

Transbronchial lung cryobiopsy for the diagnosis of lepidic-predominant lung adenocarcinoma

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ABSTRACT

Lung cancer is one of the most common malignancies globally with lung adenocarcinoma as the most common type of lung cancer. With new classification of lung cancers in 2011, it has become pertinent that adequate tissue is obtained for the diagnosis and subtyping of lung adenocarcinoma particularly for prognostication. Transbronchial cryobiopsy is a minimally invasive procedure which helps obtain adequate tissue and avoid surgical lung biopsy.

KEY WORDS: Bronchoalveolar carcinoma, cryobiopsy, lepidic growth, lung adenocarcinoma, transbronchial biopsy

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INTRODUCTION

In 2011, the International Association for the Study of Lung Cancer, American Thoracic Society, and European Respiratory Society revised the classification of lung adenocarcinoma.^[1] The idea, behind this proposed change, was to provide a uniform terminology based on morphological criteria which would also help with prognosis and would be easier to communicate among practitioners.^[1] Different subtypes of lung adenocarcinoma, such as lepidic, acinar, papillary, micropapillary, and solid, were included in the study.^[1] Lepidic pattern (formerly known as bronchoalveolar carcinoma) was defined as a tumor composed of neoplastic cells lining the alveolar lining with no architectural disruption, and no lymphovascular or pleural invasion.^[2]

Given the importance of accurate morphological diagnosis which in turn affects the treatment and prognosis,^[3] it is required that the biopsy specimen has a good representation of the lung parenchyma including alveoli,

interstitium, lymphatics, and blood vessels. Therefore, historically surgical lung biopsy was considered the gold standard for the diagnosis of bronchoalveolar carcinoma, and bronchoscopy with transbronchial biopsy was not considered adequate. The situation was similar to patients with interstitial lung disease, and surgical lung biopsy was considered the preferred modality to obtain the lung biopsy.

Transbronchial cryobiopsy is the new tool which uses cryoadhesion to biopsy the area of interest in the lung, it provides with adequate tissue for the diagnosis and has less crush artifact.^[4] Cryobiopsy is now commonly used in patients with diffuse parenchymal lung disease/interstitial lung disease;^[5] however, it has not been used for the diagnosis of lepidic-predominant lung adenocarcinoma (bronchoalveolar carcinoma). We report two cases of lepidic-predominant lung adenocarcinoma which were diagnosed with transbronchial cryobiopsy.

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How to cite this article: Pathak V, Zhou C. Transbronchial lung cryobiopsy for the diagnosis of lepidic-predominant lung adenocarcinoma. Lung India 2019;36:434-7.

Access this article online	
Quick Response Code: 	Website: www.lungindia.com
	DOI: 10.4103/lungindia.lungindia_325_18

CASE REPORTS

Case 1

A 60-year-old female with a history of 20 pack-year smoking presented for the evaluation of chronic cough. She had a persistent nonproductive cough for 4 months and had quit smoking a month before the presentation without any help. Cough was worse on bending over or lying down. She denied any fever, chills, rigors, or hemoptysis. She did not have any sinus drainage, running nose, or allergies. She did not have any history of asthma and denied any occupational or environmental exposures. She did endorse shortness of breath on exertion particularly when going up and down the stairs. She had been treated with antibiotics empirically multiple times in the past 6 months for presumed pneumonia. On examination, her vitals were normal except her oxygen saturation which was in low 90s on room air. Chest, cardiovascular, abdominal, and neurologic examinations were normal. Spirometry showed the restrictive ventilatory defect. The previous chest X-ray showed bilateral pulmonary infiltrates.

Computerized tomography (CT) of the chest showed bilateral ground-glass opacity [Figure 1].

The patient was scheduled for bronchoscopy and transbronchial biopsy using cryoadhesion. Cryobiopsy was done in the right upper lobe. The pathology showed airspaces lined by nonmucinous neoplastic epithelium consistent with adenocarcinoma, and the tumor was predominantly lepidic with many areas also showing papillary architecture [Figures 2-4]. There was no invasion; overall, it was diagnosed as lepidic-predominant nonmucinous type adenocarcinoma. Immunohistochemical staining showed the tumor to be thyroid transcription factor 1 positive and negative for CDX-2, providing evidence that this tumor represented a pulmonary primary. Further molecular markers showed epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ROS-1 negative, and programmed death-ligand 1 (PD-L1) tumor proportions score of 1%. The patient was referred to oncology for treatment.

