# Convex probe endobronchial ultrasound guided transbronchial/transoesophageal fine needle aspiration (C-EBUS-TBNA/EUS-B FNA) of pleural lesions: A single center experience and review of literature

**Mario Tamburrini[1], Dipesh Maskey[2], Nirupam Sharan[3], T.K. Jayalakshmi[4], Umberto Zuccon[1], Giuseppe Deda[5]**

*[1]Interventional Pulmonologist, AAS5 Friuli Occidentale, Pordenone, Italy; [2]NH MMI Narayana Multispeciality Hospital, Raipur, India; [3]Pulmonologist, The Happy Lungs, Ranchi, India; [4]Apollo Hospitals, Navi Mumbai, India; [5]Anatomopathologist, AAS5 Friuli Occidentale, Pordenone, Italy*

## Abstract

The evaluation of pleural diseases has been well established. If pleurocentensis is non-diagnostic, the second investigation depending upon availability could be either closed pleural biopsy or image guided pleural biopsy or thoracoscopic pleural biopsy (medical or surgical). Pleural disease presenting as thickness/mass/nodule in the mediastinum is difficult to access through ultrasound or computed tomography and will need thoracoscopy. Thoracoscopy is an invasive procedure which can be difficult to perform in localized mediastinal pleural disease without effusion or poor health condition not suitable for general anesthesia. An alternative method that can be utilized is sampling of pleural lesion through convex probe endobronchial ultrasound (C-EBUS) either through the central large airways or from esophagus if the lesions are in proximity. We present our center's experience in diagnosing pleural lesion using C-EBUS in 4 patients along with review of the literature.

Correspondence: Dr Mario Tamburrini, Interventional Pulmonologist, AAS5 Friuli Occidentale, Pordenone, Italy.
Tel. +39.349.0091667.
E- mail: mario.tamburrini@aas5.sanita.fvg.it

Key words: Endobronchial ultrasound; EBUS, EUS-B; pleural lesion.

Contributions: MT, UZ, DG, were involved in patient management; DM, NS, JTK, did the literature search and wrote the manuscript.

Funding: None.

Conflict of interest: The authors declare no conflict of interest.

Received for publication: 30 November 2019.
Accepted for publication: 15 May 2020.


*Monaldi Archives for Chest Disease 2020; 90:1207*
*doi: 10.4081/monaldi.2020.1207*



## Introduction

Convex Probe Endobronchial Ultrasound guided Fine Needle Aspiration (C-EBUS-FNA) has become the standard of practice in real-time sampling of mediastinal and hilar adenopathy as well as staging in lung cancer with improved yield [1]. C-EBUS bronchoscope can be passed into the esophagus and approach lesions in the mediastinum, lungs, liver and left adrenal glands giving pulmonologist more access to diagnosis and can be done in the same setting. Lesions in the mediastinal pleura that are close to trachea and main bronchi or esophagus can also be approached by C-EBUS. We report a single center experience of using C- EBUS guided FNA either through bronchus or esophagus in getting a diagnosis at department of pneumology in a tertiary hospital in Pordenone, North Italy.

## Case #1

A 67-year-old male, former smoker, is known patient of hypertension, COPD, gastroesophageal reflux. He was a former metal worker. He was being evaluated for persistent cough and pleural thickening with effusion since 2015 in other hospital. In 2016, he underwent thoracocentensis that was negative for malignancy. In 2017 repeat CECT chest showed right sided contrast enhanced diffuse pleural thickening extending into minor and major fissures with maximum thickness of 35mm in the basal paramediastinal area. The thickness of 23mm is seen at the subcarinal area. There is hilar and mediastinal lymphadenoapathy (Figure 1a). EUS-B FNA using EBUS was done to sample the pleural thickening at subcarina. The procedure was uneventful. ROSE was positive for malignant cells. Cytology and cell block for IHC revealed epitheloid cell mesothelioma (Figure 1b). He was referred to oncology center for further management.

## Case #2

A 64-year-old female with 10 pack year smoking presented with progressive dyspnea associated with loss of appetite and weight for 3 months after a brief episode of flu like illness on July 2019. CT chest showed thickened pleura with pleural deposits including

mediastinal pleura along with pleural effusion (Figure 2a). Pleural fluid analysis was inconclusive. She underwent C-EBUS-TBNA (Olympus EBUS with Cooks Procore needle 22 gauge) from pleural deposit that was accessible through right main bronchus (Figure 2b). Rapid On Site Examination (ROSE) was positive for malignant cells (Figure 2c). Subsequent cell cytology and cell block including immunohistochemistry showed epitheloid cell mesothelioma.

