Radial probe endobronchial ultrasound (R-EBUS) guided transbronchial cryobiopsy in the diagnosis of peripheral solitary pulmonary nodule

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SUMMARY

Solitary pulmonary nodule (SPN) always raises suspicion for early lung cancer, in which accurate and less invasive biopsy is needed. We report a case of transbronchial cryobiopsy of right upper lobe SPN under radial endobronchial ultrasound (R-EBUS) guidance after an inconclusive computed tomography guided transthoracic needle aspiration. A diagnosis of Stage 1B adenocarcinoma of the lung was made. Patient subsequently underwent curative right upper lobectomy after ruling out mediastinal lymph node involvement. To the best of our knowledge, this is the first report of R-EBUS guided transbronchial cryobiopsy case reported from Malaysia.

INTRODUCTION

Solitary pulmonary nodule (SPN) always raises suspicion for the presence of early lung cancer, in which accurate and less invasive biopsy is needed. Computed tomography (CT) guided transthoracic needle aspiration (TTNA) reported high diagnostic yield however at the expense of high complication rate, especially pneumothorax. Radial endobronchial ultrasound (R-EBUS) is a novel technique in guiding bronchoscopic biopsy of SPN with low complication rates while transbronchial cryobiopsy is able to provide larger biopsy specimen for analysis; which is important to guide personalized treatment of lung cancer in this era of targeted and immunotherapy. We report a case of transbronchial cryobiopsy of SPN under R-EBUS guidance.

CASE REPORT

A 68-year-old man with a smoking history of 60 pack years presented with chronic cough for six months. He was previously well with no chronic medical illness and report no family history of malignancy. Physical examination was unremarkable with no evidence of distant metastasis. Chest radiograph and contrast enhanced CT thorax revealed a spiculated 2.1x2.2cm SPN at the posterior segment of right upper lobe (Figure 1A, 1B). Initial CT guided TTNA was inconclusive and hence was scheduled for R-EBUS guided transbronchial cryobiopsy. A navigational route to the sub-segmental bronchi of the posterior segment of right upper lobe (RB2bii) was planned after analysing the CT scan for bronchus sign (Figure 1C).

Under conscious sedation, segmental airway was examined cautiously via trans-nasal route by a flexible therapeutic bronchoscope, which did not reveal any abnormality. A concentrically orientated lesion was successfully localized by the 2.0mm 20Hz R-EBUS probe with guide sheath (UM-S20-20R, Olympus Medical) at the planned sub-segment of RB2bii (Figure 1D). The radial probe was then removed while locking the guide sheath and bronchoscope in place. A 1.9mm flexible cryoprobe (1150mm ERBE, Medizintechnik, Germany) was then inserted into the guide sheath that acted as a conduit to the target lesion under guidance of fluoroscopy (Figure 1E). Transbronchial cryobiopsy was then obtained by freezing the tip of cryoprobe for five seconds and withdrawn en-bloc with the bronchoscope. The tissue was retrieved by thawing in normal saline. Two cryobiopsies were attempted and there was minimal intra-procedure post biopsy bleeding which was manageable by suction and local adrenaline flush. Biopsy specimen measured around 5mm in size (Figure 2A) and histopathological examination confirmed adenocarcinoma of the lung. Microscopically, the specimen showed fibrous tissue infiltrated by gland forming malignant cells, which was positive for CK7 and TTF-1 on immunohistochemistry staining (Figure 2B, 2C). No sensitising mutation was detected on epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) rearrangement on molecular study.

