ENDOBRONCHIAL ULTRASOUND-GUIDED TRANS-BRONCHIAL NEEDLE ASPIRATION FOR THE DIAGNOSIS OF GRANULOMATOUS VERSUS NON GRANULOMATOUS LUNG DISEASES

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ABSTRACT

Objective: To evaluate the diagnostic accuracy of Endo-bronchial ultrasound guided transbronchial needle Aspiration in patients with mediastinal lymphadenopathy and mass lesions especially in the context of granulomatous versus non granulomatous lung disorders.

Study Design: Open label, unblended prospective observational cohort.

Place and Duration of Study: Department of Pulmonology, Pak Emirates Military Hospital Rawalpindi, from Jul 2015 to Mar 2016.

Patients and Methods: All patients presented during study periods with meditational lymphadenopathy or lesions in which the initial bronchoscopy did not reveal any diagnosis were included in the study. Endobronchial ultrasound-guided transbronchial needle aspiration was performed in the bronchoscopy suit under conscious sedation and local anesthesia. Rapid on site evaluation was available for most of the cases. The procedure was performed using an integrated fibreoptic bronchoscopy with 22G TBNA needle by an experienced Bronchoscopist. The data was analyzed by using SPSS version 21

Results: A total of 53 patients with mean age of 44 years underwent endobronchial ultrasound-guided transbronchial needle aspiration for evaluation of meditational or hilar lesions between Jul 2015 to Apr 2016. There were 43 (81.1%) male and 10 (18.8%) female patients. A total of 108 Lymph nodes were sampled in 53 patients, rapid on site evaluation was available in 41 (77.3%) patients. Adequate representative sample could be obtained in 45 of 53 (84.9%) patients. The overall diagnosis were chronic granulomatous lesion in 27 (50.9%) patients, squamous cell carcinoma in 10 (18.8%), lymphoproliferative disorder in 2 (3.7%), thymoma in 1 (1.3%) and reactive hyperplasia in 5 (9.4%) of cases. No major complication of the procedure was observed.

Conclusion: End bronchial ultrasound-guided transbronchial needle aspiration was found useful diagnostic modality for lymph nodes sampling in patients with lymphadenopathy and mass like lesions in mediastinum.

Keywords: EBUS–TBNA, Lung cancer, Mediastinoscopy, ROSE.

INTRODUCTION

Patients with mediastinal lymphadenopathy or suspected lung cancer require accurate tissue diagnosis to determine the optimal treatment. This has been a challenging task for pulmonologist especially in developing countries. Though mediastinoscopy is considered gold standard investigative technique for obtaining tissue sections from mediastinal lymph nodes mediastinoscopy has its confines that it is invasive procedure and not all the mediastinal stations can be accessed and there is associated morbidity of the procedure[1]. The conventional transbronchial nodal aspiration (TBNA) is often underutilised and reported yields are often low[2]. Real time endobronchial ultrasound guided transbronchial needle aspiration is a method that combines endoscopic visualisation, with high frequency ultrasound imaging which is used to obtain cytology and histology samples of the lesion adjacent to the transbronchial tree. The EBUS-TBNA has gained wide spread recognition as an accurate and minimally invasive technique for the evaluation of lymph nodes in patients with lung cancer

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Received: 12 Dec 2017; revised received: 06 Feb 2018; accepted: 05 Mar 2018

(diagnosis/staging), mediastinal tumors and diagnosis of benign granulomatous lesions[3-4]. Endobronchial ultrasound (EBUS) is a bronchopic technique that uses ultrasound to visualize structures within the airway wall, lung and mediastinum[5-6]. It expandes the bronchoscopist view beyond the lumen of the airways. There are two types of EBUS, radial probe EBUS (RP-EBUS) and convex probe EBUS (CP-EBUS). CP- EBUS is used to acquire tissue, while RP- EBUS is often used to locate target lesions suitable for sampling. Transbronchial needle aspiration (TBNA) is the aspiration of material using a needle that is passed through the endobronchial wall-Bronchoscopy is used to direct the operator to the target lesion (eg. lung mass or lymph node). It can be performed as a blind procedure during conventional white light bronchoscopy (bronchoscopic–TBNA) or under image guidance using Endobronchial ultrasound (EBUS-TBNA). EBUS-TBNA is now widely recognized, minimally invasive and safe technique with high diagnostic accuracy. It is now the preferred first step procedure for large, centrally located tumors and for suspicious nodal involvement in the anterior and superior mediastinum. The preference is based upon the high sensitivity of EBUS–TBNA to stage and diagnose NSCLC and its ability to access more nodal station than the traditional gold standard cervical mediastinoscopy[7-8]. Most of the published literature on EBUS-TBNA is concentrated on investigative and staging characteristics of lung cancer. Literature on the utility of this modality from developing countries and especially in setting with high prevalence of tuberculosis is limited.

