Original Article

Transbronchial Lung Biopsy in Diffuse Parenchymal Lung Disease: Diagnostic Yield and Complications

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Abstract

Background. Diffuse parenchymal lung diseases (DPLDs) represent a group of disorders with overlapping clinical and radiological features. Lung biopsy is usually required to make an aetiological diagnosis of DPLD. Open lung biopsy which is still considered as the gold standard for the diagnosis of DPLDs, is associated with significant mortality and morbidity. Transbronchial lung biopsy (TBLB) through fibreoptic bronchoscope is safe and less invasive method in patients with DPLDs.

Objectives. To describe the diagnostic yield and complications of TBLB in patients with DPLD seen at our centre.

Methods. We prospectively studied patients with DPLD who underwent TBLB over a 2-year period.

Results. A total of 102 patients were enrolled in the study. TBLB confirms a diagnosis in 80 (78.4%) patients. Granulomatous inflammation (30 [37.5%]), non-specific interstitial pneumonia (15 [18.7%]), neoplasia (13 [16.2%]) were the most common histological findings. No procedure-related mortality was observed. Seven (6.8%) patients developed pneumothorax. Major bleeding that requires admission to intensive care unit was reported in 1 (0.9%) patient only.

Conclusions. Transbronchial lung biopsy is a safe and useful procedure for diagnosis of DPLDs. The yield of TBLB is high when centrilobular and perilymphatic involvement is found radiologically. At least four to six biopsies per TBLB should be taken to improve the overall yield of TBLB. **[Indian J Chest Dis Allied Sci 2017;59:9-12]**

Key words: Diffuse parenchymal lung diseases, Transbronchial lung biopsy, Bronchoscopy.

Introduction

Diffuse parenchymal lung diseases (DPLDs) represent a heterogeneous group of diseases with overlapping clinical and radiological features. Their diagnosis frequently needs histopathological findings based approach.[1] Lung biopsy is usually required to make an aetiological diagnosis of DPLD. Open lung biopsy, which is still considered as the gold standard for DPLD, is associated with significant mortality and morbidity. Hence, a safer, less invasive method, transbronchial lung biopsy (TBLB) is gaining wide acceptance.[2] The introduction of the flexible bronchoscope in the late 1960s increased the popularity of the technique and demonstrated that TBLB with the flexible instrument may be obtained with minimal mortality and morbidity.

Currently TBLB is a well-established diagnostic technique used by almost all bronchoscopists. The main utility of the TBLB rests in the possibility of making a specific diagnosis in a patient with DPLD and avoiding a surgical lung biopsy. However, according to the joint consensus statement of the American Thoracic Society and the European Respiratory Society on idiopathic interstitial fibrosis (IPF), TBLBs are not helpful in making a diagnosis of usual interstitial pneumonia (UIP), and the presence of a UIP pattern on high-resolution computed tomography (HRCT) is sufficient for the diagnosis of IPF in patients not subjected to a surgical lung biopsy.[3]

The diagnostic yield of histopathologic assessment of TBLB is variable,[1,4,5] and is influenced by the factors like size of samples[6] and presence of crush artefacts left by biopsy forceps.[7] The present study was designed and planned to assess the diagnostic yield and complications of TBLB in patients with DPLD at our centre.

Material and Methods

This is a prospective study conducted at the Kempegowda Institute of Medical Sciences (KIMS),

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Bangalore. All consenting consecutive patients with DPLD were enrolled in the study. Patients who had UIP pattern on HRCT of thorax, bilateral, basal, subpleural reticulations with honey-combing and/or traction bronchiectasis were excluded from the study. Immunocompromised patients and patients who had contraindications to undergo bronchoscopy, i.e. presence of a coagulation disorder (platelet count <50,000/mm^3, international normalised ratio >1.5), hypoxaemia (pO_2 <60 mmHg), and unstable heart disease (uncontrolled cardiac arrhythmia, active myocardial ischaemia) were also excluded from the study. Patients with images typical of UIP and honeycombing pattern on HRCT were also excluded from the study.

Informed written consent was taken from all the patients and the study protocol was approved by the KIMS Institutional Ethics Committee. Detailed history was taken from the patients including occupation, family, smoking and drug intake. Flexible bronchoscopy was performed using Olympus BF type 1T 150 under conscious sedation and local anaesthesia (nebulisation with 4% lidocaine and 2% lidocaine for anaesthetising the vocal cords and central airways). TBLB was done using the biopsy forceps FB-20C-1. The segments and the lobes for biopsy were selected based on the disease pattern on HRCT of thorax. Upper lobe biopsy was avoided due to the higher incidence of pneumothorax. Biopsies from both the lungs were also avoided because of the chances of bilateral pneumothoraces. On an average, 4-6 biopsies were taken in each patient. All the lung biopsy specimens were fixed in 10% formalin and sent to the department of pathology. TBLB specimens were processed and embedded in paraffin wax. Serial sections of 4-5 micron thickness were obtained and stained with Haematoxylin and Eosin. Special stains, like Periodic-Acid-Schiff (PAS), Silver methenamine, Zeihl-Neelsen (ZN), Masson's trichome and immunohistochemistry were done wherever necessary. TBLB sample was considered inadequate, when the pathologist could not interpret the sample due to inadequate tissue material (a minimum of 20 alveoli is required).

