The utility of ROSE (rapid on-site evaluation) in endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA): Is the picture rosy?

ABSTRACT

Background: Mediastinal lymphadenopathy (ML) presents a diagnostic challenge. The technique to sample the lymph nodes has evolved from conventional “blind” transbronchial needle aspiration (TBNA) to the present day endobronchial ultrasound (EBUS)-guided procedure that improves the accuracy of sampling.

Objective: This study was undertaken to evaluate the utility of “rapid on-site evaluation” (ROSE) in EBUS-guided TBNA (EBUS-TBNA) for the diagnosis of ML.

Patients and Methods: This prospective study included 80 patients who underwent EBUS-TBNA for computed tomography/positron emission tomography (CT/PET) diagnosed ML over a 4-month period at a single tertiary care center. All 80 of these patients underwent histopathological evaluation (HPE) in addition to cytology. Three out of these 80 (3.7%) patients were excluded in view of inadequate material on EBUS-TBNA. After the sampling of nodes was done, the slides were stained with rapid hematoxylin and eosin (H&E) and then on-site evaluation was done. The tissue derived was also processed for HPE in all cases.

Results: ROSE revealed granuloma in 27 patients and malignancy in 14 patients, and the remaining patients showed nonspecific inflammation. Concomitant histopathology revealed granuloma in 34 patients and malignancy in 14 patients. Considering HPE as gold standard, the overall sensitivity and specificity of EBUS-TBNA for diagnosis were 85.4% and 89.6%, respectively. For malignancy alone, the sensitivity and specificity were 100% and 98.4%, respectively.

Conclusion: This novel approach is safe, has good diagnostic yield, and has an excellent potential in assisting safe and accurate diagnostic interventional bronchoscope.

Key words: Endobronchial ultrasound (EBUS), mediastinoscopy, rapid on-site evaluation (ROSE), transbronchial needle aspiration (TBNA)

Introduction

Mediastinal lymphadenopathy (ML) presents a diagnostic challenge. Infections, granulomatous diseases, reactive hyperplasias, and malignancies can cause enlargement of the mediastinal lymph nodes.1,2 These nodes need to be sampled to reach a diagnostic conclusion. Various
techniques are available to sample the lymph nodes, these include blind conventional bronchoscopic transbronchial needle aspiration (TBNA), transesophageal ultrasound-guided needle aspiration, computed tomography (CT)-guided transthoracic needle aspiration, and mediastinoscopy. Most of these techniques come with certain drawbacks, namely need for general anesthesia, low yield, and poor accessibility. Endobronchial ultrasound-guided TBNA (EBUS-TBNA) is the most recent advancement in the field of pulmonary medicine, and it has revolutionized the scene for the pathologist and pulmonologist. TBNA is performed real time under direct visualization of the needle using simultaneous ultrasound (USG) and optical imaging. A Doppler mode is used that allows vascular structures to be visualized, and the accurate localization of lymph node stations can be done. This technique uses a 21-gauge needle and allows for procurement of material for cytology and histopathology simultaneously. ROSE or rapid on-site evaluation of the cytology aspirate is done, which improves the diagnostic yield and aids in clinical decision-making. Our study was first of its kind in the Indian scenario and was done to evaluate the utility of ROSE in EBUS-TBNA for the diagnosis of ML. We sought to specifically address two questions:

1. Does ROSE EBUS-TBNA give the same adequacy and accuracy of sampling as the gold standard that is histopathology?
2. If yes, does it affect the clinical decision-making?

Patients and Methods

This was a prospective single-center study conducted at a superspeciality hospital in Bangalore. Eighty patients, who underwent EBUS-TBNA for CT/PET and were diagnosed with ML over a 5-month period from February 2014 to June 2014, were included in this study. A 21-gauge needle was used to puncture the lymph nodes. After sampling the nodes, slides were stained with rapid H&E and ROSE was done. The material was also procured for histopathology in each case. The assessment for the sample adequacy was performed as follows: It was based on counting the lymphocyte numbers in the most cellular areas under 40× magnification. A score of 0 was given if the number of lymphocytes was below 40, a score of 1 was given if the number of lymphocytes were between 41 and 200. A score of 2 was given if the number of lymphocytes was more than 200 and a score of 3 was allotted if there were more than 200 lymphocytes noted in the confluent sheets with or without germinal center formation [Table 1].

Results

Of the 80 cases, 3 (3.7%) were excluded in view of inadequate material on EBUS-TBNA. Of the 77 cases, 49 were males and 28 were females. The average age of the patients was 54 years. An average time of 34 min was spent on each case. Mostly, 3-5 passes were made into each node and around 3-7 slides were made from each station. The most common lymph node to be sampled was station 7 followed by station 4R [Table 2]. Of the 77 patients examined on site, a diagnosis of malignancy was given for 14 cases [Figure 1a and b], granuloma [Figure 1c] for 27 cases, and nonspecific lymphadenitis for 36 cases [Table 3].