The rationale of this study was to endorse our preliminary experience on the utility of EBUS-TBNA from a tertiary care hospital.

MATERIAL AND METHODS

We analyzed fifty three patients who underwent EBUS-TBNA at the department of Pulmonology PEMH for the evaluation of meditational or hilar lesions fulfilling inclusion criteria between July 2015 to March 2016. Demographic characteristics, type of biopsied lesions (lymph node and/or mass), number of puncture per procedure, complication rate, pathological results, ROSE (Rapid on site evaluation), FNAC fine needle aspiration cytology, histopathology findings were recorded . Informed transcribed consent for the procedure was obtained from all the patients. ROSE rapid on site evaluation was done for most of the patients. Patients reported 8 hour fast on the procedure day. Recent CT scan of the thorax was available for all the patients. Latest prothrombin time, APTT, platelet counts and hemoglobin values were available from all the patients.

The procedure was performed using an integrated fibreroptic bronchoscopy (convex probe EBUS) with a dedicated 22G TBNA needles by a bronchoscopist. Sites for TBNA were chosen based on clinical tumor stage, CT scan thorax findings and intra procedural findings; care was taken to avoid neighboring vascular structure using integrated color flow images. EBUS- TBNA was performed in all cases under conscious sedation with midazolam and fentanyl, local anesthesia was achieved using lignocaine spray in the pharynx immediately prior to the procedure.

Additional 2% lignocaine boluses were also used as required throughout the procedure. Patients were monitored with continuous cardiac monitoring including pulse blood pressure as well as pulse oximetry without any anesthetist. Supplemental oxygen was administered via nasal cannulae and I/v access was established before starting the procedure. Balloon application on the ultrasound probe was not done routinely it was used only in cases when sampling from lymph node stations 2 or 4 were required. Material obtained from EBUS_TBNA was transferred to glass slides, air dried and fixed with 95% alcohol for ROSE. The cytologist assessed the adequacy of the sample defined by the presence and number of lymphocytes and whether there was diagnostic material present after each aspiration. Fast staining was done using diff quick stain, the rest of material was put into formalin containing pot to generate a cell block. In patients with a

suspected diagnosis of TB and in cases where frank pus was aspirated or rose showed granuloma, aspirates were also sent for acid fast bacillus staining, mycobacterium tuberculosis cultures and gene expert MTB_Rif test.

Data Analysis

The data obtained was entered in SPSS version 21. Categorical variable were expressd as frequency (percentages) and quantitative variable were expressed as mean.

RESULTS

A total of fifty three patients were included in the study. Average mean age of the study group was 44 ± SD. There were 43 (81-1%) males and 10 (18.8%) females. Overall 108 lymph node stations and three mass lesions were sampled in 53 patients with a median of two stations sampled per patient. The median number of needle punctures per patient was three and ranged from two to six punctures per patient. The most recurrentlytested lymph node stations were the subcarinalstation[7]. Sufficient and descriptive samples were obtained in 45 of 53 patients (84.9%). The overall diagnosis included granulomatous lymphadenopathy in 27 (50%) patients squamous cell carcinoma in 10 (18.8%), lympho proliferation in 2(3.7%) thymoma in 1 (1.8%) reactive hyperplasia in 5 (9.4%) of cases (table). Out of 27 granulomatous cases 21 (77.7%) were diagnosed as sarcoidosis and 6 (22.2%) were diagnosed as tuberculosis. Diagnosis of tuberculosis was made in one patient with positive culture, 02 patients with positive MTB gene Expert and in 03 patients with typical histopathology of cassation necrosis. Rose was available in 42 of the cases and out of 8 cases of inadequate samples 05 were without rose. No major complication of the procedure was observed, minor complication included transient hypoxemia, minor bleeds and hypoglycemia.

Table: Histopathological diagnosis in patients.

