

Diagnostic Accuracy of Endoscopic Ultrasound and Endoscopic Ultrasound Guided Fine Needle Aspiration in The Diagnosis of Tuberculous Mediastinal Lymphadenopathy

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Author's Contribution

^{1,2} Conceived the topic and review the study

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Introduction

Tuberculosis is one of the oldest infectious disease known to mankind.¹ It can involve the lung parenchyma (Pulmonary Tuberculosis) or any other part of the body (extra pulmonary Tuberculosis). Therefore, mediastinal lymphadenopathy or pleural effusion, without

ABSTRACT

Objective: To determine diagnostic accuracy of Endoscopic Ultrasound (EUS) for diagnosis of Tuberculous Mediastinal Lymphadenitis.

Methodology: A cross sectional study conducted in a period of six months at the Gastroenterology and Hepatology Department of Holy Family Hospital. 97 patients with radiographic finding of mediastinal lymphadenopathy were selected for EUS. During the procedure aspiration biopsy of significant lymph nodes was done. The diagnosis was made on the basis of specific EUS findings and histopathology report of mediastinal lymph nodes (ML).

Results: Age range of patients was 14 years (youngest) to 80 years (oldest). Out of 97 patients 49 (50.5%) were males and 48 (49.5%) were females. On analysis of data it was found that sensitivity of the EUS was 82.9% and specificity as 58%. Hence it was also calculated that the diagnostic accuracy of the procedure was found to be 70%.

Conclusion: This study suggests that EUS is a useful minimally invasive procedure that can be used to provide strong supportive evidence for the diagnosis of tuberculous lymphadenitis involving the mediastinum. In addition, it also suggests that in patients with no positive finding suggestive of Tuberculosis other diagnosis should be considered and further work up should be done.

Keywords: words: Endoscopic Ultrasonography, EUS, T.B, Tuberculous Mediastinal Lymphadenopathy, FNAC, EUS-FNA.

radiographic abnormalities in the lungs, constitute a case of extra pulmonary Tuberculosis (T.B).²

There are many causes of mediastinal and hilar lymphadenopathy. It can be due to infections, granulomatous diseases or malignancies.¹The most common cause of mediastinal lymphadenopathy in

developing countries like Pakistan is T.B. A significant number of patients with symptoms suggestive of T. Bonly have mediastinal lymphadenopathy.

Many other diagnostic modalities are available for the diagnosis of Tuberculosis. These include sputum analysis for Acid Fast Bacilli (AFB), CT chest and PET scan.³ However, in patients where there is only mediastinal lymphadenitis and no parenchymal involvement due to tuberculosis chances of detection of AFB in sputum smear is very less. CT chest also has draw back of poor visualization.⁴

Mediastinoscopy is still the gold standard for detection of mediastinal lymph nodes in various diseases. However, it cannot be done without General Anesthesia and has a morbidity and mortality of 2% and 0.08% respectively. Moreover, it cannot be used to evaluate hilar lymph nodes.^{5, 6, 7}

EUS-FNA is simple, cost effective and versatile technique, which has the advantage of possessing the ability to detect lesions that are not clearly visualized by other techniques. Indications of EUS-FNA are numerous, few to mention are intra-abdominal or mediastinal lymph nodes and pancreatic cysts or masses. It can provide a diagnosis in 85-90 % of the cases.

The aim was to highlight the significance of EUS in the diagnosis of tuberculous lymphadenopathy, keeping in mind its attribute of being safe and minimally invasive procedure before starting any empirical therapy, or before considering surgery as an option. Till to date it is not considered n priority basis due to absence of sufficient literature.

Methodology

It was a cross section (validation) study carried out in Gastroenterology and Hepatology division of MU-1 of Holy Family Hospital, Rawalpindi in a duration of six months. Sample size was calculated using WHO sample size calculator keeping Confidence level 95%, Sensitivity 84.7%, Desired precision 86.4%. The estimated prevalence of T.B was 54.4%.³ Calculated sample size was 97. Age of patients included in this study ranged was from 14 - 80 years. Only those patients who had clinical suspicion of Tuberculosis along with radiographic finding suggestive of mediastinal lymphadenopathy were included in this study. Patients excluded from this study were those who were assessed to be high risk for the procedure, and in whom the etiology of lymphadenopathy was already established.

