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Transesophageal Bronchoscopic Ultrasound-guided Cryobiopsy (EUS-B-Cryo) for mediastinal lesions in critical airway obstruction: a case series with a systematic review

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Key words: mediastinal neoplasms, cryosurgery, Endobronchial Ultrasound-Guided Needle Aspiration, airway obstruction, Superior Vena Cava Syndrome.

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Abstract

Tissue diagnosis of mass lesions in the mediastinum poses a challenge, particularly when the mass is not in direct contact with the chest wall, rendering techniques such as Ultrasonography (USG) or Computed Tomography (CT) guided biopsies ineffective. In cases of Critical Airway Obstruction (CAO), utilizing routine endobronchial ultrasound-guided biopsies can lead to complications, including respiratory failure. As an alternative technique, Transesophageal Bronchoscopic Ultrasound-Guided Fine Needle Aspiration (EUS-FNA) is utilized. However, when smears yield inconclusive results for histopathological diagnosis, mediastinoscopy remains the preferred modality. We present two cases of CAO where Transesophageal Bronchoscopic Ultrasound (EUS-B)-guided cryobiopsy was performed, eliminating the necessity for mediastinoscopy. Histopathological examination of the cryobiopsy samples revealed squamous cell carcinoma and small cell carcinoma. A detailed systematic review only revealed two similar studies in the past. Thus, EUS-B-guided cryobiopsy emerges as a novel technique with the potential to diagnose lesions located in the concealed regions of the mediastinum.

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Introduction

Endosonography of the esophagus was initially introduced in the field of gastroenterology for the diagnosis and evaluation of carcinoma of the esophagus. Later, in the 1990s, it became popular for diagnosing airway and mediastinal lesions by providing real-time visualization of mediastinal lymph nodes and masses.¹ Endobronchial Ultrasonographic-Trans Bronchial Needle Aspiration (EBUS-TBNA) has high diagnostic accuracy for metastatic lymph nodes; however, the sample obtained is limited, which may sometimes be insufficient for diagnostic evaluation of certain malignancies and benign diseases requiring histopathological samples.² EBUS Trans-Mediastinal Cryobiopsy (TMC) has a higher diagnostic yield in such cases than EBUS-TBNA, especially if molecular testing is needed for the treatment of underlying malignancy.³ Narrow airways due to subglottic stenosis or central airway obstruction are a relative contraindication for EBUS, as they can lead to hypoxemia and respiratory failure. Transesophageal Bronchoscopic Ultrasound (EUS-B)-guided is an alternative tool for making a diagnosis in such patients.⁴

Here, we present two cases of critical airways in which successful EUS-B-Cryo sampling from mediastinal lesions using an EBUS scope was performed.

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Case Report

Case 1

A 26-year-old non-smoker woman presented with complaints of progressive dyspnea, hoarseness of voice, and dry cough for 30 days. On examination, stridor was present. Chest radiograph showed mediastinal widening. Computed Tomography (CT) of the chest reported a mass originating from the posterior wall of the upper one-third trachea, causing more than 70% luminal narrowing, diagnosed as CAO (Figure 1a). Check bronchoscopy revealed a slit-like trachea. Since the patient presented with critical airway narrowing, the mass was visualized using EUS-B via the esophagus (Figure 1b). TBNA (Olympus 21-gauge EBUS needle) passes were performed. However, Rapid Onsite Evaluation (ROSE) was inconclusive. To proceed with EUS-B cryobiopsy, air insufflation was done through the suction port of the scope, for visualization of the needle insertion site (through which Fine Needle Aspiration Cytology, FNAC, was done) in the esophagus. Under direct visualization and guidance of EBUS scope in the esophagus, a 1.1 mm miniature flexible cryoprobe (ERBE,

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Medizintechnik, Tübingen, Germany) was then advanced through the port (Figure 1c), into the lymph node, crossing mucosa, sub-mucosa, and node capsule. Two cryobiopsies were done (Figure 1d) under real-time visualization, which were thawed in saline and fixed in formalin (Figure 1e). The Histopathology (HPE) and Immunohistochemistry (IHC) showed well-differentiated keratinizing squamous cell carcinoma (Figure 1f).