S. No.	Diagnosis	Percentage (%)	No
1	Granulomatous lesion	50	27
2	Squamous cell carcinoma	18.8	10
3	Lymphoproliferative disorder	3.7	2
4	Thymoma	1.8	1
5	Reactive hyperplasia	9.4	5

DISCUSSION

The primacy role of EBUS_TBNA in patients with suspected lung cancer is to diagnose primary Tumor and help determine the N component of the TNM system. In addition, it can also help determine the T component. In cases of meditational lymphadenopathy of unclear etiology, the most common use for convex probe EBUS_TBNA is to distinguish sarcoidosis from lymphoma or granulomatous from non-granulomatous conditions. In the past patient suspected to have sarcoidosis with negative transbronchial biopsy were referred for mediastinoscopy, the availability of EBUS TBNA is a less Invasive safe and more economical alternative for obtaining a pathologic diagnosis of mediastinal lymph nodes. Several reports have confirmed the diagnostic value of EBUS TBNA for the biopsy of meditational lymph nodes in patients with suspected sarcoidosis[9-10] as an example one study of 258 patients with suspected cases found that the diagnostic yield increased from 66 to 78 when TBNA was Added to transbronchial biopsy[11]. More recent studies have reported a high diagnostic yield of EBUS-TBNA for the diagnosis of sarcoidosis. Tremblay *et al* reported a significantly higher diagnostic yield of EBUS-TBNA (83.3%). A systemic review and meta analysis reported a pooled diagnostic accuracy of 79% of EBUS-TBNA for the diagnosis of sarcoidosis[12]. In present study, 27 patients had chronic granulomatous lesions. Twenty one patients were with sarcoidosis and 6 patients with tuberculosis with percentage representation of sarcoidosis as 77.7% and for tuberculosis as

22.2%. The results were in consistent with another study of 165 patients in which a diagnosis of sarcoidosis and tuberculous lymphadenitis made in 118 patients as (71.5%) and 47 (28.8%) respectively[13]. The diagnosis of sarcoidosis was based on a compatible clinical and radiographic picture with demonstration of non-necrotizing granulomatous inflammation on tissue biopsy in the absence of inciting organism. A number of reports of infections diagnosed via TBNA have appeared. The diagnosis of mediastinal mycobacterial adenitis (due to either Mycobacterium tuberculosis or mycobacterium avium intracellulare) using EBUS-TBNA has been described in immunocompetant as well as immunocompromised patients[14,15]. Most thoracic granulomatous lymphadenopathy comprise tuberculous lymphadenopathy and sarcoidosis differentiating between these using a histological examination alone is difficult. In present study, of 06 patients diagnosed as having tuberculosis lymphadenitis only 01 patients had positive culture for mycobacterium tuberculosis, 2 patient had MTB Gene expat positive, 03 had typical histological findings of granuloma with caseation. The results of current study was in line of another study done by Eom *et al* in South Korea in which of 46 patients with IGL[16], with tuberculosis and 30 with sarcoidosis were identified and Mtb culture were positive in (3/16) 19% patients the remaining 13 patients were diagnosed based on histological results or clinical or radiological improvement after anti-tuberculous treatment[16]. The most important role of EBUS TBNA in patients with meditational lymphadenopathy is to prevent mediastinoscopy. As mediastinoscopy require general anesthesia allows access only to paratracheal, and subcarinal lymph nodes and in many cases require an inpatient stay. Patients are left with visible scar above the suprasternal notch which can be cosmetic issue in young people. Although complication from mediastinoscopy are rare they may be catastrophic and include vocal cord paralysis, innominate vein damage and even death[17], EBUS TBNA on the other hand is generally a safe procedure. A systemic review of 18 observational studies, reported no serious complication of the use of convex probe EBUS for EBUS TBNA of regional lymph nodes[18]. In present study no major complication was observed. ROSE (rapid on site evaluation) facilities if available are useful in the context of interventional pulmonology training. Studies have demonstrated that ROSE canallow reduction in the procedure time of TBNA, the number of needle punctures, decrease in complication rates, reduce procedure time and costs, improve diagnostic yield[19,20]. For patients with isolated hilar or mediastinal lymphadenopathy EBUS-TBNA is a reliable first line diagnostic investigation[21], especially in developing and tuberculous endemic areas it's scope has gone beyond lung cancer and useful for the diagnosis of granulomatous diseases. Although cost of the equipment and level of expertise makes it availability limited. Our data suggest that EBUS-TBNA has much to offer to the prescribing clinician in a setting especially where procedures like mediastion scopy or high risk empirical treatment is the only other option left.

CONCLUSION

Endobronchial Ultrasound-guided trans-bronchial needle aspiration was found useful diagnostic modality for lymph nodes sampling in patients with lymphadenopathy and mass like lesions in mediastinum. Its ability has evolved beyond lung cancer and now being increasingly utilized in the diagnosis of benign illnesses. ROSE appears to be useful as it increases diagnostic accuracy of EBUS-TBNA.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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