## Case #3

A 78-year-old male, former carpenter and reformed smoker with COPD presented with acute exacerbation in May 2019. He had past history of right pleural decortication for empyema 39 years back. CECT chest showed contrast enhanced focal pleural thickening 40X20mm in left marginal-costal postero-inferior border along with thin plaques of pleural thickening in margino-costo-antero-superior border. Another lesion of similar characteristic measuring 25X15 mm is seen in right postero-superior paravertebral pleura (Figure 3a). Bilateral upper lobe predominant centrilobular emphysema was seen along with subcentimeter hilar and mediastinal adenopathy. PET CT showed hyperintense uptake in these nodules along with uptake in cervical, submandibular, axillary, right internal mammary, anterior costophrenic, mesenteric, paraaortic and external iliac lymphnodes. There was hyperintense uptake in right axillary soft tissue and diffuse bone marrow uptake (Figure 3b). Clinically they were not feasible for biopsy. So EUS-B FNA was performed from the right pleural uptake through EBUS scope with 22G Cooks Procore needle and no complications were observed. ROSE showed multiple lymphnodes (Figure 3c) so cell cytology, cell block for immunohistochemistry and flow cytometry were sent. The result showed Non-Hodgkin B cell lymphoma.

## Case #4

A 77-year-old female, non-smoker, hypertensive in regular treatment presented with right chest pain that was persistent since one and half years, along with significant weight loss. She had worked in a cotton textile factory and retired 43 years ago. CT Chest showed pleural thickening with effusion encasing the lung with enlarged subcarinal, right paratracheal lymphnodes (Figure 4a). She underwent EUS-B FNA from the mediastinal node and pleural mass in the mediastinum as flexible bronchoscopy revealed narrowing of right main bronchus lumen (Figure 4b). The ROSE was positive for malignant cells from pleural mass and subcarinal nodes. Multiple passes were taken for cell block, histology with final diagnosis of epitheloid malignant mesothelioma (Figure 4c).

## Discussion

Convex Probe EBUS has revolutionized the approach to mediastinal structure that are located around the trachea and main bronchi

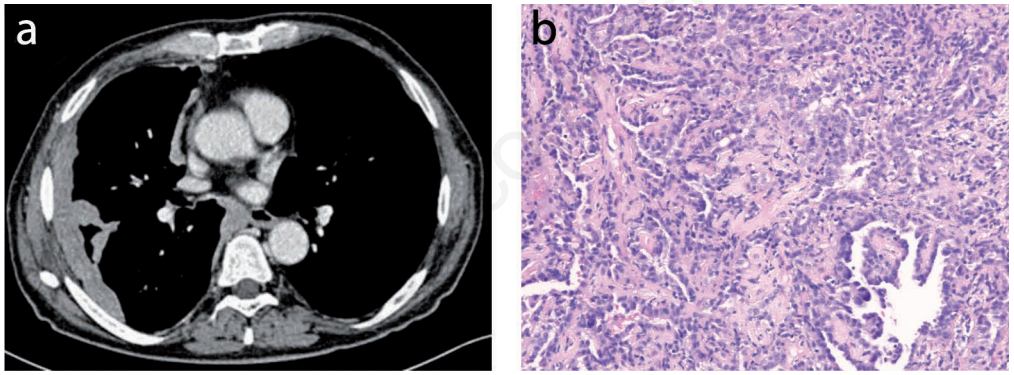


**Figure 1. a) CT chest showing pleural thickening including the mediastinum. b) H&E stain showing sheets of epitheloid malignant mesothelial cells.**

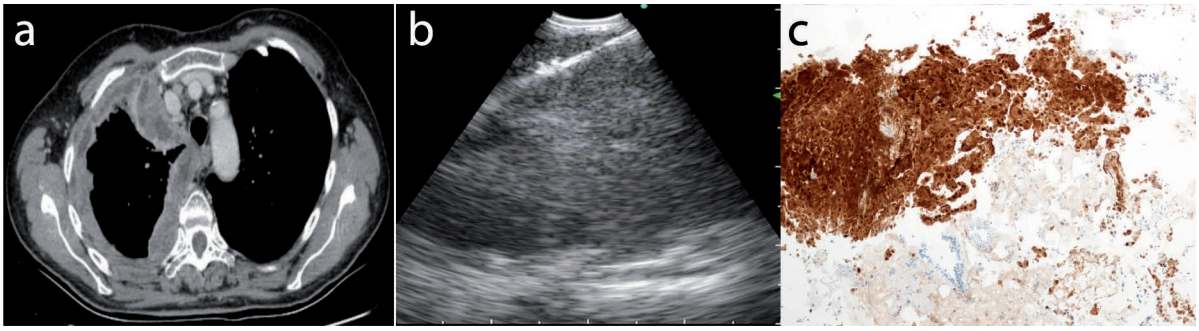


**Figure 2. a) CT showing circumferential pleural thickening including the mediastinum. b) EBUS TBNA from pleural mass. c) IHC of cell block showing calretinin positive in malignant mesothelial cells.**

