ORIGINAL RESEARCH PAPER

Volume-7 | Issue-7 | July-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ROLE OF TRANSBRONCHIAL LUNG BIOPSY IN THE DIAGNOSIS OF DIFFUSE PARENCHYMAL LUNG DISEASES

Pulmonary Medicine

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ABSTRACT

Background : Diffuse Parenchymal Lung diseases (DPLDs) are a diverse group of disorders which involve more than 200 clinical entities. The common feature in DPLDs is inflammation and fibrosis of the lung parenchyma which produces derangement of the alveolar architecture. The approach to diagnosis is multidisciplinary involving clinical, radiological and pathological findings. Although open lung biopsy is considered the gold standard for diagnosis, it is associated with higher morbidity and longer hospital stay. Transbronchial lung biopsy(TBLB) is a relatively safer procedure which can be used to obtain a biopsy sample from the lung. There is no prior study in Goa where TBLB has been used to diagnose DPLDs. Hence we undertook this study to evaluate the utility and safety of TBLB in the diagnosis of DPLDs.

Materials and Methods: A prospective study on 45 patients presenting to the Department of Pulmonary Medicine, Goa Medical College with radiological features suggestive of diffuse parenchymal lung disease.

Results: The overall tissue yield of TBLB was 44% and the diagnostic yield was 31.1%. The most common histological patterns found were carcinoma, followed by tuberculosis and sarcoidosis. There was no mortality associated with the procedure. Iatrogenic pneumothorax occurred in three patients (6.6%).

Conclusion: TBLB is a safe and effective tool in the diagnosis of DPLD, however the rate of diagnosis varies. It is a useful test when the radiological diagnosis is uncertain.

KEYWORDS

Diffuse Parenchymal Lung Disease, Transbronchial Lung Biopsy

INTRODUCTION

Diffuse Parenchymal Lung diseases (DPLDs) are a diverse group of disorders which involve more than 200 clinical entities. Many factors play a role in the pathogenesis of DPLDs such as environmental and occupational agents, drugs, radiation and genetic predisposition. The common feature in DPLDs is inflammation and fibrosis of the lung parenchyma which produces derangement of the alveolar architecture. While evaluating a suspected case of DPLD, history is of utmost importance. A thorough history including occupational, drug and exposure history is irreplaceable. Further evaluation involves chest radiography, high resolution computed tomography, pulmonary function tests and a lung biopsy for tissue diagnosis. Thus the approach to diagnosis is multidisciplinary. As the histological patterns seen by pathologists usually allow for better separation of these entities than the imaging patterns seen by radiologists, the joint statement of the American Thoracic Society (ATS) and European Respiratory Society (ERS) advises surgical lung biopsy, particularly for the diagnosis of idiopathic interstitial pneumonias (IIPs), unless contraindicated.[1]

Various methods of obtaining a lung biopsy are open lung biopsy (OLB), VATS lung biopsy and Transbronchial lung biopsy (TBLB). Of these, OLB is considered the gold standard for diagnosis. But it is also associated with higher morbidity and longer hospital stay. Transbronchial lung biopsy is a relatively safer procedure but with lower diagnostic yield. The diagnosis of DPLDs is often delayed because most clinicians attribute the symptoms to more common diseases like chronic obstructive lung disease and tuberculosis. An attempt should be made to diagnose these diseases at the earliest so that appropriate therapy can be initiated before the changes of end stage disease set in. This involves creating awareness among the practitioners about DPLDs and the various methods of diagnosis.

There is no prior study in Goa where TBLB (without fluoroscopic guidance) has been used to diagnose DPLDs. Hence we undertook this study to evaluate the usefulness of TBLB in the diagnosis of DPLDs. The hospital has no facility for fluoroscopic guidance and so this unguided approach was taken in order to find out the utility in resource crunched and peripherally situated health institutions. The study was undertaken in the Department of Pulmonary Medicine of Goa Medical College. This department serves as a tertiary referral centre for the state of Goa and neighbouring districts of Maharashtra and Karnataka.

MATERIALS AND METHODS

This is a prospective study conducted on 45 patients in the Department of Pulmonary Medicine, Goa Medical College, over a three year period. Informed consent was taken from all the patients in the study. The study was approved by the Ethics Committee .The following were the inclusion and exclusion criteria.

Inclusion Criteria:

All patients presenting to the Department of Pulmonary Medicine, Goa Medical College with features suggesting diffuse parenchymal lung disease on HRCT were included in this study after taking an informed consent.

Exclusion Criteria:

Patients who had contraindications to undergo bronchoscopy, i.e.presence of a coagulation disorder (platelet count <50,000/mm3, international normalised ratio >1.5), hypoxaemia (pO2 <60 mmHg), and unstable heart disease (uncontrolled cardiac arrhythmia, active myocardial ischaemia) were also excluded from the study.