Case 2

A 49-year-old man, a chronic smoker with a smoking index of 40 pack years, presented with complaints of facial puffiness, dyspnea in the lying down position, facial plethora, distension of neck veins, and hoarseness of voice for 10 days. Chest radiograph showed mediastinal widening. Contrast-Enhanced Computed Tomography (CECT) was suggestive of mediastinal mass compressing the superior vena cava and trachea (Figure 2a). He also had enlarged 4L, 7, 10R, 10L lymph nodes. (Figure 2b) Bronchoscopy was attempted for sampling; however, because of vocal cord edema, further bronchoscopy was not proceeded with. Under EUS-B guidance, mass was

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visualized (Figure 2c). FNA passes were taken. ROSE revealed the possibility of neuroendocrine tumor vs lymphoma, requiring immunohistochemistry for further confirmation. Cryobiopsy was done using the same method as explained in the previous case (Figure 2d, 2e). HPE is suggestive of a tumor made up of sheets of small round cells with a high N/C ratio, which is likely small cell carcinoma (Figure 2f). The same was confirmed with IHC.

Discussion

EUS was initially designed for gastrointestinal tract malignancies; however, EUS-FNA gained importance in diagnosing and staging lung cancer. Stations 4L, 7, 8, and 9 can be sampled easily via EUS. Station 2 and 4R cannot be assessed by EUS due to the presence of air between the node and ultrasound probe; however, if the size of the 4R lymph node is huge, it can be sampled by EUS.⁵ Meta-analysis has shown a combined sensitivity of EBUS-FNAC and EUS FNA to be 86% and a specificity of 100% for staging lung cancer.⁶ However, studies have shown a low sensitivity of EUS-FNA for the diagnosis of lymphoma. A prospective study by Hedenstrom *et al.*

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has shown the sensitivity of diagnosing lymphoma by EUS-FNA is 9% and by EUS-FNB (fine needle biopsy) is 55%.⁷ Mediastinal lymph node cryobiopsy is a novel tool for diagnosing mediastinal tumors, especially lymphoma or histopathological sampling in lung cancer for running molecular markers. A study by Zhang *et al.* has shown that the overall diagnostic yield in mediastinal cryobiopsy was 91.8% as compared to EBUS-TBNA, which was 79.9% (p=0.001).⁸ Our patients presented with mediastinal mass leading to critical airway narrowing, due to which EBUS was not feasible. Hence, the decision to use EUS-guided cryobiopsy was made so that diagnosis and ancillary studies could be done simultaneously and the patient could be started on appropriate therapy.

Systematic review

A literature review was conducted in the PubMed, Medline, and Lilacs databases using the search terms “Mediastinal” AND “Cryobiopsy” AND “Transesophageal.” Database was searched from inception up to March 2024. Title/abstracts identified were

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screened for full-length articles and English language; a total of 4 articles were identified. After excluding review articles, 2 case reports were included in the final evaluation (Figure 3).

Thus, currently, the literature on using EUS cryobiopsy for diagnosing mediastinal lesions is scarce. There are only 2 case reports published using trans-esophageal cryobiopsy for the diagnosis of mediastinal mass (Table 1). A study by Huang *et al.* showed no evidence of malignancy in the EUS-FNA sample; however, when cryobiopsy done from the same site, it suggested the diagnosis of lymphoma.⁹ In a case report by Ariza-Prota *et al.*, the decision of EUS-cryo biopsy was taken as the patient was at high risk of developing respiratory failure. They used a 1.1mm cryoprobe after making a tract using a 22G needle. The diagnosis of squamous cell carcinoma was made, and the sample was sufficient to run molecular markers.¹⁰ Theoretically, complications of EUS cryobiopsy could be the same as those of EBUS-TMC, like bleeding, pneumomediastinum, and mediastinitis; however, there was no complication noticed in either of the two cases published in the literature or any of the present case

Conclusions

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Endoesophageal mediastinal cryobiopsy is a novel technique. The above cases highlight the importance of EUS-cryobiopsy in patients with critical airway obstruction and its role in early treatment initiation. Literature on the use of EUS cryobiopsy is scarce and will require further studies to understand complications, the number of biopsies required, and the locations that can be biopsied.