leading to better visualization of lesions such as lung mass, mediastinal mass or lymphnodes as well as bronchial cysts [1]. With real time guidance a dedicated transbronchial needle can be used to puncture the central airways and reach these lesions and aspirate materials for cytology, cell block for immunohistochemistry, molecular markers, microbiology as well as core biopsy for histology thereby improving yield [1]. With better experience and understanding of ultrasound imaging, the bronchoscopists have also used the same EBUS bronchoscope into the esophagus and got access to paraesophageal lymphnodes and even left adrenal mass [2-4] and is called EUS-B FNA. The advantage of EUS-B is better tolerance by patients with minimal cough, desaturation, and less sedation however the disadvantage being poor bronchoscopic view of the esophagus with high risk of scope damage by the needle if unable to see the guidesheath exit properly. In our institute, we confirm guidesheath exit from the working channel through the ultrasound image while performing EUS-B.

The use of C-EBUS for pleural sampling is unusual as the standard approach to pleural disease is first pleural fluid analysis followed by image guided pleural biopsy or thoracoscopic guided pleural biopsies in case of undetermined exudative pleural effusion [5,6]. But the latter is more invasive, need moderate to deep sedation and requires inpatient care. In patients with diseased pleura, which present with either thickening, mass or nodule with or without effusion, that are in the vicinity of the central airways, bronchi or esophagus, the lesions can be approached using C-EBUS and under real time perform fine needle aspiration acquiring adequate cells for cytology, cells blocks, core biopsy for molecular analysis, IHC as well as microbiology.

In last two years, we have performed C-EBUS/EUS-B guided direct pleural aspiration with positive diagnosis in all four patients. The procedure was safe with no immediate or late complications. Three procedures were performed through transesophageal approach while one procedure was done from the right bronchus. Three patients had malignant mesothelioma and the other patient had lymphoma deposit in the pleura.

We searched the literature for EBUS guided pleural aspiration and core biopsy in Pubmed, EMBASE and Google Scholar using key words "Endobronchial ultrasound OR EBUS OR EUS-B AND pleura OR pleural mass OR pleural nodule or pleural thickening" and came across only six cases published till date (Table 1) [7-12].

Lococo *et al.* first reported use of EBUS-TBNA from pleural nodule adjacent to right costovertebral recess accessed through posterior wall of right main bronchus and diagnosed mesothelioma which was later confirmed from surgery [7]. Thoracoscopy, either medical or surgical, is more invasive than EBUS FNA. Gaspard *et al.* performed EBUS-TBNA from pleural mass with EBUS bronchoscope inserted into right lower lobe in a 50 years man with past history of inguinal synovial sarcoma. FNA was positive for synovial sarcoma and confirmed after surgical resection of the tumor from the right pleura [8]. The reason for selection of the procedure was twofold. First was for staging of tumour and the second was to assess endobronchial lumen and feasibility of FNA. Guinde *et al.* performed both EBUS-TBNA and CT guided biopsy sequentially to confirm diagnosis of dry pleural mesothelioma thereby confirming the role of EBUS FNA in diagnosing pleural disease [9]. A study of 736 patients undergoing EBUS-TBNA for thoracic lesions described

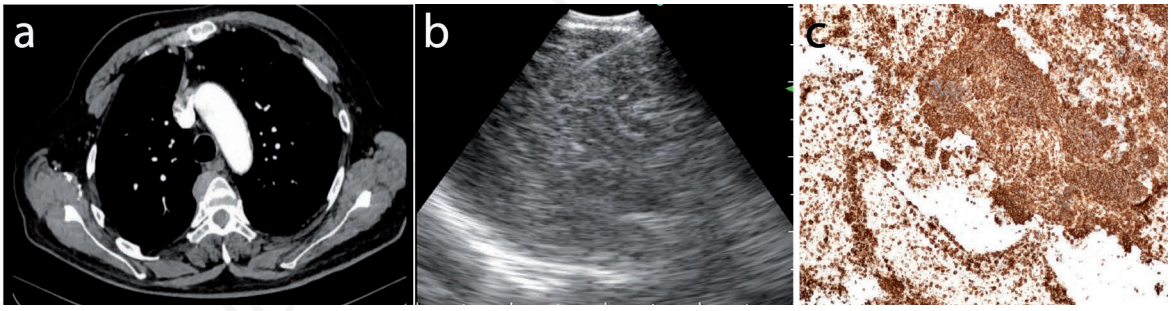


**Figure 3. a) CT chest showing right mediastinal pleural nodule. b) EUS-B FNA from right pleural nodule. c) IHC of cell block showing positive CD20 lymphocytes of B cell lymphoma.**

