

OPEN

Bronchoscopic Transbronchial Cryobiopsy Diagnosis of Recurrent Diffuse Large B-Cell Lymphoma in the Lung: A Promising New Tool?

To the Editor:

The yield from conventional transbronchial biopsy of the lung for pulmonary lymphoma is often hampered by small samples afflicted by crush artefacts. Consequently, surgical lung biopsy, the only alternative available until recently, is often required to establish a diagnosis. Many patients are comorbid and unable to tolerate such a surgical procedure which itself is associated with significant risks. Endobronchial cryotherapy has been used for many years with success due to its ability to remove much larger specimens compared with conventional forceps. Its use ranges from sampling endobronchial lesions to recanalization of airway lumen from lung cancers.¹ In addition to providing large specimens, the ease of handling the cryoprobe and relatively low set up cost has led to cryotherapy being investigated as a means of sampling lung parenchyma. Transbronchial cryobiopsy (cryo-

TBB) has been examined as a diagnostic tool for diffuse or interstitial lung disease² as well as in after lung transplant surveillance.³ In these studies, the size of specimens retrieved by cryoprobe were significantly larger than those obtained by conventional forceps. Samples were generally between 5 and 7 mm in maximum diameter, contained less crushed artefacts and greater preserved architecture. Adverse effect profiles from cryo-TBB appear slightly higher compared with conventional forcep transbronchial biopsy in terms of bleeding and pneumothorax, but without any increase in mortality risk. The use of cryo-TBB in these lung conditions may become more widespread in the future as the community develops experience and provide evidence of its efficacy.

To our knowledge, there are no large studies examining the use of cryo-TBB in pulmonary lymphoma. Ours is the second case reporting on the successful use of cryo-TBB as a diagnostic tool for diffuse large B-cell lymphoma (DLBCL) presenting in pulmonary parenchyma. The other case report illustrates the use of cryo-TBB in diagnosing primary pulmonary DLBCL.⁴ Our case has 2 unique features in that the patient presented as a late relapse and her presentation was isolated to lung parenchyma with pleural effusion, without lymphadenopathy. Relapse from treated DLBCL after 5 years or later is very rare with a described rate of around 3.6%.⁵ Furthermore, isolated pulmonary parenchymal DLBCL is uncommon for both first presentation and recurrence, prompting the need for a definitive diagnosis.

In our patient, flexible bronchoscopy with transbronchial forcep and cryobiopsies were

performed in the operating theater. Anesthesia was induced and maintained with propofol, dexmedetomidine, and alfentanil and the patient was breathing spontaneously throughout the procedure. She was intubated with a laryngeal airway mask and an endobronchial blocker was placed prophylactically in the bronchus intermedius. Radial endobronchial ultrasound with guide sheath was performed with the 1.8 mm radial probe (UM-S20-17S Olympus) to aid location of abnormal lung parenchyma. Fluoroscopy was used to confirm the position of the probe within the lateral segment of the right middle lobe (Fig. 1) at least 2 cm away from the lung edge. The following sampling methods were performed sequentially: cytology brush, forcep, needle aspiration, and 2 cryobiopsies (1.9 mm, ERBE, Germany). The cryogen gas used was carbon dioxide and freezing time was 3 seconds. The cryoprobe and bronchoscope were removed en bloc after each cryobiopsy. A second bronchoscope was inserted immediately to inspect for bleeding distal to the endobronchial blocker. No significant bleeding occurred after both biopsies, and a chest x-ray performed an hour after the procedure confirmed no pneumothorax had occurred.

Specimens from the brush, needle aspirate, and forcep had significant crush artefacts and contained atypical lymphoid cells. The cryobiopsy specimens measured 6 × 4 and 6 × 3 mm. One contained inflamed lung parenchyma without evidence of neoplasia, while the other showed lung parenchyma infiltrated by singly distributed large, atypical lymphoid cells showing pleomorphic and irregular nuclei with prominent

Disclosure: There is no conflict of interest or other disclosures.

The Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/LBR.0000000000000354



FIGURE 1. Fluoroscopy image of cryoprobe extending into right middle lobe and endobronchial blocker within bronchus intermedius.

nucleoli. Immunohistochemistry stains confirmed these as abnormal B cell infiltrates (positive labelling for CD20, CD79a, BCL6, CD10), which have a Ki67 proliferative index of 80% to 90%. Comparison with the original inguinal lymph node histology found similar features, thereby confirming recurrence of DLBCL of the lung.

In our patient, the cryo-TBB specimen was the only diagnostic specimen, while the other results were merely suggestive. Without the cryobiopsy specimen, a definitive diagnosis of DLBCL recurrence would not have been possible. This case highlights the potential value of transbronchial cryobiopsy as a diagnostic modality for pulmonary parenchymal lymphoma. Further larger case studies are required to establish the efficacy and safety of cryo-TBB in this setting, but cryo-TBB could be considered in patients presenting with lung parenchymal abnormalities where lymphoma is suspected, particularly if preexisting

comorbidities prohibit surgical lung biopsy.

Elaine Yap, FRACP*

Irene Low, FRACP†

Departments of *Respiratory

†Histopathology, Middlemore Hospital
Auckland, New Zealand

REFERENCES

- Schumann C, Hetzel M, Babiak AJ, et al. Endobronchial tumor debulking with a flexible cryoprobe for immediate treatment of malignant stenosis. *J Thorac Cardiovasc Surg.* 2010;139:997–1000.
- Pajares V, Puzo C, Castillo D, et al. Diagnostic yield of transbronchial cryobiopsy in interstitial lung disease: a randomized trial. *Respirology.* 2014;19:900–906.
- Fruchter O, Fridel L, Rosengarten D, et al. Transbronchial cryo-biopsy in lung transplantation patients: first report. *Respirology.* 2013;18:669–673.
- Schiavo D, Batzlaff C, Maldonado F. Pulmonary parenchymal lymphoma diagnosed by bronchoscopic cryoprobe lung biopsy. *J Bronchol Intervent Pulmonol.* 2016;23:174–176.
- Larouche JF, Berger F, Chassagne-Clement C, et al. Lymphoma recurrence 5 years later or following diffuse large B-cell lymphoma: clinical characteristics and outcome. *J Clin Oncol.* 2010;28:2094–2100.

Combined Typical Carcinoid-Adenocarcinoma Lung Tumor

To the Editor:

Combined tumors are those with a mixed histologic pattern. Combined neuroendocrine tumors consist of a neuroendocrine component as well as at least one other distinct tumor population. Although combinations of neuroendocrine tumors with non-neuroendocrine carcinomas (NNEC) can occasionally be found in the lungs, the neuroendocrine component of these tumors tends to be small cell lung carcinoma (SCLC) or large cell neuroendocrine carcinoma as opposed to typical or atypical carcinoids. We report a case of combined endocrine tumor of the lung consisting of typical carcinoid mixed with adenocarcinoma, one of only a few reported cases of its kind. Cavazza et al¹ were one of the first and only to report a similar finding in 2001.

A 59-year-old white male, 90 packs per year smoker with non-alcoholic steatohepatitis cirrhosis being evaluated for liver transplantation, presented with an incidental right middle lobe 1.6 × 1 cm nodule with associated right upper lobe (RUL) punctuate nodules (Fig. 1A). Other pertinent history includes non-Hodgkin lymphoma in remission since 2007 and Crohn disease. A positron emission tomography scan revealed hypermetabolic activity with a standardized uptake value of 3.2 and 5.8 in the right middle lobe nodule and RUL punctuate nodules, respectively (Fig. 1B).

Disclosure: There is no conflict of interest or other disclosures.
DOI: 10.1097/LBR.0000000000000359