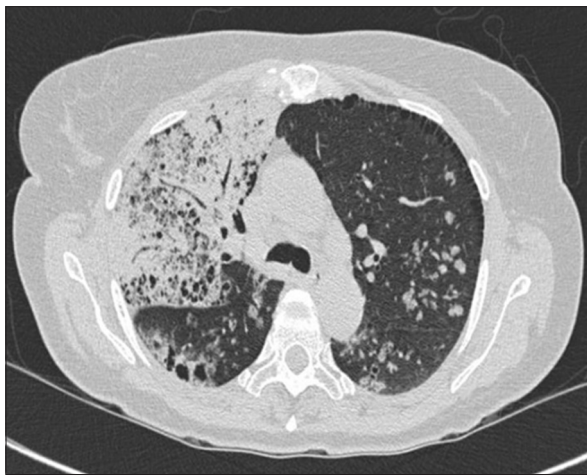


Figure 1: Computerized tomography of the chest showing consolidation with air bronchogram

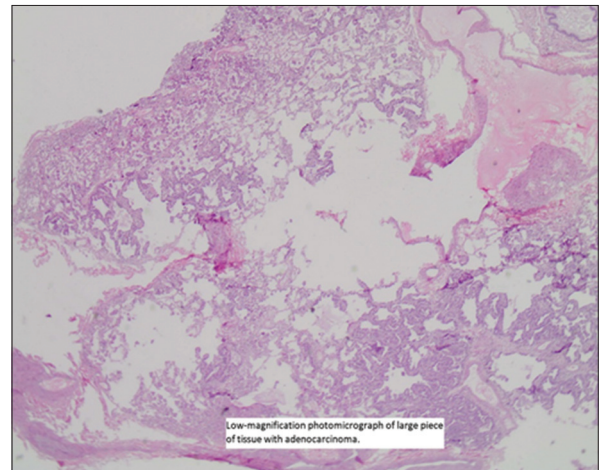


Figure 2: Low-magnification photomicrograph of lung biopsy showing adenocarcinoma with lepidic-predominant features

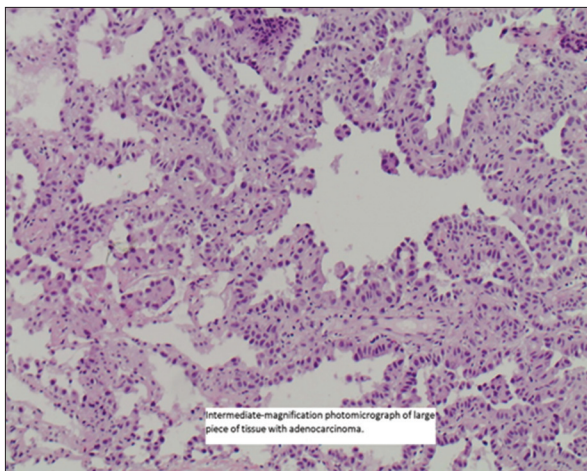


Figure 3: Intermediate magnification photomicrograph of lung biopsy showing adenocarcinoma with lepidic-predominant features

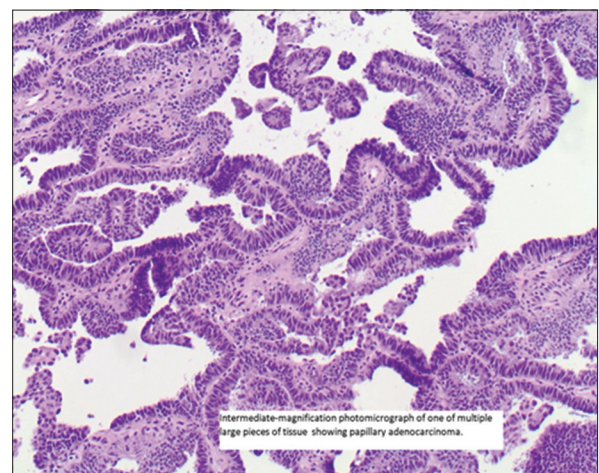


Figure 4: Intermediate magnification photomicrograph of one of multiple lung biopsy fragments showing moderately differentiated adenocarcinoma with papillary features