Chest radiograph was done in all the patients one hour after the procedure to rule out pneumothorax. Severity of bleeding was classified as minor bleeding (bleeding requiring suction or instillation of cold saline) and major bleeding (bleeding causing haemodynamic or respiratory instability, requiring admission to intensive care unit). Patients were kept under observation for 24 hours after the procedure.

Results

A total of 102 patients who fulfilled the inclusion and exclusion criteria were enrolled in the study. Age of the patients ranged from 21-86 years with a mean age of 52 years. Sixty-three (61.7%) were males and 39 (38.2%) were females. Bilateral reticulonodular opacities were the most common finding on HRCT. Other HRCT findings included bilateral ground-glass opacities, mediastinal and hilar lymphadenopathy, bilateral patchy consolidation, tree-in-bud appearance and mosaic pattern.

Twenty-two (21.5%) biopsy samples were reported as inadequate. A histological diagnosis consistent with the final clinical diagnosis was achieved in 80 (78.4%) (Table 1). Granulomatous inflammation (37.5%), non-specific interstitial pneumonia (18.7%), neoplasia (16.2%) were the most common histological findings.

Among the granulomatous inflammation (Figure 1), tuberculosis was the most common finding (Table 2). UIP pattern (Figure 2) was found in 11 (13.7%) patients, even though patients with IPF pattern on HRCT thorax were excluded. We also found certain rare causes of DPLD, like eosinophilic lung disease (Figure 3) and lymphangioleiomyomatosis.

Table 1. Histological diagnosis consistent with the final clinical diagnosis

Histological Diagnosis	No. of Patients (%)
Granulomatous inflammation	30 (37.5)
Non-specific interstitial pneumonia	15 (18.7)
Neoplasia	13 (16.2)
Usual interstitial pneumonia	11 (13.7)
Organising pneumonia	4 (5)
Diffuse alveolar damage	3 (3.7)
Pneumoconiosis	2 (2.5)
Eosinophilic lung disease	1 (1.2)
Lymphangioleiomyomatosis	1 (1.2)

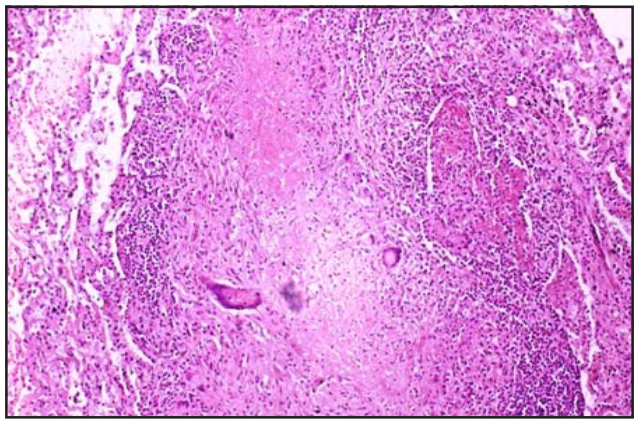

Figure 1. Photomicrograph showing epithelioid granuloma with central area of caseation necrosis surrounded by lymphocytes and Langhans' giant cells (Haematoxylin and Eosin × 400).

Table 2. Aetiology of granulomatous inflammation

Aetiology of Granulomatous Inflammation	No of Patients (%)
Tuberculosis	17 (21.2)
Sarcoidosis	9 (11.2)
Hypersensitive pneumonitis	3 (3.7)
Granulomatosis with polyangiitis	1 (1.2)

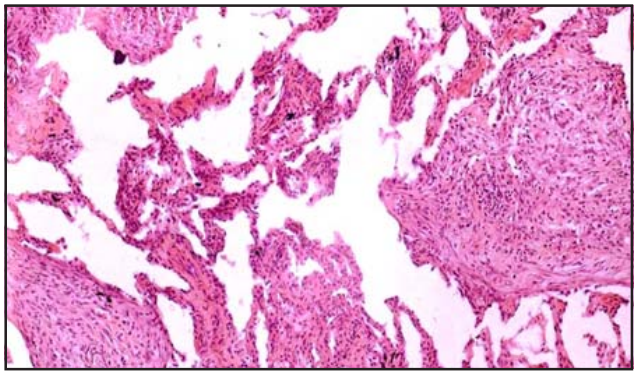

Figure 2. Photomicrograph showing patchy interstitial fibrosis and chronic inflammation along with normal alveoli in usual interstitial pneumonia (Haematoxylin and Eosin × 100).

