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The complimentary role of transbronchial lung cryobiopsy and endobronchial ultrasound fine needle aspiration in the diagnosis of sarcoidosis

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ABSTRACT

Purpose: Transbronchial lung cryobiopsy (TBLC) is a novel technique that has proved to be useful in diagnosing various interstitial lung diseases (ILD). The use of TBLC to diagnose sarcoidosis in an unselected patient population is unknown, and could be complimentary to endobronchial ultrasound fine needle aspiration (EBUS-FNA).

Methods: A retrospective analysis of 36 patients in a single, tertiary-care, academic medical center was conducted to describe the yield of both EBUS-FNA and TBLC in the diagnosis of suspected sarcoidosis over a three year period. A grading system to evaluate the presence and extent of specific radiographic features on computed tomography chest imaging studies was compared to the results of EBUS-FNA and TBLC. Complications associated with the procedures were also noted.

Results: The overall diagnostic yield in our cohort (all pathologic diagnosis considered) was 80.6% (29 out of 36 patients had a definite pathologic diagnosis). Eighteen patients referred for possible sarcoidosis had a positive bronchoscopic specimen confirming the diagnosis of sarcoidosis. For those patients with a pathologic diagnosis of sarcoidosis, the diagnostic yield for EBUS-FNA and TBLC was 66.7% each (12 out of 18 patients), while the combined diagnostic yield for EBUS-FNA and TBLC increased to 100%. For all cases, the pneumothorax rate was 11.1%.

Conclusions: TBLC appears to be a safe and complimentary technique to diagnose sarcoidosis and could be considered part of the diagnostic armamentarium in bronchoscopic centers.

1. Background

Sarcoidosis is a multisystem disorder of unknown cause. It frequently presents with bilateral hilar and mediastinal adenopathy, pulmonary infiltrates, and ocular and skin lesions. The diagnosis is established when clinicoradiological findings are supported by histological evidence of noncaseating epithelioid cell granulomas [1]. Even with tissue confirmation, diagnosis is never secure and follow-up over a number of years is required to be fully confident of the diagnosis [2].

The ATS/ERS/WASOG Statement on Sarcoidosis written in 1999 recommends transbronchial lung biopsy (TBLB) as the procedure of choice for tissue diagnosis [1]. However, the diagnostic yield of TBLB ranges 40%–90% [3–6]. Factors influencing yield of TBLB include chest X ray (CXR) appearance and experience of the operator. Specimens from TBLB may lack sufficient quality due to crush artifact and are generally too small for diagnosis of diffuse lung disease [7]. If TBLB is negative, other diagnostic modalities include endobronchial ultrasound bronchoscopy (EBUS) [8–10], the more invasive video assisted thoracoscopic surgical (VATS) lung biopsy, or open lung biopsy (OLB). VATS lung biopsy is costly, requires general anesthesia, in-patient care and has a mortality rate ranging 0%–4.4% [11–13]. OLB probably has a similar complication rate at least [14].

Transbronchial lung cryobiopsy (TBLC) is a novel technique

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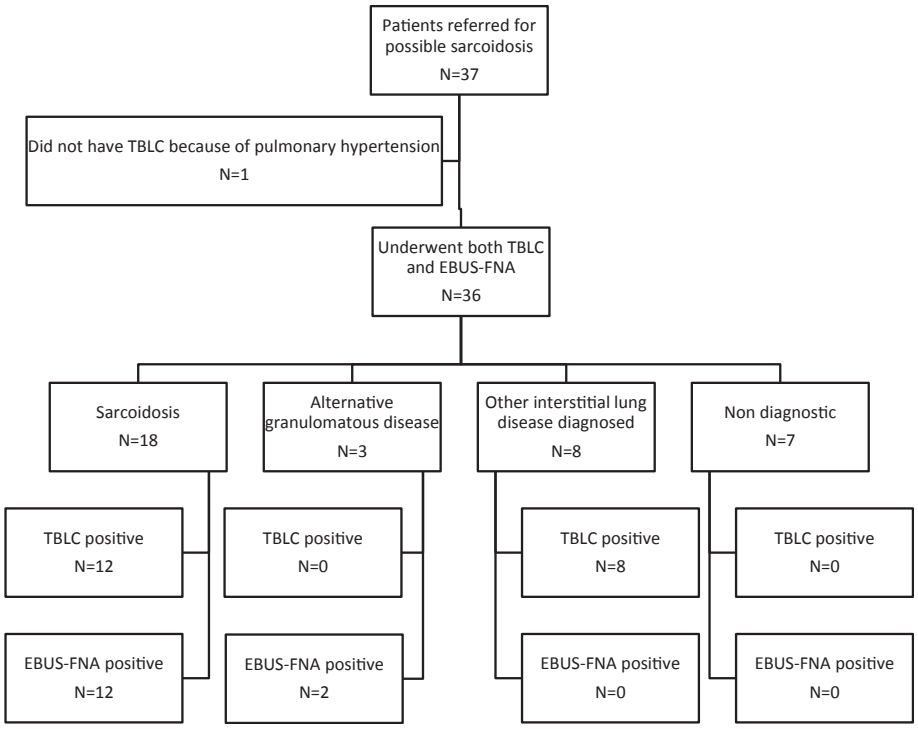