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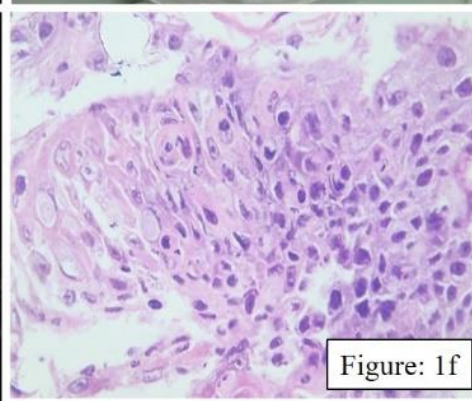
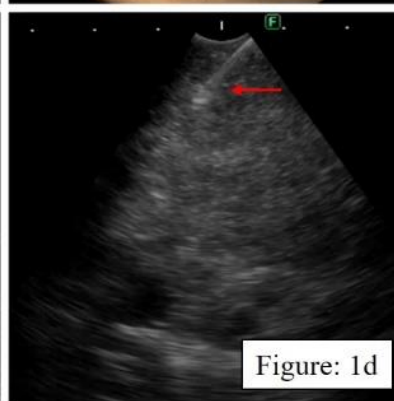
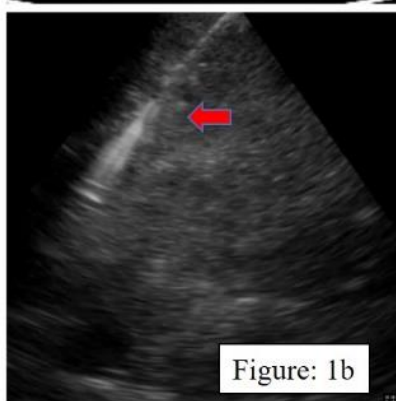
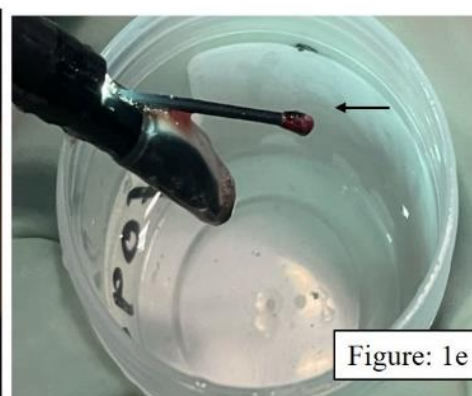
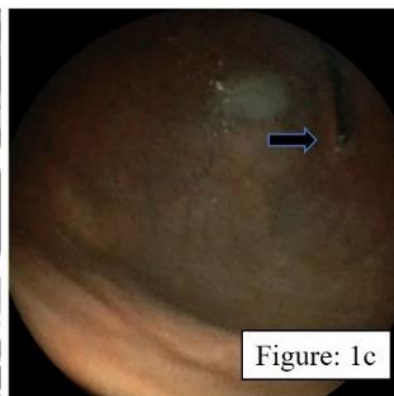
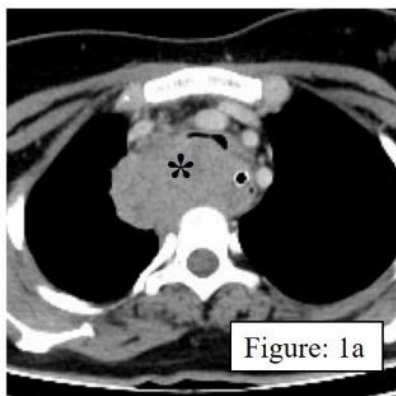
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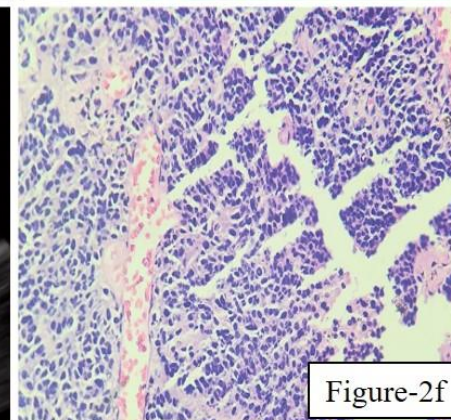
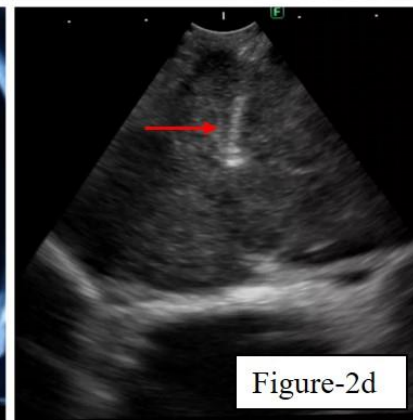
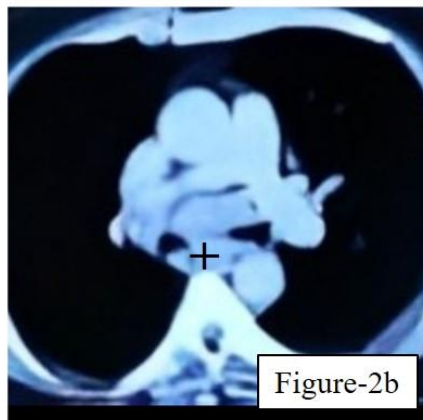
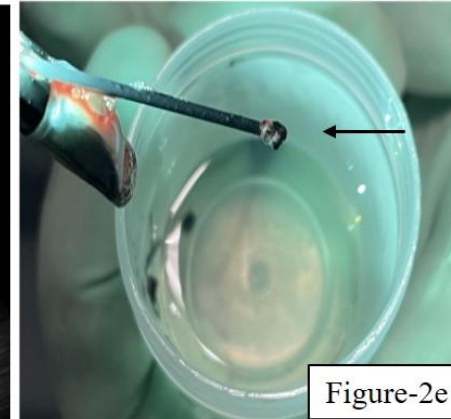
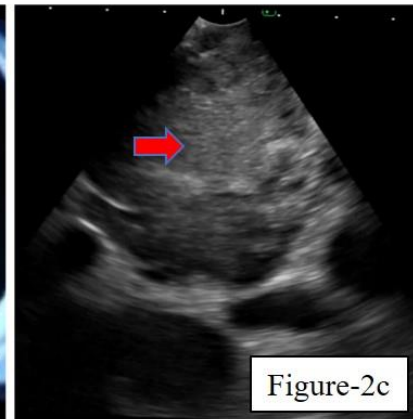
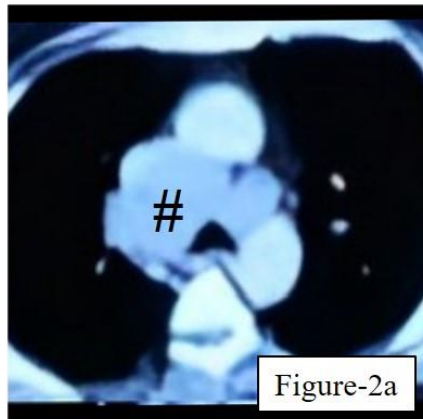
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Figure 1. **a)** Tracheal mass compressing trachea; **b)** ‘red arrow’ shows Endoscopic Ultrasound Fine-Needle Aspiration (EUS-FNA) from the mass; **c)** cryoprobe insertion in the distended esophagus; **d)** ‘red arrow’ shows cryoprobe in the lesion; **e)** cryobiopsy specimen; **f)** Histopathology (HPE) (400x) squamous cell carcinoma.

