Case Report

EBUS guided trans-esophgeal cryobiopsy-two case reports

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ABSTRACT

Endobronchial ultrasound (EBUS) guided mediastinal cryobiopsy is a novel technique which can be combined with EBUS -TBNA to improve the diagnostic yield. Recent studies report, this technique is safe and superior to EBUS TBNA alone in terms of acquisition of larger tissue samples and thereby a better diagnostic yield and adequacy of tissue for molecular studies. However, safety of this technique in patients do not tolerate a bronchoscopic procedure due to hypoxia or respiratory distress is not clarified yet. Alternatively, EBUS guided FNA via trans-esophageal route(EUS-B-FNA) is a proven technique with a similar diagnostic yield as EBUS TBNA with a better tolerance and a more patient comfort. We report two patients here, in whom EUS- B guided cryobiopsy was successfully done via trans-esophageal route, due to intolerance for bronchoscopic procedure and inconclusive ROSE reports.

KEY WORDS: Cryobiopsy, endobronchial ultrasound, mediastinal adenopathy

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Submitted: 02-Nov-2023 **Revised:** 20-May-2024 **Accepted:** 21-Oct-2024 **Published:** 29-Apr-2025

BACKGROUND

Endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) is a standard technique for obtaining tissue samples from mediastinal mass lesions around the large airways. Trans-esophageal EBUS-guided fine needle aspiration (EUS-B-FNA) is also a good technique for sampling lesions in the mediastinum around the esophagus. If a patient is not fit for a bronchoscopic procedure due to large airway obstruction or hypoxia, the trans-esophageal route is a good alternative, which can be done safely with less incidence of hypoxia and lesser requirement of sedation. Though these needle techniques show a high yield for diagnosis of lung cancer and tuberculosis, the adequacy of the samples for molecular testing, and diagnosis of sarcoidosis and lymphoma have always been debated. Recently, studies have shown that EBUS-guided transbronchial cryobiopsy is possible by introducing a 1.1 mm size flexible cryoprobe trans-bronchially. Though this technique has not yet been standardized and safety is not well established, it is shown to be superior to EBUS TBNA in terms of diagnostic yield. We report two cases here who have undergone EUS-B guided trans-esophageal cryobiopsy of mediastinal lesions due to their intolerance for bronchoscopy or inconclusive Rapid onsite evaluation (ROSE).

Access this article online

Quick Response Code:

Website: https://journals.lww.com/lungindia

DOI: 10.4103/lungindia.lungindia_531_23

How to cite this article: Santhakumar S, Deshmukh K, Mehta SS, Muthusamy RK, Venugopal J, Deepak TH, *et al*. EBUS guided trans-esophgeal cryobiopsy-two case reports. Lung India 2025;42:252-5.

CASE REPORTS

Case 1 [Figure 1]

A 45-year-old female came with complaints of cough, fever, breathing difficulty, and chest pain for three weeks. Her room air SPO2 was 92%, BP-120/70 mmHg and respiratory system examination was unremarkable. CT scan of the chest showed large mediastinal nodes at the right paratracheal and sub-carinal region, compressing the trachea, carina, and the right main bronchus with minimal pleural effusion on the left side. Pleural fluid analysis was non-diagnostic. During bronchoscopy, she had significant hypoxia due to excessive dynamic airway collapse (EDAC) at the level of the lower trachea and right main bronchus, and further bronchoscopy was not possible due to significant hypoxia. Hence, we decided to proceed with EUS-B-FNA, and the subcarinal node was sampled by trans-esophageal FNA. Rapid on-site evaluation (ROSE) was inconclusive. Hence, the 1.1 mm cryoprobe was introduced at the same entry point as the needle, and cryobiopsy was obtained. The patient did not have any complications. Histopathological examination revealed features suggestive of Hodgkin's lymphoma and subsequent immunohistochemistry (IHC) confirmed CD 30 positivity.

Case 2

A 65-year-old male had PET Positive mediastinal adenopathy with a left paratracheal node being the largest (2.1 mm, short axis) and with the highest uptake (SUV-6.5) during evaluation for pyrexia of unknown origin. EBUS TBNA was done but ROSE was inconclusive. Transtracheal cryobiopsy was attempted but failed due to difficulty in introducing the cryoprobe due to angulation of the trachea. Hence, he was subjected to EUS-B cryobiopsy from the left paratracheal node. The histopathology was reported as Hodgkin's lymphoma and the samples were adequate for subsequent immunohistochemistry which confirmed the disease.

