMUGAN N, RIBEIRO A. EUS-guided FNA and diagnosis of a malignant pleural effusion in pancreatic cancer. *Gastrointest Endosc* 2007; 66: 1058-1060.
- 6) CHANG KJ, ALBERS CG, NGUYEN P. Endoscopic ultrasound-guided fine needle aspiration of pleural and ascitic fluid. *Am J Gastroenterol* 1995; 90: 148-150.
- 7) LARGHI A, LOCOCO F, RICCI R, GALASSO D, CARNUCCIO A, UCHIDA N, COSTAMAGNA G. Pleural tuberculosis diagnosed by EUS-guided fine-needle tissue acquisition. *Gastrointest Endosc* 2010; 72: 1307-1309.
- 8) EL HAJJ II, LUZ L, DIMITROV R, AL-HADDAD M. Pleural metastases from pancreatic cancer diagnosed by EUS-guided FNA. *Gastrointest Endosc* 2012; 76: 703-705.
- 9) LARGHI A, VERNA EC, RICCI R, SEERDEN TC, GALASSO D, CARNUCCIO A, UCHIDA N, RINDI G, COSTAMAGNA G. EUS-guided fine-needle tissue acquisition by using a 19-Gauge needle in a selected patient population: a prospective study. *Gastrointest Endosc* 2011; 74: 504-510.
- 10) ANNEMA JT, VAN MEERBEECK JP, RINTOUL RC, DOOMS C, DESCHEPPER E, DEKKERS OM, DE LEYN P, BRAUN J, CARROLL NR, PRAET M, DE RYCK F, VANSTEENKISTE J, VERMASSEN F, VERSTEEGH MI, VESELIĆ M, NICHOLSON AG, RABE KF, TOURNOY KG. Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: a randomized trial. *JAMA* 2010; 304: 2245-2252.
- 11) SHARPLES LD, JACKSON C, WHEATON E, GRIFFITH G, ANNEMA JT, DOOMS C, TOURNOY KG, DESCHEPPER E, HUGHES V, MAGEE L, BUXTON M, RINTOUL RC. Clinical effectiveness and cost-effectiveness of endobronchial and endoscopic ultrasound relative to surgical staging in potentially resectable lung cancer: results from the ASTER randomised controlled trial. *Health Technol Assess* 2012; 16: 1-75.
- 12) ANNEMA JT, VESELIĆ M, RABE KF. EUS-guided FNA of centrally located lung tumours following a non-diagnostic bronchoscopy. *Lung Cancer* 2005; 48: 357-361.
- 13) TOURNOY KG, RINTOUL RC, VAN MEERBEECK JP, CARROLL NR, PRAET M, BUTTERY RC, VAN KRALINGEN KW, RABE KF, ANNEMA JT. EBUS-TBNA for the diagnosis of central parenchymal lung lesions not visible at routine bronchoscopy. *Lung Cancer* 2009; 63: 45-49.
- 14) YASUDA I, TSURUMI H, OMAR S, IWASHITA T, KOJIMA Y, YAMADA T, SAWADA M, TAKAMI T, MORIWAKI H, SOEHENDRA N. Endoscopic ultrasound-guided fine-needle aspiration biopsy for lymphadenopathy of unknown origin. *Endoscopy* 2006; 38: 919-924.
- 15) PERIC R, SCHUURBIERS OC, VESELIĆ M, RABE KF, VAN DER HEIJDEN HF, ANNEMA JT. Transesophageal endoscopic ultrasound-guided fine-needle aspiration for the mediastinal staging of extrathoracic tumors: a new perspective. *Ann Oncol* 2010; 21: 1468-1471.