After approval from ethical review board of Holy Family Hospital informed consent was taken from the patients.

Patients fulfilling the inclusion criteria were included in the study. Their demographic details were recorded. Endoscopic Ultrasonography was conducted by a Consultant Endoscopist with Linear EUS Machine Model EVS-240 Series of Olympus. Fine Needle aspiration of the mediastinal lymph nodes was carried out in each case with needle model NA-200H-8022, width 22g, length - 80mm. All biopsy specimens were sent to histopathologist for interpretation to minimize the observer bias. Biopsy results were collected and documented.

Variables included in this study were age, sex, true positives, true negatives, false positives and false negatives . SPSS version 17 was used for data analysis. Mean and standard deviation for age was calculated. Diagnostic accuracy was calculated keeping histopathology as standard.

Results

97 patients were recruited in this study after taking informed consent. Patients with clinical suspicion of T.B and evidence of mediastinal lymphadenopathy on X-rays or Computed Tomography were included in this study. Ages of patients included in this study ranged from 14 to 80 years with the mean age of 44.23±9.34. Among these 97 patients 49 (50.5%) were males and 48 (49.5%) were females. Our study results showed that there were total 39 (40.2%) true positives, 29 (29.8%) true negatives, 21 (21.6%) false positives and 8 (8.2%) false negatives.

Our study results showed that EUS-FNA has a sensitivity of 82.9% and Specificity of 58%. The Positive and Negative Predictive Value (PPV) in overall study population was 57.3 % and 78.3% respectively. Hence diagnostic accuracy was found to be as 70%. (Table#1)

Table I: Diagnostic accuracy of the EUS keeping histopathology as Gold Standard.

Parameter	Value
Sensitivity	83%
Specificity	58%
PPV	65%
NPV	37%
Accuracy	70%

Discussion

Tuberculosis is recognized as a chronic, communicable granulomatous disease which is caused by mycobacterium tuberculosis. It is more common in South East Asia due to poverty, lack of sanitization and health care facilities. According to the surveys conducted by WHO and Government of Pakistan, estimated prevalence of T.B in Pakistan is 54.7% and 54.4%.⁸ Tuberculosis is

classified as Pulmonary or Extra pulmonary .Pulmonary T.B refers to a disease in which lung parenchyma is involved only. Involvement of any other part of body comes under the domain of extra pulmonary T.B.⁹ A common presentation of extra pulmonary tuberculosis is in the form of non -specific symptoms with mediastinal lymphadenopathy and its diagnosis remains a challenge.¹⁰ Early diagnosis and treatment of Mycobacterium tuberculosis can help decrease morbidity and mortality to a significant extent.¹¹ Among the factors that contribute to the diffusion of M. tuberculosis is its ability to adopt a dormant state that helps it to survive for years.^{12, 13} In few patients, secondary T.B occurs when the pulmonary disease spreads from its primary focus in the lungs to other parts of body through self-inoculation. This can occur through infected sputum, blood, or lymphatic system.¹⁴ The global number of new TB cases is rising at a rate of 2% per year. Therefore, more advanced investigation modalities, with high degree of sensitivity and specificity, are required to make an early diagnosis, to assess the prognosis, and also to monitor the recurrence of disease.¹⁴ This study was conducted to identify patients with mediastinal lymphadenopathy in whom EUS-FNA can give a definitive diagnosis. This can help physicians to start anti tuberculous treatment in time or to consider other diagnosis. The results of this study will help in improving our population's general health and in adjusting the health budget according to the needs. Through the introduction of this minimally invasive investigation technique, physicians will be able to diagnose the cause of mediastinal lymph nodes with more confidence as it is still a difficult field of diagnostics despite the incorporation of clinical, radiological, pathological and microbiological examinations.