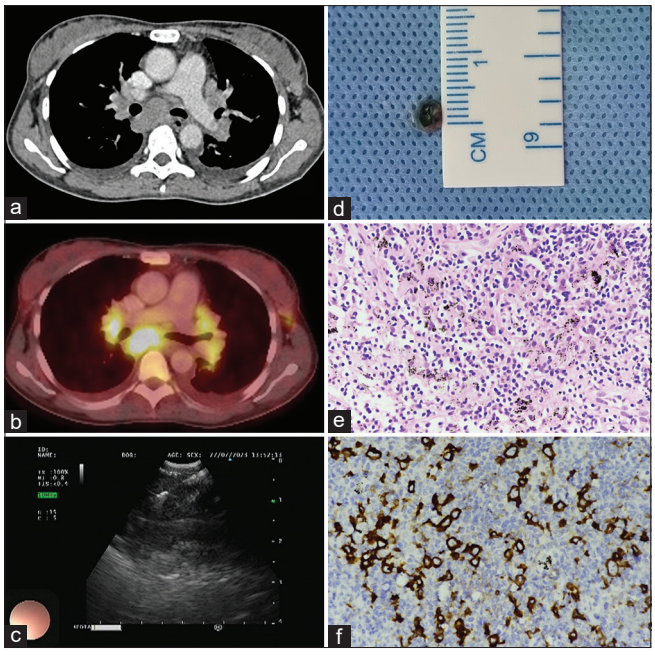

Figure 1: Case 1. (a) CT thorax showing mediastinal Adenopathy (b) PET-CT showing hypermetabolic paratracheal and subcarinal mediastinal lymph nodes (c) EUS-B cryobiopsy (d) Cryobiopsy specimen (e) High power of lymph node with large atypical cells in polymorphous background, H and E 40x (f) Atypical large cells with CD 30 immunoreactivity, 40x

Procedural details [Figure 2]

In both patients, the procedure was done under deep sedation using a Gastro laryngeal mask airway, which is a dual channel supraglottic airway (LMA Gastro™Cuff Pilot™ Airway - LGA; Teleflex® Medical, Athlone, Ireland). The EBUS scope (Olympus BF-UC190F, AMERICA Inc) was introduced through the esophageal channel of LMA, negotiated through the esophagus gently and the lesion of interest in relation to the thoracic vascular landmarks was located by endosonography. Initially, FNA was done using 21 G (ViziShot EBUS-TBNA-Olympus), under sonographic guidance, and subjected to ROSE. The decision to proceed with cryobiopsy was made based on ROSE. Before cryobiopsy, a 19 G EBUS Needle was introduced along with the sheath in the same puncture site, to make it larger, so that the cryoprobe can be passed easily. Subsequently, a 1.1 mm flexible cryoprobe (ERBE CRYO® 2, USA INC) was introduced through the same entry point until the tip reached the center of the lesion (to avoid biopsy of the esophageal wall) under sonographic guidance, and cryoactivation was done for 3–4 seconds, followed by withdrawal of EBUS scope and cryoprobe assembly in total and tip of the cryoprobe was thawed in warm saline. The procedure was repeated until 3 cryobiopsy specimens were obtained. During the procedure, heart rate, ECG, Pulse oximetry, blood pressure, and End-tidal

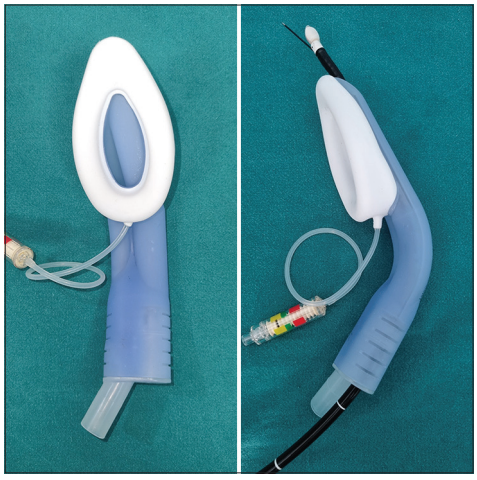

Figure 2: Dual channel Gastro LMA used for the procedure. On the right-side assembly of EBUS scope (through the esophageal channel of LMA) and cryoprobe. EDAC - Excessive Dynamic Airway Compression; EUS-B - Endoscopic Ultrasound - Biopsy; EUS FNA - Endoscopic Ultrasound Fine Needle Aspiration; RMB - Right Main Bronchus, NSCLC - Non-small Cell Lung Carcinoma, LMB - Left Main Bronchus, SCLC- Small Cell Lung Cancer

CO_2 were monitored. Post-procedure, patients' vital parameters were observed for 2–4 hours in the day-care unit. A Chest X-ray was done to rule out pneumothorax or pneumomediastinum. Since an esophageal puncture was done, patients were given 5 days of oral antibiotics to prevent mediastinitis. None of the patients had any intra or post-procedural complications.