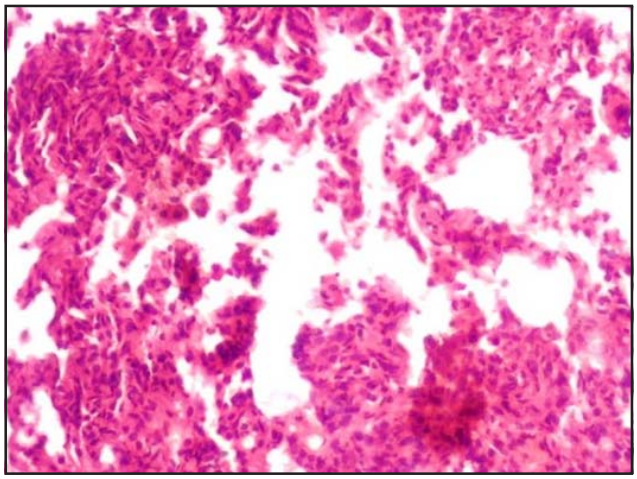

Figure 3. Photomicrograph of eosinophilic lung disease showing alveolar filling by mixed inflammatory cells including many eosinophils (Haematoxylin and Eosin × 100).

No procedure-related mortality was observed. Seven (6.8%) patients developed pneumothorax, three of whom required chest tube for 2-3 days. Minor bleeding during the procedure was controlled either by suction or by instillation of cold saline. Major bleeding causing haemodynamic instability was reported in one patient (0.9%) only and required admission to intensive care unit for a day.

Discussion

Lung biopsy is an important diagnostic tool in patients with DPLD. The question of what kind of biopsy should be performed to diagnose DPLD has a long and controversial history. Although the surgical lung biopsy provides substantially more material for pathological study, the procedure requires general anaesthesia, and one or more days in the hospital with a chest tube in place. Moreover, studies[8,9] have shown that surgical lung biopsy may be associated with increased morbidity and mortality in certain conditions. Lettieri *et al*[8] reported a median mortality of 4% to 6% within 30 days following surgical lung biopsy for UIP.[8] Biopsy performed at the time of acute exacerbation (AE) resulted in higher 30-day mortality (28.6%) compared to non-AE cases.[9]

In contrast, fibreoptic bronchoscopy can be done as an outpatient procedure, usually with minimal morbidity and mortality.[10] Even though the size of the biopsy specimen obtained with the bronchoscope is small, the clinician can often combine the clinical, radiologic, microbiologic, and cytologic and histopathologic information to arrive at a diagnosis.[11]

Although TBLB is gaining wide acceptance for the diagnosis of interstitial lung disease in certain circumstances, the yield of this technique has come under question in the context of some DPLDs.[12] The yield of TBLB is high when centrilobular and perilymphatic involvementis found radiologically[1,13] and lower in predominantly peripheral processes, such as UIP.[11] According to joint American–European guidelines,[3] TBLB is not helpful in diagnosis of UIP and the presence of a UIP pattern on HRCT is sufficient for the diagnosis of IPF in patients not subjected to surgical lung biopsy.[3]

In the present study, a confident histological diagnosis consistent with the final clinical diagnosis was achieved in 78.4% patients, which was similar to other studies.[1,4,5] We also observed in our study that diagnostic yield was higher when centrilobular and perilymphatic involvement was seen on HRCT thorax, like tuberculosis, sarcoidosis, neoplasia and organising pneumonia. Even though we excluded IPF patients in our study, 13.7% patients had UIP pattern on histology, which also suggests that histological evidence of UIP can be found in the absence of IPF pattern on HRCT thorax.

In the present study, we observed that for a good diagnostic yield for more common diseases presenting with diffuse infiltrates, like sarcoidosis, neoplasia, and hypersensitive pneumonitis, four to six biopsies per TBLB are required. Findings of our study are comparable to that proposed by Descombes *et al*[2] (five to six biopsies) and Gilman *et al*[14] (four biopsies).

The main complication of TBLB is bleeding. Some amount of bleeding occurs virtually in all TBLB procedures and in some cases it can be substantial. Bleeding is a major concern during the procedure as limited options are available to manage excessive bleeding through flexible bronchoscope. Hence, evaluation of patient prior to the TBLB procedure is crucial for reducing the chances of this complication. In our study patients, minor bleeding was controlled either by suction or by instillation of cold saline. The complication rates (major bleeding 0.9% and pneumothorax 6.8%) in our study was comparable to other studies (1% and 5% respectively). [15,16]

Conclusions

Transbronchial lung biopsy is safe and potentially useful for the diagnosis of DPLDs under experienced professionals. HRCT thorax is crucial prior to the procedure to know about the disease pattern and for selecting the lobe or the segment to be biopsied. The yield of TBLB is higher when centrilobular and perilymphatic involvement is found radiologically. At least four to six biopsies per TBLB should be taken to improve the overall yield of TBLB.

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