The patients were evaluated as follows:

1. Detailed history and clinical examination including occupational history, drug history, history related to connective tissue disorders, etc.
2. Radiological Investigations- CXR and HRCT Thorax
3. Laboratory Investigations- Connective tissue profiles, Serum ACE levels, etc
4. Pulmonary Function Tests – Pre and Post bronchodilator values.
5. Pre-Bronchoscopic evaluation
6. Bronchoscopy and Transbronchial Lung Biopsy

Bronchoscopy was performed with a flexible video-bronchoscope under local anaesthesia as per standard protocol (BTS guidelines).2 The area from which the TBLB samples would be taken was determined after reviewing the HRCT report, taking care to biopsy only one lung in one setting. Transbronchial lung biopsy was performed for all patients using alligator forceps and the number of biopsy bites varied from 2-6.The biopsy tissue was mounted on Whatman's filter paper. While doing so care was taken to ensure that the mucosal surface faced upwards. The filter paper was then dipped into formalin and transported in air tight bottles. A chest x ray was done for all patients to look for iatrogenic pneumothorax. Patients who did not have any post procedure complications were discharged after 24 hours of hospital stay.

RESULTS

We enrolled a total number of 45 patients of which 27 were males and

18 were females. The mean age was 51 years. Table 1 shows the radiological findings seen on HRCT. The most common finding was that of bilateral reticulonodular opacities.

Table 1: Radiological features of patients with DPLDs.

Radiological Findings	No. Of cases(%)
Reticulonodular opacities	44%
Lymphadenopathy	27%
Ground Glass Opacities	11%
Consolidation	10%
Honeycombing	9%

Table 2: Subtypes of DPLDs included in the study (Based on Radiological and hiistopathological features)

Subtype of DPLDs	No. Of cases(%)
Interstitial Pulmonary Fibrosis	10
Sarcoidosis	8
Carcinoma	7
Connective tissue related DPLDs	6
Tuberculosis	4
Occupational lung disease	2
Others	8

Table 3 – Comparison between HRCT and TBLB

	HRCT DIAGNOSTIC	HRCT NOT DIAGNOSTIC
TBLB DIAGNOSTIC	**10**	**4**
TBLB NOT DIAGNOSTIC	**27**	**4**

On bronchoscopic evaluation the tracheobronchial tree was normal in all the patients, no intrabronchial growth or mucosal irregularity was evident. Of the 45 patients enrolled, an adequate biopsy sample could be obtained in 44.4% and a confirmatory diagnosis could be established in 14 patients, i.e 31.1%. The most common histological findings were Carcinoma, followed by tuberculosis and sarcoidosis.

Below mentioned are the Chest X Ray, CT thorax and histopathology images (Figs. 1,2 and 3 respectively) of a case of Silicosis that was diagnosed by TBLB.

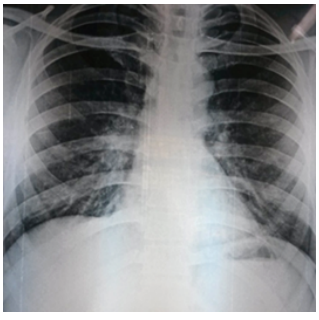

Fig. 1 -CHEST RADIOGRAPH

- Bilateral hilar prominence
- Reticulonodular shadows in mid and lower zones bilaterally
- Δ – Early Interstitial Lung Disease

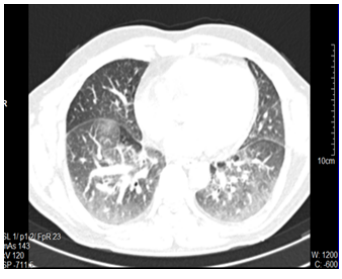

Fig. 2- HRCT THORAX

- Interstitial thickening with nodular appearance
- Multiple nodules in both perihilar regions and upper lobes
- Bilateral mediastinal lymphadenopathy with peripheral calcification
- Differential Diagnosis- Sarcoidosis, Silicosis

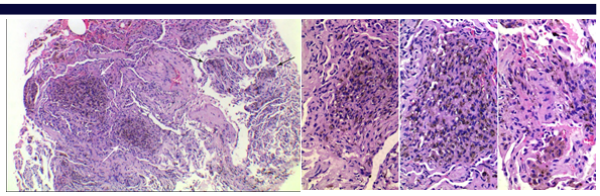

Fig. 3- The Transbronchial Lung biopsy specimen showed small rounded fibroblast proliferation with dust laden macrophages. Polarisation showed silica crystals.