Subsequently, a complete mediastinal staging was performed with convex probe EBUS to the mediastinal lymph node stations systematically. The right paratracheal lymph node (Station 4R) was sampled via transbronchial needle aspiration (TBNA) under convex probe EBUS guidance, which revealed only benign lymphoid tissue. Patient was diagnosed Stage 1B (cT2aN0M0) adenocarcinoma lung of the right upper lobe. Pre-operative assessment deemed patient a low risk surgical candidate with a predicted post-op FEV1 for right upper lobectomy of 80%. Patient subsequently underwent video assisted thoracoscopy (VATS) right upper lobectomy and lymph node dissection uneventfully. Resected specimen showed good margin clearance with negative hilar and right paratracheal lymph node - pathological Stage 1B (pT2aN0M0). Patient remained well post lobectomy and no adjuvant therapy was given. The latest CT surveillance one year after showed no evidence of recurrence and patient remained well with on-going radiological surveillance. His lung function remained stable with FEV1 of 91%.

This article was accepted: 29 May 2019
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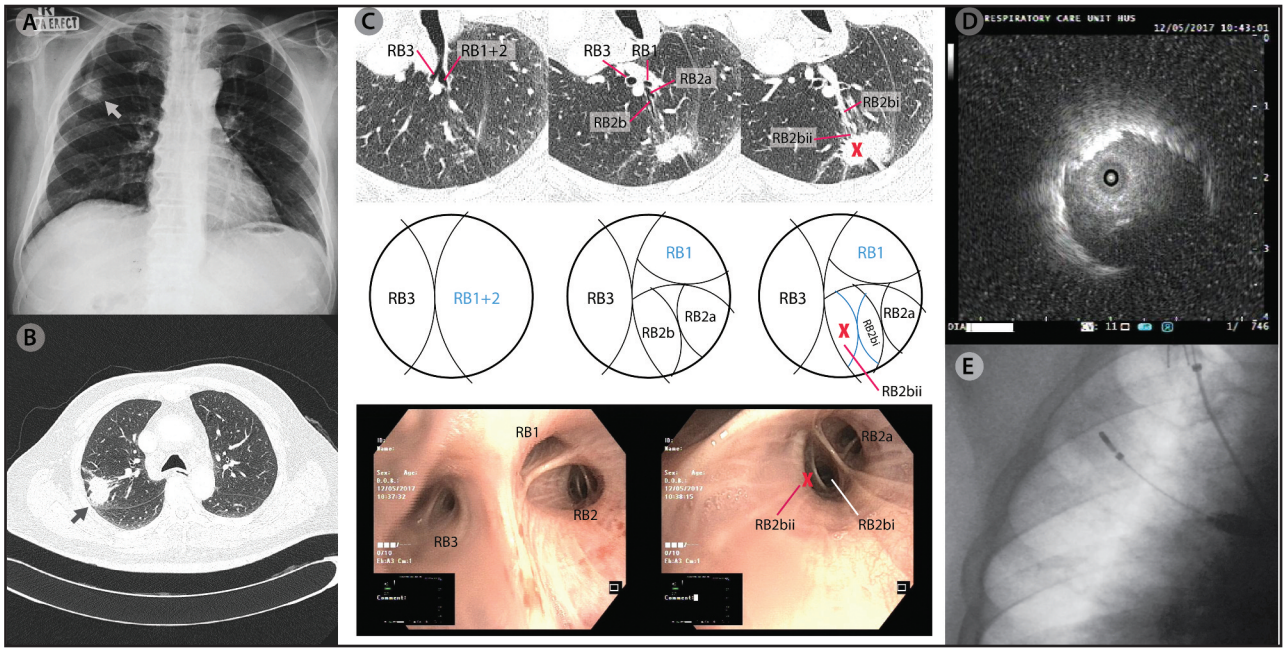

Fig. 1: (A) Chest radiograph demonstrating a right upper lobe nodule (arrow).
(B) A 2.1x2.2cm spiculated solitary pulmonary nodule at the posterior segment of right upper lobe on axial CT scan.
(C) The planned navigational route for the solitary pulmonary nodule via analyzing CT bronchus sign.
- Top panel: Axial CT scan slices rotated counter-clockwise to simulate actual bronchoscopic vision for right upper lobe access. All segmental bronchi* leading into the target lesion (RB2bii) were identified and labeled.
- Middle panel: Schematic drawing of the navigational route into the target sub-segmental bronchi of RB2bii.
- Low panel: Actual bronchoscopic image of right upper lobe bronchus correlating with the planned navigational route to RB2bii.