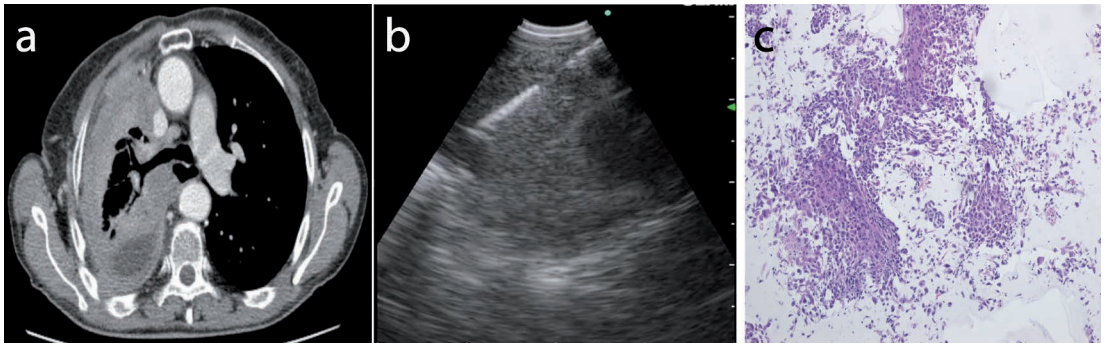


**Figure 1. a) CT chest showing pleural thickening including the mediastinum. b) H&E stain showing sheets of epitheloid malignant mesothelial cells.**

four patients of pleural mesothelioma diagnosed from tissue sampled from pleura, mediastinal mass and subcarinal lymphnode [10]. Kassirer *et al.* performed EUS-B FNA from pleural mass and EBUS-TBNA from subcarinal and right paratracheal lymphnode and diagnosed metastatic renal clear cell lymphoma from both pleural deposit and lymph nodes [11]. Donghi *et al.* performed EBUS-TBNA from pleural mass due to inadequate sample from lung mass for molecular analysis and received adequate sample to perform the molecular testing including Programmed death-ligand 1 (PD-1) [12]. The EBUS was done to stage lung cancer as well as perform tissue sampling at the same setting rather than to repeat the lung biopsy followed by staging thus minimizing multiple procedures.

The common feature in all the cases published so far including ours is the location of pleural lesion around the mediastinal pleura which were easily accessible through airway or esophagus to perform the procedure. EBUS TBNA was the most common procedure performed. Endosonography (EUS) of the pleura and pleural effusion have been well described in literature [13] but there is paucity of literature using EBUS. Likewise, EUS guided fine needle aspiration from the pleural lesions by gastroenterologists have been published earlier [14-16].

From the cases published so far and with our experience, malignant pleural mesothelioma (MPM) is the most common disease diagnosed. MPM commonly presents with pleural effusion and thickening involving both parietal and visceral pleura. Kato *et al.*, in his review of 327 CT imaging of MPM found localized pleural thickening in the mediastinum in 77% [17]. Utility of diagnosis of pleural mesothelioma through EBUS guided mediastinal lymphadenopathy is well known [18-20]. It is also helpful in staging of mesothelioma for choosing the therapy and is now getting established [21]. None of the published cases including ours experienced complications due to the procedure establishing the safety of the procedure.

All patients underwent procedure with conscious sedation with fentanyl and midazolam, and none of them required deep sedation with or without ventilation. So in high volume centres and deep sedation may not be required, but it cannot be denied that in few cases they may be warranted. With current EBUS needles, core biopsies are possible leading to dramatic improvement in diagnosis. Moreover, with advent of cell block preparation it is easier to get proper diagnosis, so we do not think it is now a major limitation for the procedure. In an inexperienced hand it can be an issue.

In conclusion, convex probe EBUS-TBNA or EUS-B FNA is a safe, tolerable and minimal invasive procedure for performing pleural biopsy that are accessible through either central airways or esophagus. It can be performed with minimal sedation with adequate specimen for diagnosis. In an appropriate setting, we suggest to perform the procedure before thoracoscopic pleural biopsy as it reduces hospitalization as well as cost. We have proposed this technique as an alternative method where thoracoscopy is risky or contraindicated and also less invasive. It is by no means to say that this method should replace thoracoscopy. However, by our study it may open an area of research for comparative study in future.

