Transbronchial Cryobiopsy in Diffuse Parenchymal Lung Diseases in a Community Medical Center

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ABSTRACT

Background: Transbronchial cryobiopsy (TBC) has recently emerged for the assessment of diffuse parenchymal lung disease (DPLD) as a less invasive procedure than surgical lung biopsy. The diagnostic usefulness and safety of TBC is still controversial.

Objectives: To evaluate the safety and diagnostic yield of TBC in a peripheral community medical center.

Methods: We retrospectively reviewed the charts of all patients with DPLD who underwent TBC from January 2015 to January 2020.

Results: The study comprised 97 patients. Three samples were taken from each patient with an average diameter of 0.59 cm. The histologic diagnostic yield was 54% (52 of 97 procedures). The most frequent histopathologic diagnoses were usual interstitial pneumonia in 13 patients (13%), bleeding was observed in 19 cases (19%) and only one patient (1%) had severe bleeding. Pneumothorax developed in seven patients (7%) and one patient (1%) suffered from interstitial lung disease exacerbation.

Conclusions: TBC was found to be safe; however, the diagnostic yield was rather low compared to other studies, which emphasizes the need for interstitial lung disease centers with expert in this field.

KEY WORDS: diffuse parenchymal lung disease (DPLD), idiopathic pulmonary fibrosis (IPF), interstitial lung diseases (ILD), transbronchial cryobiopsy, usual interstitial pneumonia (UIP)

Transbronchial cryobiopsy (TBC) emerged recently for the assessment of DPLD. Cryobiopsy is a less invasive procedure, more cost effective, and associated with lower complication rates than surgical lung biopsy. The major advantages of TBC are larger tissue samples with a higher percentage of alveolar tissue, fewer crush artifacts, and less atelectasis, which correlates with a greater and a better diagnostic yield than a simple transbronchial biopsy. The reported estimated diagnostic yield in former studies is over 80% [3,5,7-9].

In the last 2 years, expert statements were published trying to standardize the procedure [10], practically each center does it differently in the context of indication threshold, study population, number of biopsies, and use of anesthesia. In this report we describe 5 years of experience with TBC at our Institution, Carmel Medical Center, a community medical center with 500 beds located in northern Israel. We evaluated the safety and diagnostic accuracy and compared it with previous research studies on the use of TBC at interstitial lung disease (ILD) centers with greater experience.

PATIENTS AND METHODS

We searched the clinical records of patients with DPLD who underwent a cryobiopsy at our institution from January 2015 to January 2020 and analyzed the medical records for demographic data, procedure specific complications, and pathological results.

All patients were referred to cryobiopsy when a specific diagnosis could not be made confidently by a multidisciplinary discussion based on clinical, radiographic, and blood test studies [1].

All the procedures were done on intubated deeply sedated patients under general anesthesia. A flexible cryo-probe (ERBE, Tubingen, Germany) with an outer diameter 2.4 mm was introduced through the working channel of a bronchoscope and passed into the distal airways under fluoroscopic guidance. In a distance of approximately 1–2 cm from the thoracic wall a biopsy was taken by cooling the probe using nitrous oxide for 3–4 seconds. Then, the entire bronchoscope was retracted with the frozen lung tissue being attached on the probe’s tip. The frozen specimen then thawed in saline to release it from the probe [7,10]. At the same time a suction catheter was inserted through the endotracheal tube to suction blood if present in the airway while awaiting for the bronchoscope to be released from the frozen cryoprobe. This last

Diffuse parenchymal lung diseases (DPLDs) are a heterogeneous group of disorders that affect the pulmonary parenchyma. The evaluation is best achieved by a multidisciplinary approach combining clinical, radiological and pathologic features. Lung biopsy may be necessary for an accurate diagnosis in cases of atypical presentation [1,2].

Surgical lung biopsy is the gold standard for the diagnosis of DPLD. Specimens obtained via video assisted thoracoscopic surgery or thoracotomy have diagnostic yields in the range of 90–95% [3-5]. Nevertheless surgical biopsy in that population has significant morbidity and in-hospital mortality of approximately 1.7% for elective procedures and 16% for non-elective procedures [6].

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manner is unique to our center and may be a simple alternative to endobronchial blocker in some cases.

Three biopsies were generally obtained from one or two lobes, which appeared to have the most active disease on high resolution computed tomography (HRCT). When possible, the right lower lobe was preferred; since bleeding can be more easily managed and the bifurcation angle at the carina the suction catheter enters the right lung. Within 2 hours after the procedure, a chest X-ray was performed to exclude pneumothorax and then patients were discharged.