Fig. 1. Outcome of all patients.
TBLC = transbronchial lung cryobiopsy; EBUS-FNA = endobronchial ultrasound guided fine needle aspiration.
Alternative granulomatous disease: 1 patient with EBUS-FNA culture positive for *M. tuberculosis*; 1 patient with BAL positive for *M. kansasii*; 1 patient with EBUS-FNA compatible with mantle cell lymphoma (confirmed with VATS excision of right paratracheal lymph node station) *Other ILD diagnosed*: 7 patients with RB-ILD, 1 patient with emphysema.

under investigation to overcome limitations of TBLB and could be complimentary to EBUS. It has proved useful in diagnosing various interstitial lung diseases (ILD) [15–17].

2. Methods

A retrospective analysis of patients with suspected sarcoidosis in a single, tertiary-care, academic medical center who had been referred for bronchoscopic evaluation was performed. All patients were considered for both endobronchial ultrasound-guided fine needle aspiration (EBUS-FNA) and TBLC. Cases were seen over a three year period (October of 2013 and October of 2016). The following data was extracted from the patients' charts: age, gender, body mass index, radiographic data, procedure and pathology reports, and complications. All patients were classified by the American Society of Anesthesiologists (ASA) scoring system prior to the procedure. Clinical data, post procedural outcomes, pathologic diagnosis and outpatient follow-up (at least 6 months after lung biopsy) were recorded. This retrospective chart review protocol had been approved by the University of Cincinnati Institutional Review Board (Study #: 2016-0867).

All patients underwent bronchoscopy under general anesthesia through a laryngeal mask airway (LMA). Alternatively, if a patient had features suggestive of a difficult airway or had baseline home oxygen >4L per minute, an endotracheal tube (ETT) was used. Bronchoscopies were performed by board certified interventional pulmonologists at the University of Cincinnati Medical Center. Our cryobiopsy technique has been described previously [18].

The final diagnosis was made based on clinical presentation, radiographic information, pathologic examination, and clinical course of patients. Patients diagnosed with sarcoidosis met ATS/ERS/WASOG criteria, with alternative diagnosis excluded.

The pathologic diagnosis of sarcoidosis was confirmed with histological evidence of noncaseating epithelioid cell granulomas, and the following:

- Negative bacterial, fungal and mycobacterial stains/cultures.
- Cytology samples negative for disease processes other than sarcoidosis.

Radiologic evaluation of patients with suspected sarcoidosis was done with computed tomography (CT) chest imaging. A thoracic radiologist (RTS) reviewed the CT chest scans, blinded to results of bronchoscopy. The pattern and extent of disease was described with a grading system based on a Likert score: none, mild, moderate and severe, for five different CT chest findings: adenopathy; bronchovascular bundle thickening (large airway bundles); centrilobular nodularity (small airway bundles and/or ground glass opacities); pleural nodularity (along peripheral and fissural pleura); and fibrosis. CT chest studies were also classified according to the Scadding criteria [19]. See pictures section for representative imaging studies and yield of EBUS-FNA, TBLC or both combined (see Fig. 2).

Complications associated with the bronchoscopic procedure included acute respiratory failure, acute coronary syndromes, new cardiac arrhythmias requiring short or long term therapy, pneumonia, lobar atelectasis, pneumothorax, bleeding, thromboembolic disease, and death, regardless of cause, within 30 days of the procedure.

Bleeding at time of bronchoscopy was classified using a modification of a previously reported scale [18]. Bleeding was scored as Grade 0: traces of blood not requiring suctioning; Grade 1: mild bleeding that only requires suctioning and hemostatic wedging up to 2 min (two 1-min cycles); Grade 2: moderate bleeding requiring hemostatic wedging for 3 or more minutes; Grade 3: severe bleeding requiring topical instillation of epinephrine or cold saline;