CASE REPORT

Transbronchial Lung Cryobiopsy for Diagnosis of Pediatric Interstitial Lung Disease

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Received: January 02, 2017;
Initial review: April 10, 2017;
Accepted: March 08, 2018.

Background: Tissue diagnosis of Childhood interstitial lung diseases is of paramount importance to outline management. **Case characteristics:** A 10-year-old boy with prolonged cough, and computed tomography of thorax with features suggestive of primary Langerhans's cell histiocytosis. **Intervention:** Transbronchial cryobiopsy of lung using flexible cryoprobe, revealed a final diagnosis of Surfactant protein C/ABCA3 deficiency. **Message:** Transbronchial cryobiopsy of the lung can provide adequate lung tissue for a categorical diagnosis of interstitial lung diseases in children.

Keywords: *Childhood interstitial lung disease, Langerhan's cell histiocytosis, Lung biopsy, Video-assisted thoracic surgery.*

The term 'diffuse pediatric lung disease' has been used interchangeably with Childhood interstitial lung disease (ChILD) [1]. In the work-up of ChILD, tissue diagnosis with surgical lung biopsies/video-assisted thoracic surgery (SLB/VATS) is the gold standard, but is associated with significant risks [2]. Other option include Transbronchial forceps lung biopsy (TBFB), but has limitations of small specimen, and crush artifacts [3]. Newer diagnostic options for ChILD include Transbronchial Cryobiopsy (TBCB), which is increasingly being utilized for diagnosis of interstitial lung disease (ILD) in adults [4-6]. We report use of TBCB for a categorical diagnosis in ChILD.

CASE REPORT

A 10-year-old boy presented with history of dry cough, exertional dyspnea and intermittent wheezing, with inability to gain weight and height for four years. There was no significant antenatal or perinatal history, or recurrent infections requiring prolonged intubation or ventilation. There was no history of aspiration, swallowing dysfunction, or any exposure to pets, birds, farm dust, metallic dust, fumes, or animal dander.

On examination, he was afebrile, and had heart rate 90 beats per minute, respiratory rate 24 breaths per minute, blood pressure 100/66 mm Hg, and oxygen saturation 95% on room air. The height (119 cm) and weight (15 kg) were below 3rd centile. Clubbing was present on all digits. Chest examination showed basal bilateral fine crackles with end-expiratory wheeze.

The complete blood count, coagulation profile and urine analysis was normal. Pulmonary function tests showed mixed airway disease (FVC 23.8%, FEV1 19.8%, FEV1/FVC 81% predicted) with significant post-bronchodilator reversibility (30.5%). Echocardiography was normal. Chest computed tomography (CT) showed diffuse reticular opacities, multiple bilateral small thin walled irregular cysts with relative basal sparing, and diffuse ground glass opacities (***Fig.* 1**). A clinical diagnosis of primary Langerhan's cell histocytosis (PLCH) was considered.

For diagnosis, a comprehensive discussion of the options (TBFB *vs* TBCB *vs* VATS) was done. The parents were unwilling for VATS, and with the limitations of TBFB, a TBCB of the lung was planned. The segment for biopsy was decided based on the CT of the chest, targeting a significantly involved area (lingula). Rigid bronchoscopy (ventilating bronchoscope, 6.5 mm) was performed under general anesthesia. A flexible bronchoscope (diagnostic scope, channel 2.2 mm, Olympus Corporation) was introduced through the rigid scope to facilitate passage of flexible accessories. A Fogarty balloon (5 mm) was positioned at the entrance of the lingula, to restrict any bleeding to that segment. A standard flexible cryoprobe (ERBE, Germany, 90 cm length and 1.9 mm diameter) was introduced into the inferior lingula under fluoroscopic guidance *via* the flexible bronchoscope. The biopsy site was approximately 15-20 mm from the pleural surface. The biopsy process involved cooling for 3-4 seconds, and adhering lung tissue to the cryoprobe tip (cryoadhesion). The cryoprobe was then pulled with the adherent specimen, removing the cryoprobe with the bronchoscope as a unit. Simultaneously, with cryoprobe withdrawal, the appropriately positioned Fogarty balloon was inflated to

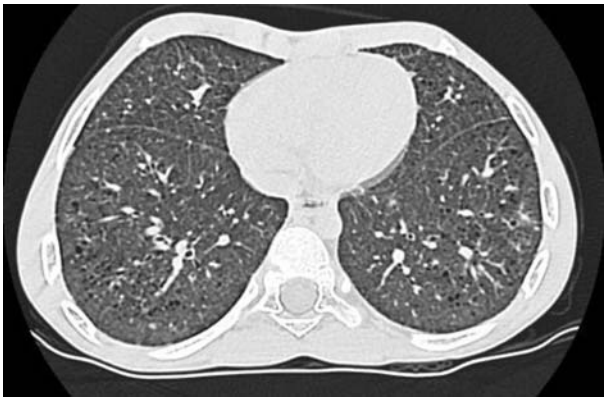

FIG. 1 *Computed tomography of chest shows diffuse reticular opacities with multiple bilateral small thin walled irregular cysts.*

restrict any bleeding. The frozen specimens (largest 27 mm^2) were thawed in saline and sent for histopathology [7]. Recovery was uneventful with no complications, and the child was discharged the next day.

Microscopy of the sample (60 alveoli) showed focal organizing pneumonia, indicated by tufts of fibroblasts extending into the airspaces with interstital fibrosis and organizing lung injury. This was suggestive of surfactant protein C deficiency or *ABCA3* mutation, pending genetic diagnosis. Immunohistochemistry showed negative CD1a stain, ruling out PLCH.

DISCUSSION

SLB is considered the gold standard for the diagnosis of ChILD's [8], but is associated with significant morbidity (persistent air-leak, persistent chest pain, cardiac arrhythmias, and infectious complications) and mortality (2-4% at 90 days) [2]. TBFB pieces are too small to define histology and TBCB offers an option between these two modalities. The application of cryotherapy for lung biopsy is based on the principle of cryoadhesion. Compressed carbon dioxide passing through the probe expands suddenly at the tip, leading to rapid cooling (– 89ºC). This freezes the tissue in contact for biopsy, with preservation of architecture due to cooling.

The most common complications reported in c ryobiopsy for ILD are pneumothorax (4.5-7.5%) [5,9] and bleeding (1.4%) [6]. Pneumothorax risk can be minimized by fluoroscopy [6]. Bleeding, though mild in most reports, can be controlled by Fogarty balloon tamponade [6]. The rigid bronchoscope enables both cryoprobe and Fogarty to be placed and utilized sequentially rapidly, which is important to control bleeding.

The limitations of TBCB in the children include difficulty in application. The rigid ventilating bronchoscope has to accommodate both the flexible bronchoscope and the Fogarty balloon at the same time, and hence a certain minimal size is essential. In our experience, this requires a minimal rigid scope diameter of 6.5 mm. Hence, it may not be possible to perform this procedure in children less than 6 years of age [10].

We demonstrated TBCB to be possible and safe for obtaining a categorical diagnosis in ChILD. TBCB provided adequate lung tissue, and allowed rapid recovery and discharge.

Acknowledgments: Dr Megan K Dishop, Pediatric Pathologist and Medical Director of Anatomic Pathology Children's Hospitals and Clinics of Minnesota, Minneapolis, USA for interpretation of cryobiopsy sample.
Contributors: All authors were involved in patient management, and contributed to the review of literature. All authors approved the final version of the manuscript.
Funding: None; *Competing interest*: None stated.

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