There was no mortality associated with the procedure. Pneumothorax was observed in 3 patients (6.6%). All three patients improved after passing an intercostal tube to drain the pneumothorax. Minor bleeding was seen in six patients which was controlled by instillation of cold saline. During the procedure about 10 patients developed desaturation which prompted us to withdraw the scope and prematurely terminate the procedure. Most of the patients improved after withdrawal of the scope, propped up positioning and starting on high flow oxygen, while some required a stat dose of injectable steroids.No serious complications occurred in any of the enrolled 45 patients.

DISCUSSION

This study was undertaken to evaluate the diagnostic efficacy of TBLB in diffuse parenchymal lung diseases as well as to evaluate the procedure related complications. The diagnostic yield in this study was found to be 31.1% and the tissue yield was 44.4%. The diagnoses obtained included malignancy (5 patients), sarcoidosis(3 patients), tuberculosis (2 patients), pulmonary fibrosis (2 patient), silicosis (1 patient) and hamartoma (1 patient). It is to be noted that although the total number of patients diagnosed is less, the procedure of TBLB aided in obtaining the diagnosis in these patients. With advancements in computed tomography, most of the DPLDs can be diagnosed by HRCT alone. It is only when a confirmatory diagnosis cannot be obtained radiologically, attempts are made to obtain a biopsy sample. These are the cases where the role of TBLB appears to be particularly important. In the patients diagnosed as carcinoma, the mass was not amenable to CT guided biopsy, neither was any growth seen intrabronchially. In two of the five cases of bronchogenic carcinoma, the radiological diagnosis was not suggestive of carcinoma – one being given as lipoid pneumonia and the other as ILD. Therefore TBLB was helpful in obtaining a cell type. In the patient diagnosed as Silicosis, the radiological diagnosis was uncertain (the differential diagnosis given was of sarcidosis/tuberculosis/silicosis). TBLB clinched the diagnosis in the patient showing small rounded fibroblast proliferation with dust laden macrophages; polarisation showed silica crystals, thus confirming the diagnosis of silicosis.

Many factors influence the tissue yield in TBLB, including use of fluoroscopic guidance, expertise of the bronchoscopist, type of DPLD, number of tissue samples collected, processing and evaluation of the samples by the pathologist and lastly the respiratory reserve of the patients. The yield of our study was comparably less possibly due to the absence of fluoroscopic guidance which is required not only for the localisation of the lesions but also to detect any pneumothorax developing as a result of the procedure. Most of the studies conducted previously have evaluated the efficacy of fluoroscopically guided TBLB. The inability to accurately guide the forceps into the area of interest in the absence of fluoroscopic guidance may be one of the reasons why a representative sample could not be obtained. Secondly the diagnostic rate of TBLB depends on the clinical skill and expertise of the bronchoscopist. As we have only recently started performing this procedure, the rate of diagnosis was low for the initial cases but kept improving over time as we did more procedures. Also, we have included all types of DPLDs in this study. However as is well known, the yield of TBLB is higher only when there is peribronchial involvement by the disease e.g in diseases like sarcoidsis, lymphangitic carcinomatosis, etc.[4] Whereas in diseases like IPF, vasculitis, connective tissue related ILDs the yield is low. This is probably another reason why the overall rate of diagnosis is lower. Another factor which is of importance is the number of samples taken Usually about 4-6 samples are needed to make an accurate diagnosis.[3] However, as we had no anesthetist assisting the procedure nor any ICU facilities on campus, we had to prematurely terminate the procedure in about ten patients when they desaturated during the procedure. This limited the number of samples that could be taken in some cases. Once the samples are obtained, they should be properly

handled and transported to the laboratory for evaluation. As the size of the biopsy specimen is very small, care should be taken while processing the samples. In our study the individual samples were mounted onto a filter paper bit (with the mucosal surface upwards) and then inserted in formalin and transported to prevent loss of material and to aid in cutting the sample with the mucosal side above and the alveolar side below thus maintaining the orientation of the tissue. These were then transported to a specialist centre in Mumbai to be studied by a pathologist trained in evaluating the small TBLB samples. Lastly most of the patients presenting with DPLDs have a poor lung function and may thus not be able to withstand the procedure for a prolonged period of time. Also the risk of pneumothorax and the subsequent consequences need to be considered in these patient with an already low pulmonary reserve.

CONCLUSIONS

To conclude, TBLB is a safe investigation in the diagnosis of diffuse parenchymal lung diseases. However, the diagnostic yield depends on a number of factors. With fluoroscopic guidance and adequate expertise on the part of the bronchoscopist and pathologist, the yield can be improved. Most of the DPLDs can be diagnosed by HRCT alone; however when the radiological diagnosis is uncertain, TBLB plays an important role.

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