DISCUSSION

EBUS TBNA is a guideline-recommended first-line investigation for sampling the mediastinal mass lesions, lymphadenopathy, and lung cancer staging.[1,2] EUS-B-FNA is also a standard technique that enhances the diagnostic yield when combined with EBUS TBNA, or it may be used alternatively where EBUS TBNA is not feasible.[3-5] Though these are the preferred techniques in lung cancer diagnosis, the adequacy of the samples obtained for molecular analysis and next-generation sequencing (NGS) has always been debated. A recent meta-analysis showed the adequacy of the EBUS TBNA sample for NGS is uncertain.[6] The sensitivity of EBUS TBNA is much lower in the diagnosis of sarcoidosis and lymphoma.[7,8]

Transbronchial EBUS-guided mediastinal cryobiopsy is a recently developed novel technique that can give larger tissue. As compared to the standard EBUS TBNA, tissue adequacy for molecular studies in lung cancer patients is favorable with this technique.[9,10] However, though transbronchial procedures are minimally invasive, it is challenging to obtain tissue samples in patients with hypoxia and in patients who do not tolerate an airway procedure due to their poor general condition. EUS-B-FNA holds an advantage over EBUS TBNA as it is safer in patients with hypoxia or large airway obstruction and in children because there is no additional airway obstruction caused by the EBUS scope itself.[11] Studies have shown that trans-esophageal approach is a good alternative in such patients, which provides greater patient comfort with the same diagnostic yield.[12-14] Nakashima *et al*.,[15] have demonstrated safety and utility of EUS-B-FNA in patients with respiratory failure or poor général condition. Molecularly targeted drugs are effective in improving performance status (PS) or respiratory conditions in driver oncogenes positive non-small cell lung cancer (NSCLC) patients even with poor performance status (PS)[16,17] or respiratory condition.[18] Therefore, it would be interesting to explore a safe technique that can give adequate tissue to patients not fit for the trans-airway approach.

There are only two case reports available in the literature mentioning the possibility of trans-esophageal cryobiopsy[19,20] of mediastinal mass lesions. To the best of our knowledge, ours is the first case series report with regards to EUS-B-Cryobiopsy. Technically introducing a cryoprobe through the esophagus is challenging due to, 1) the cryoprobe has to be guided by sonographic vision only as the endoscopic vision through EBUS scope is much poorer due to the collapsing and moving nature of the esophagus, 2) Unlike transbronchial approach, the track created by the needle quickly disappears due to presence of thick smooth muscle layer in the esophagus. We had to use the 19 G EBUS needle (ViziShot 2 FLEX 19 G-Olympus) before introducing cryoprobe, to make the track larger.

Possible complications of the technique include bleeding, perforation of the esophagus, and mediastinitis. Studies report the complication rate of EUS-B-FNA is minimal and rare.[21,22] Though both of our patients had no complications during or post-procedure, it is too early to comment on the safety of this technique because a blunt probe is introduced through the esophagus and there is a theoretical possibility of perforation. Extreme caution should be observed and only experienced operators in the field can do, so until strong evidence of safety is available by a larger trial to analyze the utility and safety of this approach.

SUMMARY

EUS-B guided trans-esophageal mediastinal cryobiopsy may be a possible option to obtain larger tissue samples for diagnosis and molecular studies in patients with mediastinal lesions who are not fit for EBUS approach (due to poor general condition and respiratory failure) or in ROSE negative EUS-B-FNA cases. This procedure should not be practiced routinely without experienced operators until strong evidence of safety is clear by larger randomized studies. Larger studies are needed to know more details about the safety and utility of this approach.

Abbreviations

EBUS: Endobronchial ultrasound
TBNA: Transbronchial Needle Aspiration
FNA: Fine Needle Aspiration
EUS-B: Endoscopic ultrasound with bronchoscope
ROSE: Rapid On-Site Evaluation
EDAC: Excessive Dynamic Airway Collapse
LMA: Laryngeal Mask Airway
CT: Computed Tomography
PET: Positron Emission Tomography
NSCLC: Non-Small Cell Lung Cancer

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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