

## Original Research Article

# Unveiling mediastinal pathology: role of EUS guided fine needle aspiration in diagnosing mediastinal lesions

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## ABSTRACT

**Background:** Mediastinal lesion is the focus of investigation in diagnosis of infective, granulomatous or neoplastic pathology of respiratory system. Metastatic mediastinal node assessment is an integral part of oncological management. EUS provides access to sampling of mediastinal mass, sub-carinal and aorto-pulmonary nodes. This study aims to assess the clinical impact, diagnostic yield and safety of EUS guided FNA for mediastinal lesions.

**Methods:** Retrospective analysis of prospectively collected data of 72 cases of mediastinal lesions between January 2014 and December 2017 was done. EUS-FNA was performed with a linear echoendoscope using a 22- or 25-gauge needle. Adequacy of cellularity was assessed by on site pathologist. Patient data (demographics, intervention and follow-up) were prospectively collected and introduced in a predefined computer database for later review.

**Results:** EUS-FNA was performed from 57 lymph nodes and 15 mediastinal masses. Adequate samples were obtained in 67 of 72 patients (93.05%). All mediastinal masses were malignant and were identified in the 3<sup>rd</sup>, 5<sup>th</sup> and 6<sup>th</sup> decade of life. Of the 57 lymph nodes, 15 were malignant, 28 had granulomatous lymphadenitis of which 16 individuals became asymptomatic after anti tubercular therapy. Sample was inadequate in 5 circumstances. No major complications were encountered with the procedure in any of the individuals.

**Conclusions:** EUS guided tissue diagnosis is a safe technique and our data supports the use of EUS-FNA in work-up of mediastinal lesions. It is minimally invasive, accurate and has easy access to mediastinum. It has significant impact on patient diagnosis, management and should be considered over other invasive techniques.

**Keywords:** Endoscopic ultrasound, FNA, Mediastinal mass, ROSE

## INTRODUCTION

Mediastinum is often referred to the Pandora's Box in Greek mythology due to its relative inaccessibility for tissue sampling. Presently various techniques are available for obtaining specimens from mediastinum. These include CT guided biopsy, mediastinoscopy, thoracotomy, transbronchial FNAC and endoscopic ultrasound (EUS). Each technique has its advantages and limitations. EUS has evolved over the past two decades and it combines the use of flexible endoscopy with high

frequency ultrasonography. Introduction of linear scanning instruments permits easy tissue sampling and therapeutic procedures with EUS. The ability to access mediastinum makes it the state of art for workup of mediastinal lesions. The diagnostic yield of EUS-guided fine needle aspiration is of concern. Possible reasons for variable accuracy of the procedure include sampling technique used, availability of onsite pathologist/rapid onsite evaluation, needle size used and operator dependent factors.<sup>1</sup>

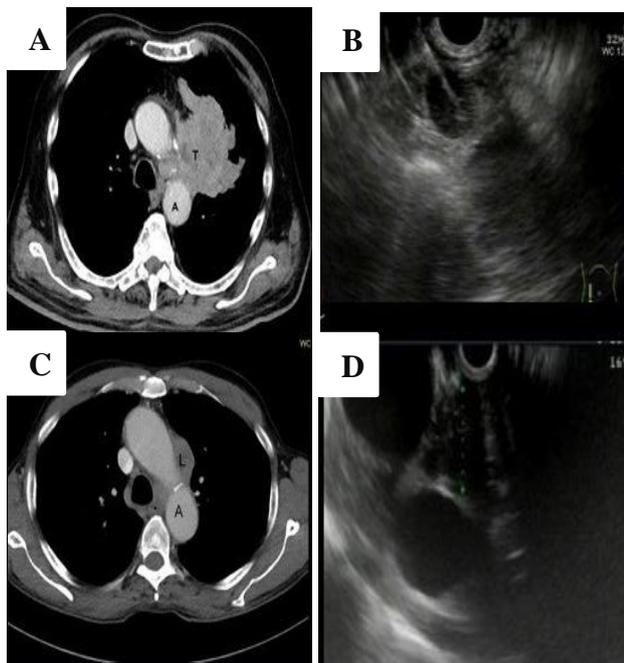
The main objective of this study was to assess the diagnostic yield and safety of endoscopic ultrasound guided fine needle aspiration (EUS –FNA) for workup of mediastinal lesions. Furthermore, this study aims to evaluate the clinical impact of EUS-FNA in patients with mediastinal lesions.