Case 2

A 55-year-old male with gastroesophageal reflux and hyperlipidemia presented with nonproductive cough and shortness of breath for 2 months. Over the last 2 months, he received two courses of antibiotics empirically for pneumonia without any help, each course lasting for 10 days. He denied any chest pain, fever, chills, or rigors; no hemoptysis, loss of weight, or loss of appetite; no prodromal symptoms or travels; no history of exposure to dust, fumes, and chemicals; not a bird feeder; no rheumatological illness; and no travels. Father and other male siblings/relatives had lung cancers. He smoked for about 15–20 years on and off. On presentation, he was hypoxic with his oxygen saturation in low 80s on room air. He was treated with supplemental oxygen for 6l/min improving the saturation to 93%. His vitals otherwise were stable. Examination of the chest did not reveal any crackles or wheeze. Normal cardiovascular, abdominal, and neurological examinations. CT chest showed bilateral ground-glass opacity particularly on the left side [Figure 5].

Bronchoscopy with transbronchial biopsy using cryoadhesion was done in the left upper and lower lobes. Pathology showed adenocarcinoma of the lung with lepidic-predominant features in both the lobes. Molecular analysis showed no EGFR, ALK, or ROS1 mutation. PD-L1 immunostain was also negative. The patient was referred to oncology for further treatment.

DISCUSSION

Initially, both patients, presented with shortness of breath and cough, were hypoxic on presentation and had bilateral ground-glass opacity with air bronchogram. The differential diagnosis included acute or chronic eosinophilic pneumonia, cryptogenic organizing pneumonia, acute interstitial pneumonia, hypersensitivity pneumonitis, idiopathic interstitial lung disease, and lung adenocarcinoma. Due to the broad differential diagnosis



Figure 5: Computerized tomography of the chest showing ground-glass opacity with air bronchograms

and the fact that larger tissue would have been required for adequate evaluation of parenchymal architecture, transbronchial lung cryobiopsy was chosen as the best diagnostic modality.

Transbronchial cryobiopsy provided adequate tissue for the diagnosis in both the cases. Both cases were diagnosed with lepidic-predominant adenocarcinoma. The tissue was also adequate for molecular markers such as EGFR, ALK, ROS1, and PD-L1.

Most of the lung adenocarcinoma has mixed histologic type; however, lepidic-predominant lung adenocarcinoma has the best prognosis. Solitary tumors, which are <3 cm in size, with pure lepidic pattern with no evidence of invasion are now termed as “adenocarcinoma *in situ*” and the term “bronchoalveolar carcinoma” is no longer used. Similarly, the tumor which is <3 cm with 5 mm or less invasion with predominant lepidic pattern is termed as “minimally invasive adenocarcinoma.”^[6]

Diagnostic bronchoscopy has significant role in the diagnosis of lung cancers. However, the forceps used for the endobronchial or transbronchial biopsy provides the specimen of approximately 2-mm diameter^[7] while cryobiopsy specimen are up to 8 mm in diameter.^[8] The bigger size accounts for better architectural and morphological review which helps with correctly subtyping the tumors. Cryobiopsy also avoids crush artifact which can be seen with forceps biopsy, thus allowing a better interpretation of anatomic structure and histopathological changes. The efficacy and safety of cryobiopsy in patients with interstitial lung disease have been studied in the past, and it is deemed a safe procedure.^[9] Cryobiopsy also allows for sample specimen to allow for molecular marker study such as EGFR, ROS1, ALK, and PD-L1.

CONCLUSIONS

Transbronchial cryobiopsy is a safe new technique which provides larger specimen permitting adequate evaluation of lung parenchyma and correctly subtyping lung cancers. It also provides sample specimen to study molecular markers. Transbronchial cryobiopsy can be done in outpatient setting, and surgical lung biopsy can be avoided, further saving the time and cost.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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