Endoscopic ultrasound guided fine needle aspiration was first described by Vilmann et. al. in 1992. It is now widely used clinically for broad range of indications. The diagnostic accuracy of EUS ranges from 70% to 100 % with 0% to 3% incidence of complications. The overall accuracy of diagnosing malignancy in the posterior mediastinum with EUS-FNA is 90%.^{15,16} The only limitation of EUS is that it is unable to access the structures in the anterior mediastinum because of the presence of air in the trachea.¹⁷ Mediastinal lymphadenopathy is difficult to diagnose and often mimics mediastinal tumor or lymphoma.¹⁸ FNA can be performed safely during EUS as a short outpatient procedure without the need of administration of general

anesthesia. FNA adds in accuracy of EUS to diagnose mediastinal lymphadenopathy.¹⁹

The management and prognosis of patients with mediastinal lymphadenopathy vary tremendously according to its etiology. Therefore, differentiating inflammatory process from malignancy is important for treatment as well as for predicting survival.^{20, 21}

In our study, EUS showed mediastinal lymph adenopathy in 60 (61%) of the 97 patients. In another study conducted in India for assessing utility of EUS in the diagnosis of tuberculous mediastinal lymphadenopathy, true positives were 55%.

In different studies conducted worldwide, mediastinal lymphadenopathy is assessed on the basis of size, contour and echo characteristics. We also assessed mediastinal lymph nodes on the basis of similar characteristics. Features that consistently favored tuberculosis as the possible cause of lymphadenopathy were matted lymph nodes, anechoic foci suggestive of caseation as well as hyper echoic foci due to calcification.

Sensitivity of a test depicts its ability to detect people who have the disease. In our study sensitivity of EUS to diagnose tuberculous mediastinal lymphadenopathy was 82.9%. It is a fairly high sensitivity and makes EUS a very useful modality for the diagnosis of the cause of mediastinal lymphadenopathy (ML).

Specificity of a test is the measure of its ability to detect people who do not have the disease. In our study, specificity of EUS was 58%. This is a low value with respect to international standards and is mainly due to much higher false positive results. This can be due to the fact that it is a relatively newer technique and is operator dependent. Moreover, there are areas in the mediastinum that are difficult to reach so the material aspirated for histopathology is usually insufficient in these cases.

Positive predicted value is precision rate of a diagnostic test. It is directly proportional to the disease prevalence. Higher the PPV value, higher is the diagnostic utility of the test. In our study PPV is 57.3 which is much higher considering the prevalence of T.B among patients with mediastinal lymphadenopathy.

Negative predictive value gives the proportion of patients with negative results who actually have no disease. More is the NPV value, the more is diagnostic utility of the test. In our study, NPV value is 78.3 which is significantly high value.

True negatives are those patients in whom there is no evidence of T.B on EUS and the results of their histopathology after EUS- FNA also did not support the

diagnosis of T.B. In our study, true negatives were 29.8% which means that in cases of ML significant number of patients will have diagnoses other than T.B.

Our study raises an important point that it is unwise to start Anti-Tuberculous drugs just on the basis of radiographic findings suggestive of mediastinal lymphadenopathy as it can be due to other causes as well. Low number of false negatives(8%) in our study suggest that we can start Anti-Tuberculous drugs if EUS findings are characteristic of T.B even before the histopathology results are available.

We also noted certain limitations in our study. There is lack of experience with this technique in our country which makes it difficult to be used as a routine investigation. It is a relatively newer technique and is not widely available. The use of sedative drug during this procedure makes it risky for patients who have certain premorbid like DCLD. The equipment used for EUS-FNA is expensive and requires regular maintenance making it difficult to manage in a developing country like us. However our study has highlighted the significance of a minimally invasive technique (EUS and EUS-FNA) in diagnosing mediastinal T.B as well as identifying other diseases that can present as mediastinal lymphadenopathy.

Conclusion

As high good accuracy is found in this study of the EUS so it could be advised to the patients for the confirmation of TB. Since there is high burden of tuberculosis in our country so the decision of administration of anti-Tuberculous regimes must be made on the basis of definite diagnostic tests. Therefore, final conclusion drawn from this study is that we can safely rely on findings of EUS and EUS-FNA for the diagnosis of tuberculous mediastinal lymphadenopathy.

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