*RB1: Apical segment of RUL; RB3: Anterior segment of RUL; RB2: Posterior segment of RUL; RB2a: Posterior sub-segment of RB2; RB2b: Anterior sub-segment of RB2; RB2bi: Posterior sub-segment of RB2b; RB2bii: Anterior sub-segment of RB2b.
(D) A concentrically orientated R-EBUS lesion successfully localized at the target segment of RB2bii.
(E) Fluoroscopic image showing placement of the 1.9mm cryoprobe within a guide sheath into the target lesion.

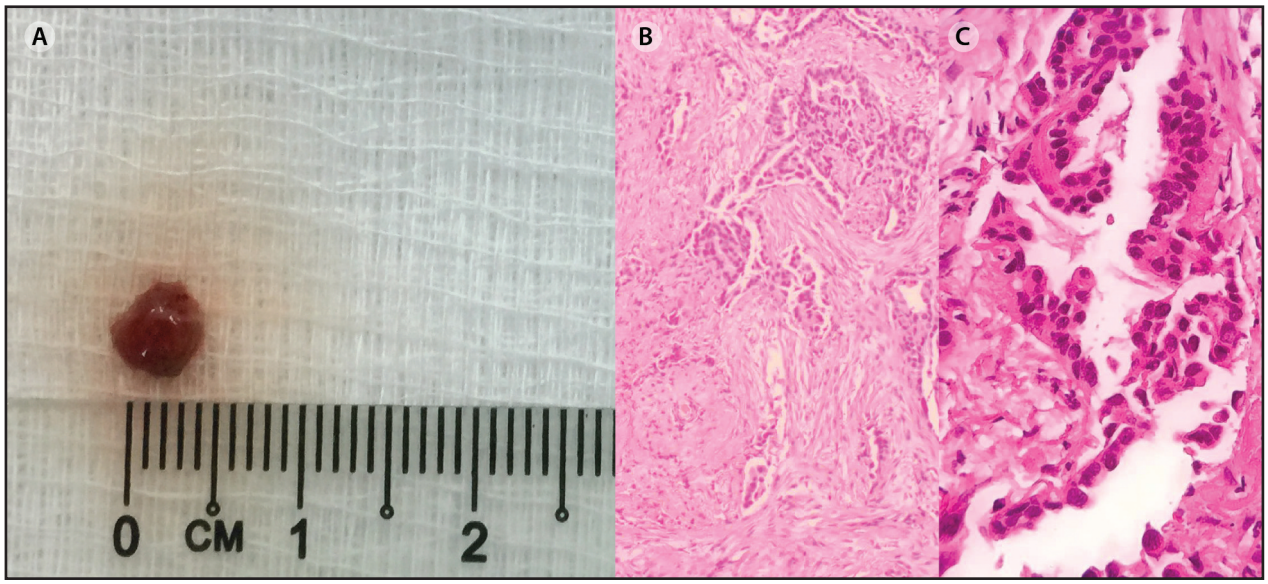

Fig. 2: (A) Gross appearance of the transbronchial cryobiopsy specimen, measured around 5mm in size
(B) Histopathological examination revealed fragments of fibrous tissue infiltrated by malignant cells forming glandular structure with desmoplastic reaction in surrounding stroma. (Hematoxylin & Eosin Stain, x10 fold magnification)
(C) The malignant cells were pleomorphic with hyperchromatic nuclei and prominent nucleoli and moderate amount of cytoplasm. (Hematoxylin & Eosin Stain, x40 fold magnification)

DISCUSSION

Lung cancer is a major cause of mortality and morbidity in Malaysia and worldwide. Most lung cancer in Malaysia present late with locally advanced disease or distant metastasis with only around 12% of cases were detected early enough to be considered for curative surgical resection.[1] Recently, widespread use of CT has led to exponential rise in detection of SPN. Lung cancers presenting as SPN are often early disease with good prognosis. Hence, there is a rising demand and expectation for more accurate and less invasive diagnostic test.