Continuous variables were presented as average with standard deviations (SD), while categorical data were presented by numbers (percentage).

RESULTS

Over a 5-year period, we performed 97 procedures in 97 patients with diffuse pulmonary infiltrates of unclear cause. The mean age of the study population was 58 ± 12.7 years, 42 (43%) were women and 55 (57%) were men; average diameter of samples was 0.59 ± 0.21 cm.

The most frequent histopathologic diagnoses were usual interstitial pneumonia (13 patients [13%]), hypersensitivity pneumonitis (9 patients [9%]), and nonspecific interstitial pneumonia and sarcoidosis (each 6 patients [6%]), respiratory bronchiolitis-associated interstitial lung disease (RB-ILD, 4 patients [4%]), organizing pneumonia, silicosis, and lipid pneumonia (each 3 patients [3%]), and langerhans cell histiocytosis (2 patients [2%]). Final histopathological diagnoses are shown in Table 1.

In 45 patients (46%) nonspecific histologic findings were described, which was not enough to make a specific diagnosis. From those, three patients underwent surgical lung biopsy and the final diagnoses were usual interstitial pneumonia, diffuse alveolar damage, and extranodal marginal cell lymphoma.

<table>
<thead>
<tr>
<th>Table 1. Final histopathological diagnosis</th>
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<tbody>
<tr>
<td>Usual Interstitial pneumonia</td>
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<tr>
<td>Hypersensitivity pneumonitis</td>
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<tr>
<td>Nonspecific Interstitial pneumonia</td>
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<tr>
<td>Sarcoidosis</td>
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<td>Respiratory bronchiolitis associated ILD</td>
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<td>Organizing pneumonia</td>
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<td>Silicosis</td>
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<tr>
<td>Lipoid pneumonia</td>
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<td>Langerhans cell histiocytosis</td>
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<td>Necrotizing granuloma</td>
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<tr>
<td>Adenocarcinoma</td>
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<td>Amiodarone Lung</td>
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This discrepancy may be partially explained by the learning curve needed for experience in performing lung cryobiopsy and the lack of international guidelines for procedure performance in the context of indication, patient selection, and technical aspects like freeze time and probe diameter. In the last 2 years expert statements were published trying to standardize the procedure [10,17], but practically each center does it differently.

Another possible reason may be the lack of expert pathologists who are familiar with transbronchial lung cryo-biopsies, which are smaller in size than the traditional surgical lung biopsies. Actually, it is a speculative issue, because we did not send the histologic specimen to a second reviewer who had experience in this field.

It should be emphasized that the reported diagnostic yield in most studies included a final diagnosis after multidisciplinary discussion, which significantly raises the diagnostic yield, in contrast to our study, which was based only on histopathology diagnosis. The diameter of the specimens in our study was 0.59 cm, which is considered as an acceptable size compared to other studies [10,18] and expected to be sufficient to make a final diagnosis of ILD.

The complication rate of pneumothorax in our study was 7%, significantly lower than the reported rate in the literature, with a pneumothorax rate in the range of 12% [3,7,13]. The low percentage of pneumothorax may indicate that the biopsies were not taken peripherally, at a distance of 1–2 cm from the thoracic
wall, as recommended by experts [10]. The bleeding rate in our study was 20%, which is similar to previous studies. Cryobiopsy can cause an exacerbation of ILD as described in some case reports [19] and also in our study.

Finally, this study highlights the limitation of performing cryobiopsy in small community hospitals. Furthermore, the relatively low yields of the cryobiopsy emphasize the need for interstitial lung diseases centers to better diagnose and manage patients with DPLD.

Despite the lower diagnostic yield of our study, we believe that cryobiopsy should be ranked first as a procedure of choice after multidisciplinary discussion in evaluating patients with DPLD and we believe that the importance will strengthen in the coming years.

CONCLUSION

Our single center study demonstrated a low diagnostic yield of 54% compared to previous studies, which emphasizes the safety of the procedure and the need for interstitial lung diseases centers with expert in this field.

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References

Imperfect future immunity

Humans are infected by several seasonal and cross-reacting coronaviruses. None provokes fully protective immunity, and repeat infections are the norm. Vaccines tend to be less efficient than natural infections at provoking immunity, and there are risks of adverse cross-reactions. Saad-Roy and colleagues used a series of simple models for a variety of immune scenarios to envisage immunological futures for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) with and without vaccines. The model outcomes showed that imperfect knowledge about the imperfect coronavirus immune landscape can give rise to diverging scenarios, ranging from recurring severe epidemics to elimination. It is critical that healthcare professionals accurately characterize immune responses to SARS-CoV-2 for translation into managing disease control.

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