## References


1. Dhooria S, Sehgal IS, Gupta N, et al. Diagnostic yield and complications of EBUS-TBNA performed under bronchoscopist-directed conscious sedation: Single center experience of 1004 subjects. J Bronchology Interv Pulmonol 2017;24:7–14.
2. Mondoni M, D'Adda A, Terraneo S, et al. Choose the best route: ultrasound-guided transbronchial and transesophageal needle aspiration with echobronchoscope in the diagnosis of mediastinal and pulmonary lesions. Minerva Medica 2015;106:13-9.
3. Hwangbo B, Lee HS, Lee GK, et al. Transoesophageal needle aspiration using a convex probe ultrasonic bronchoscope. Respirology 2009;14:843-9.
4. Crombag LMMJ, Szlubowski A, Stigt JA, et al. EUS-B-FNA vs conventional EUS-FNA for left adrenal gland analysis in lung cancer patients. Lung Cancer 2017;108:38-44.
5. Hooper C, Lee YCG, Maskell N, BTS Pleural Guideline Group. Investigation of a unilateral pleural effusion in adults: British Thoracic Society pleural disease guideline 2010. Thorax 2010;65:ii4-17.
6. McGrath EE, Anderson PB. Diagnosis of pleural effusion: A systematic approach. Am J Crit Care 2011;20:119-28.
7. Lococo F, Rossi G, Agostini L, et al. "Dry" pleural mesothelioma successfully diagnosed on endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA). Intern Med 2014;53:467-9.
8. Gaspard D, Raja H, Arya R, et al. A case report on the diagnosis of a rare pleural tumor with endobronchial ultrasound breaking new boundaries. Medicine 2015;94:e561.
9. Guinde J, Laroumagne S, Kaspi E, et al. Endobronchial ultrasound in the diagnosis of malignant pleural mesothelioma. Rev Mal Respir 2015;32:750-4.
10. Ghigna MR, Crutu A, Florea V, et al. The role of endobronchial ultrasound-guided fine needle aspiration in the diagnosis of pleural mesothelioma. Cytopathology 2016;27:284-8.
11. Kassirer M, Wiesen J, Atlan K, Avriel A. Sampling pleural nodules with an EBUS scope: A novel application. Respir Med Case Rep 2018;25:36-8.
12. Donghi SM, Prisciandaro E, Sedda G, et al. When less is more: EBUS-TBNA for the diagnosis of pleural lesions. Innovations 2019;14:473-5.
13. Sharma M, Rameshbabu CS. Endoscopic ultrasound-guided evaluation of the pleura and cases of pleural effusion. Lung India 2017;34:441-7.
14. Larghi A, Lococo F, Mainenti S, et al. EUS-guided fine needle tissue acquisition for the diagnosis of pleural metastases from endometrial cancer. Eur Rev Med Pharmacol Sci 2014;18:1379-82.
15. El Hajj II, Luz L, Dimitrov R, Al-Haddad M. Pleural metastases from pancreatic cancer diagnosed by EUS-guided FNA. Gastrointest Endosc 2012;76:703-5.
16. Sharma M, Somani P. Endoscopic ultrasound-guided fine needle aspiration of pleural deposits. Endosc Ultrasound 2017;6:51.
17. Kato K, Gemba K, Fujimoto N, et al. Fatal pleural mesothelioma in Japan (2003-2008): evaluation of computed tomography findings. Jpn J Radiol 2016;34:432-8.
18. Mukherjee I, Yi E, Utz J. Diagnosis of mesothelioma using flexible bronchoscopy with endobronchial ultrasound-guided biopsy of mediastinal lymph nodes. J Bronchology Interv Pulmonol 2009;16:207-10.
19. Ashinuma H, Shingyoji M, Yoshida Y, et al. Endobronchial ultrasound-guided transbronchial needle aspiration in a patient with pericardial mesothelioma. Intern Med 2015;54:43-8.
20. Kang B, Kim MA, Lee BY, et al. Malignant pleural mesothelioma diagnosed by endobronchial ultra-sound-guided transbronchial needle aspiration. Tuberc Respir Dis 2013;74:74–8.
21. Rice DC, Steliga MA, Stewart J, et al. Endoscopic ultrasound-guided fine needle aspiration for staging of malignant pleural mesothelioma. Ann Thor Surg 2009;8:862-9.