**METHODS**

This study was performed at the Department of Gastroenterology, PSG Institute of Medical sciences and Research, Tamil Nadu, India. This is a retrospective analysis of prospectively collected data of patients with mediastinal lesions evaluated from January 2014 until December 2017. Patient data (demographics, intervention and follow-up) were prospectively collected and introduced in a predefined computer database for later review. A total of 72 individuals with mediastinal lesions with various clinical presentations were included in the study.

**Technique of EUS-FNAC**

Informed written consent was obtained from patients. All procedures were performed using Olympus GF-UCT 140 linear echoendoscope with patient in the left lateral decubitus position.



**Figure 1: CT and corresponding EUS images of mediastinal mass and node. A) CT image of a Mediastinal mass. B) EUS FNA of the mass. C) CT image of a mediastinal node in station 5. D) EUS image of the station 5 aorto-pulmonary node.**

Patients with coagulopathy were excluded. Conscious sedation was preferred in all cases. A 22 or 25-gauge

needle (Boston scientific) was used for tissue sampling. Colour flow doppler imaging was done prior to FNAC to avoid intervening blood vessels. Once the needle was advanced into the targeted lesion, fanning technique was done to obtain sample. Suction of any form was not used in any cases. Following each pass, the collected material was smeared onto slides for immediate evaluation by an onsite cytopathologist using toluidine blue stain. On average 2 passes were required for adequate specimen in each case.

Further study of slides was done using Giemsa stain. Cell block was created in select cases. Post procedure patients were kept nil by mouth for 2 hours and vitals were monitored every thirty minutes for 2 hours. Figure 1 shows CT and EUS images of mediastinal node, mass and FNA from mediastinal mass.

**RESULTS**

Of the 72 cases that underwent EUS guided FNA, 44 were females and 28 were males. The most common clinical presentation was pyrexia of unknown origin, dysphagia and abnormal imaging findings. Table 1 shows the clinical presentation of patients who underwent EUS guided FNA.