Diagnostic yield for routine unguided bronchoscopy for SPN is less than 20%.[2] R-EBUS guided transbronchial lung biopsy of SPN is a novel technique with meta-analysis revealed overall diagnostic yield of 70.6% with a low complication rate of 2.8%.[3] In contrast, CT guided transthoracic needle aspiration although providing higher diagnostic yield, was associated with significant complication risk especially pneumothorax at 25% with at least 15% requires chest tube insertion.[2] Our case demonstrated the practicality of R-EBUS in sampling a SPN after an inconclusive CT guided TTNA. To the best of our knowledge, this is the first R-EBUS guided transbronchial cryobiopsy case reported from Malaysia.

Nonetheless, despite the use of various guidance techniques, diagnostic yield of SPN still strongly depends on the biopsy methods.[3,4] Conventional forceps biopsy frequently results in small and crushed specimens, which may not be suitable and adequate for immunohistochemical or molecular studies. On the contrary, cryobiopsy is a novel bronchoscopic sampling technique, which provide larger specimens. This technique had shown promising results in the diagnosis of diffuse parenchymal lung disease, and had since then been expanded into the diagnosis of SPN under R-EBUS guidance.[4,5] Schuhmann et al.,[4] demonstrated that transbronchial cryobiopsy with R-EBUS guidance to have higher diagnostic yield of 74.2% compared to 61.3% for conventional forcep biopsy, a larger tissue sample (11.17mm^2 for cryobiopsy and 4.69mm^2 for forcep biopsy) with no severe complications observed, especially bleeding and pneumothorax. Another proposed advantages of cryobiopsy in biopsy of SPN is the ability of cryoprobe in obtaining a spherical core of tissue surrounding the tip when it was frozen, increasing the chance of successful biopsy in lesion which was adjacently orientated to the probe.[4,5] Literature on transbronchial cryobiopsy focused on the diagnosis of diffuse parenchymal lung disease with only limited reports on the diagnosis of SPN.

Early diagnosis of lung cancer improves morbidity and mortality. Less invasive diagnostic test such as guided bronchoscopy via R-EBUS plays a pertinent role in providing an accurate and effective option for SPN biopsy. Transbronchial cryobiopsy is able to provide larger tissue specimens which is essential in the era of targeted and immunotherapy in lung cancer by providing adequate samples of specimen for immunohistochemistry and molecular study. Our case highlights the first reported case of transbronchial cryobiopsy of SPN under R-EBUS guidance in Malaysia.

REFERENCES

1. Malaysian National Cancer Registry Report, Malaysia Cancer Statistics, Data and Figure 2007-2011.
2. Memoli JSW, Nietert PJ, Silvestri GA. Meta-analysis of guided bronchoscopy for the evaluation of the pulmonary nodule. Chest 2012; 142(2): 385-93.
3. Ali MS, Trick W, Mba BI, Mohananey D, Sethi J, Musani AI. Radial endobronchial ultrasound for the diagnosis of peripheral pulmonary lesions: a systematic review and meta-analysis. Respirology 2017; 22(3): 443-53.
4. Schuhmann M, Bostanci K, Bugalho A, Warth A, Schnabel PA, Herth FJF et al. Endobronchial ultrasound-guided cryobiopsies in peripheral pulmonary lesions: a feasibility study. Eur Respir J 2014; 43: 233-9.
5. Goyal R, Gogia P, Chachra V. Endobronchial ultrasound-radial probe-assisted cryobiopsy for peripheral lung mass, a new way for better yield? J Bronchol Intervent Pulmonol 2016; 23(1): 67-70.