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Figure 2. **a)** ‘Mass compressing Superior Vena Cava (SVC); **b)** level 7 lymph node; **c)** ‘red arrow’ shows level 7 lymph node visualized by Endoscopic Ultrasound (EUS); **d)** ‘red arrow’ shows cryoprobe in lymph node; **e)** cryobiopsy specimen on cryoprobe; **f)** shows Histopathology (HPE) (400x) small cell carcinoma.

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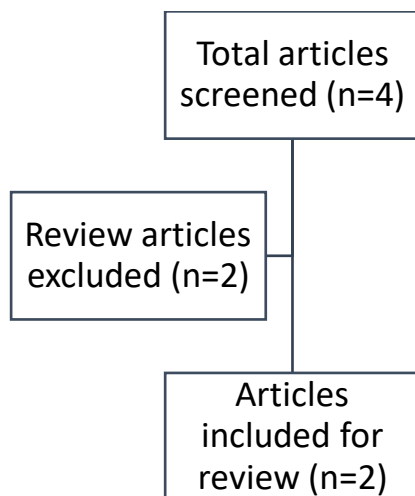


Figure 3. Flow chart for review.

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Table 1. Indication and outcomes of Endoscopic Ultrasound (EUS)-guided Cryobiopsy cases published in the literature.

Author and journal, country year	Age/sex/lymph node station	Cryoprobe used and tract made by?	Why is EBUS not used?	Diagnosis by EUS-FNA	Final diagnosis by EUS-cryobiopsy	Complication
Huang <i>et al.</i> ⁹ Respiration China, 2022	73/Female/Para-aortic	1.1 mm/High-frequency needle knife	EBUS screening negative	No atypical cells	Hodgkins Lymphoma Positive for CD20, BOB1, Pax-5, and OCT-2, Ki-67,	None
Ariza-Prota <i>et al.</i> ¹⁰ Bronconeum ologica Spain, 2023	67/Male/Subcarinal	1.1 mm/22G needle	Risk of respiratory failure	NSCLC	Squamous cell carcinoma	None
Case 1 India	26/Female/Posterior tracheal mass,	1.1 mm/21G	Critical airway narrowing	Suspicious of malignancy	Squamous cell carcinoma	None

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Case 2 India	49/Male/Subcarinal node	1.1mm/21G	Laryngeal edema	Few atypical cells	Small cell carcinoma	None
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EBUS, Endobronchial Ultrasound; EUS-FNA, Endoscopic Ultrasound Fine-Needle Aspiration; NSCLC, Non-Small Cell Lung Cancer

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