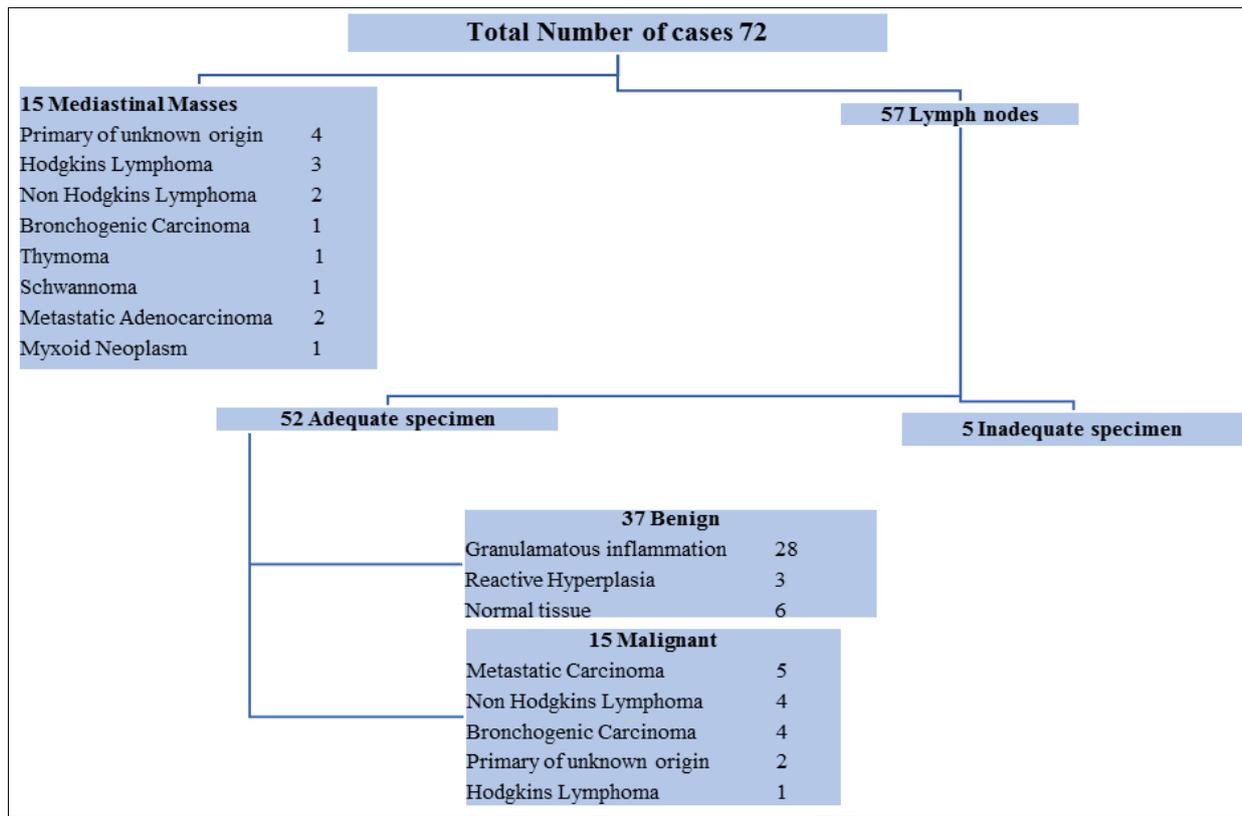
Procedure related complications included mild throat discomfort lasting for 2-4hrs following the procedure and was conservatively managed. None of the individuals had major life-threatening complications.

**Table 1: Clinical presentation of patients.**

Clinical Presentation of patients
Pyrexia of unknown origin
Dysphagia
Abnormal imaging findings (CT Thorax / Chest X ray)
Lymph node of Unknown origin
Unintentional weight loss
Hoarseness of voice
Horner's and superior vena cava syndromes

EUS guided FNA was done from 57 lymph nodes and 15 mediastinal masses. Lymph nodes included those in subcarinal, aorta pulmonary and paraesophageal region. Of the 57 lymphnodes, adequate specimen for diagnosis was obtained in 52 cases. In 5 cases tissue obtained was reported inadequate for reporting by the pathologist, though on site pathologist opined the cellularity of the samples to be adequate.

EUS-FNA obtained from mediastinal masses was diagnostic in all circumstances. 14 patients were males and 1 was female. Patients were in the 3<sup>rd</sup>, 5<sup>th</sup> and 6<sup>th</sup> decades of life. Figure 2 shows the diagnostic outcomes of FNA in mediastinal mass.



**Figure 2: Outcome from EUS-FNA in mediastinal mass.**

In present study, EUS-FNA from mediastinal masses was diagnostic in all the cases (100%). The final histopathological diagnosis included 3 cases of Hodgkin’s lymphoma, 2 cases of Non Hodgkins lymphoma, 1 case of Bronchogenic carcinoma, 1 case of thymoma, 1 case of schwannoma, 2 cases of metastatic

adenocarcinoma, 1 case of myxoid neoplasm. 4 cases were reported as malignancy, but primary site of origin could not be identified. Sampling using EUS-FNA from lymph nodes was adequate in 52/57 circumstances (93.05%). 37 out of 52 lymph nodes were benign, these included granulomatous inflammation (28/37), reactive hyperplasia (3/37) and normal lymphoid tissue (6/37).