Histopathology slides from all the 77 patients were examined and it was seen that all 14 cases that were positive for malignancy on cytology were also found to be malignant on histopathology.

Table 1: Criteria adopted for assessing the adequacy of sampling in slide

| Score | Lymphocyte numbers |
|-------|--------------------|
| 0     | <40                |
| 1     | 41 - 200           |
| 2     | >200, not confluent|
| 3     | >200 + confluent sheets/ germinal center fragments |

Adapted from Alsharif et al.

Table 2: Frequency of different lymph nodes sampled

| Lymph node station | Number of lymph nodes sampled |
|--------------------|------------------------------|
| 2R                 | 4                            |
| 2L                 | 2                            |
| 4R                 | 44                           |
| 4L                 | 28                           |
| 7                  | 66                           |
| 10L                | 3                            |
| 11R                | 40                           |
| 11L                | 29                           |
| 12R                | 10                           |
| 12L                | 1                            |

Figure 1: (a) Cytology image showing atypical lymphoid cells (H and E, ×400). (b) Granuloma composed of epithelioid cells seen (H and E, ×400). (c) Atypical cells, some of which are forming glands (H and E, ×40)
histopathology [Figure 2a and b]. Granulomas were identified in 34 cases and nonspecific lymphadenitis was the diagnosis in 29 cases [Table 4]. The most common malignancy in our study was adenocarcinoma [Table 5]. The overall sensitivity was 85.4% and specificity was 89.6%.

Discussion

EBUS-TBNA is a fairly new technique. ROSE EBUS-TBNA is a useful technique that has revolutionized the field of pulmonology. Developed initially for detecting metastasis in lung cancer patients, it is currently used in the diagnosis of sarcoidosis, tuberculosis (TB), and lymphoma. ROSE, which has been a game changer for the pathologists, helps to act as a guide for assessing the adequacy and accuracy of the sample and aid in rapid decision-making. Our study was a prospective study where we studied 80 cases. Three out of 80 were excluded in view of inadequate sample. We obtained a sample adequacy of 96.3% that was comparable to Yasufuku et al., who also reported an adequacy of 96%. Alsharif et al. reported a sample adequacy of 84.3%.

Of the 77 patients, 49 were males and 28 were females with a male-to-female ratio of 1.7. The average age of the patients in our study was 54 years that was much less as compared to Alsharif et al. and Chhajed et al. who reported the average age of their patients as 61 years and 66 years, respectively. An average time of 34 min was spent on each case. This was higher than reported in previous studies. Mostly, 3 to 5 passes were made into each node. This was in concordance with the earlier studies. The most common lymph node to be sampled was station 7 which was the case in studies of Alsharif et al. A dedicated 22-gauge needle was inserted through the working channel of the bronchoscope and lymph nodes were punctured under real-time guidance. Slides were fixed in alcohol and stained by rapid H&E for on-site evaluation and simultaneously material was sent for histopathology.

Of the 77 cases, an on-site diagnosis of malignancy was given in 14 cases. The most common malignancy in our study was adenocarcinoma. Parmaksiz et al. also reported adenocarcinoma as the most important malignancy in their study. Granuloma composed of epithelioid cells was noted in 24 out of 77 cases and a diagnosis of nonspecific lymphadenitis was given in 36 cases. When histopathology slides were examined, all 14 cases found positive for malignancy on cytology also turned out to be positive on histopathology. Hence, the concordance in this case was 100%. Granulomas were identified in 34 cases. With histopathology as the gold standard, the sensitivity and specificity in our study were 84.4% and 89.6%, respectively. Yasufuku et al. reported higher sensitivity and specificity of 95.7% and 100%, respectively.

A sensitivity of 95% and specificity of 100% was reported by Ye et al. Alsharif et al. and Parmaksiz et al. reported sensitivity and specificity of 89.2% and 100% respectively.

EBUS-TBNA is a new technique that allows for cytological sampling of lymph nodes. Cytology and histopathology samples can be procured in the same sitting. ROSE facilitates sample adequacy and also aids in rapid clinical decision-making. It equals the gold standard, that is, histopathology by mediastinoscopy in sensitivity and specificity for diagnosis of ML. This technique can also be used to procure samples for molecular analysis.
Hence, this novel approach is safe, has good diagnostic yield and has an excellent potential in assisting safe and accurate diagnostic interventional bronchoscope. The picture indeed is rosy.

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Conflicts of interest
There are no conflicts of interest.

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