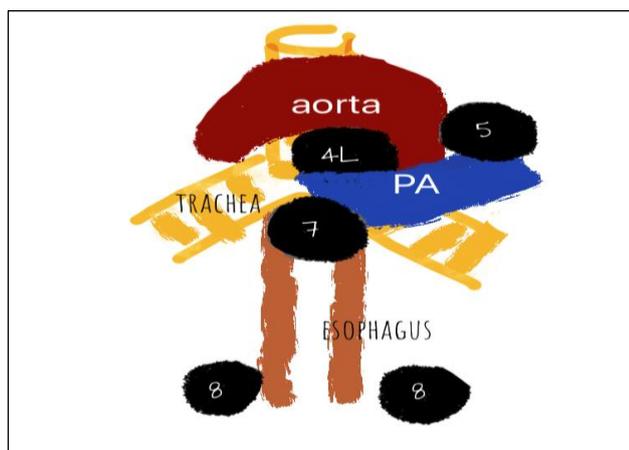
**Table 2: Final diagnosis.**

Study subjects	Diagnosis made by use of EUS FNA	Number of cases
Malignant (30)	Nonhodgkins lymphoma	7
	Metastatic carcinoma	6
	Primary of unknown origin	6
	Hodgkins lymphoma	4
	Bronchogenic carcinoma	4
	Thymoma	1
	Schwannoma	1
	Myxoid neoplasm	1
Benign (37)	Granulomatous inflammation	28
	Reactive hyperplasia	3
	Normal tissue - no significant pathology	6
Inadequate sample (5)		5

About 16 patients with granulomatous lymphadenitis had probable tuberculosis and became totally asymptomatic with anti-tubercular treatment. 15 (28.8%) out of 52 lymph nodes were malignant. These included 4 cases of Non Hodgkins lymphoma, 3 cases of bronchogenic carcinoma, 5 cases of metastatic carcinoma, 2 cases of primary of unknown origin and 1 case of Hodgkins lymphoma. Table 2 lists the final diagnosis made by use of EUS FNA, in all the study subjects.

## DISCUSSION

A decade ago, mediastinoscopy was the investigation of choice for workup of suspected mediastinal lesion. It has limitation of access to anterior part of esophagus only. Over the years EUS has evolved and has now become a vital tool for sampling mediastinal lesions. EUS guided FNA is a widely accepted technique for sampling mediastinal masses as it is safe, sensitive and has significant impact on patient management. It combines the use of endoscopy and ultra sonogram, which was initially used for evaluating the pancreas.<sup>2</sup> Echoendoscope operates across a broad range of frequencies ranging from 5 to 20MHz, with a variable depth of penetration and resolution.



**Figure 3: Mediastinal nodes accessible for EUS guided FNA.**

Computerised tomography of the chest is often the primary screening tool for evaluation of patients suspected with mediastinal mass. Sampling of mediastinal lesions has a major impact on patient management. EUS FNA is the preferred sampling method performed when the target lesion appears accessible and is paraesophageal, in the posterior mediastinum, or in the inferior mediastinum.<sup>3</sup> Station 4 L, 5, 7 and 8 were more accessible by EUS (Figure 3), whereas for mediastinal abnormalities in the anterior or superior mediastinum, endobronchial ultrasound-guided transbronchial fine needle aspiration (EBUS-TBNA) may be more appropriate.

The diagnostic yield of EUS-FNA often remains a concern. The number of passes, use of rapid on-site cytologic evaluation and fanning technique affect the diagnostic yield of EUS FNA.

### Number of passes

Even though EUS-FNA is widely available, few patients still do not receive conclusive diagnoses upon initial EUS-FNA. The exact number of passes required for adequate EUS guided tissue acquisition remains unclear. Factors influencing the number of fine needle passes required during EUS-FNA include needle size, type of lesion (solid/cystic) and presence of onsite cytopathologist during the procedure. Approximately five to seven passes are required for pancreatic masses, five passes for lymphnodes.<sup>4</sup> A core biopsy needle or 19-G FNA needle could improve diagnostic yield. Targeted sampling has better diagnostic utility than random sampling. Newer tissue acquisition needle and fine needle biopsy needle has claimed improved diagnostic yield.

Rapid on-site cytologic evaluation (ROSE): This was well described in sampling of transbronchial, percutaneous lung, pancreas and sentinel lymph nodes in breast cancer.<sup>5-9</sup> Rapid on-site cytologic evaluation informs the operator for need to obtain additional samples and increases diagnostic yield.<sup>10</sup> On average, ROSE improves the per-case adequacy rate by about 12%.<sup>11</sup>

It also allows preliminary diagnosis so that additional material can be requested for ancillary studies such as flow cytometry, microbiology cultures, or molecular studies.

### Fanning technique

Fanning technique is superior to standard technique and involves sampling multiple areas within a lesion with each pass.<sup>12</sup> The needle is positioned at four different areas within the mass and then moved back and forth four times in each area to procure tissue (4×4). Aspiration is initiated at the left margin and then “fanned” until the right margin of the mass was sampled.

Earlier evidence revealed EUS-FNA as a useful tool for workup of mediastinal lesions. A retrospective cohort study evaluated 49 patients who underwent EUS-FNA to evaluate mediastinal lymphadenopathy or a mediastinal mass. Benign diseases were detected in 24 patients (49%).

They included 8 cases of histoplasmosis, 1 case of sarcoidosis, 2 cases of leiomyoma, 2 cases of duplication cyst, 1 case of teratoma, and 10 cases of benign lymphadenopathy. EUS-FNA identified malignant mediastinal disease in 22 patients (45%). Diagnoses included 6 cases of breast cancer, 2 cases of colon cancer,

2 cases of renal cell cancer, 2 cases of testicular cancer, 1 cases of esophageal cancer, 1 case of laryngeal cancer, 4 cases of metastatic disease from an unknown site, 2 cases non-small cell lung cancer and 1 cases of small cell lung cancer. When both malignant and benign diagnoses were considered, EUS-FNA made the correct diagnosis in 94 percent of cases.<sup>13</sup> In another prospective cohort study of 35 patients suspected of having bronchogenic carcinoma but whose bronchoscopy was nondiagnostic, EUS-FNA correctly confirmed the diagnosis in 25 of the 26 patients who had bronchogenic carcinoma.<sup>14</sup> EUS-FNA had an overall diagnostic yield of 93 %, sensitivity of 71 %, specificity of 100 %, and positive predictive value of 100 % in a study of 60 consecutive patients done to evaluate the role of EUS-FNA in isolated mediastinal lymphadenopathy in patients suspected of having tuberculosis.<sup>15</sup>

In this study, the diagnostic yield of EUS FNA was 93%. The acceptable rate of tissue acquisition at our centre was probably due to the combined use of the above described techniques.

#### **Complications of EUS-FNA**

Mild throat discomfort lasting for 2-4hrs following the procedure was encountered in all individuals and was conservatively managed. There is little evidence to suggest that haemorrhage is a major a complication of EUS-FNA. Increase in needle size is associated with higher risk of bleeding complications. Trucut biopsy needle has a higher risk of bleeding when compared to FNA. Colour flow Doppler prior to FNAC to avoid intervening blood vessels reduces chance of bleed. The use of prophylactic antibiotics to prevent infection while performing EUS FNA remains controversial. Evidence suggests that infection associated with EUS-FNA ranges from 4 to 6 percent.<sup>16</sup> Risk of bacteraemia depends on the type of tissue being sampled. Solid lesions are associated with lesser risk of infection when compared to cystic lesions.<sup>17</sup> A standard diagnostic endosonography carries a risk of esophageal perforation between 0.03 and 0.06%.<sup>18,19</sup> Clinical findings of tachycardia, chest pain and air crepitus following the procedure should raise concern for perforation. In present study, none of the patients had life threatening complications and hence EUS is a safe tool for workup of mediastinal lesions.

#### **CONCLUSION**

EUS guided tissue diagnosis is a safe technique and our data supports the use of EUS-FNA in work-up of mediastinal lesions. It is minimally invasive, accurate and has easy access to mediastinum. It has significant impact on patient diagnosis, management and should be considered over other invasive techniques.

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