

Mucinous Adenocarcinoma of the Lung Diagnosed by Radial Endobronchial Ultrasound-guided Bronchoscopic Cryobiopsy and Presenting as Interstitial Lung Disease in a Patient with Systemic Sclerosis

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Abstract

We report a patient with systemic sclerosis who was diagnosed with advanced-stage mucinous adenocarcinoma of the lungs. The clinical presentation, imaging findings, pathological results, and molecular diagnoses are presented. A 64-year-old woman with systemic sclerosis was administered prednisolone and hydroxychloroquine sulfate to control her disease. High-resolution computed tomography (HRCT) revealed an interstitial pattern in both lungs during annual imaging. Connective tissue disease-associated interstitial lung disease (CTD-ILD) was diagnosed using blood tests, pulmonary function tests, and imaging findings. One year later, the patient underwent follow-up chest HRCT, which showed progressive lung disease. The patient underwent endobronchial ultrasound (EBUS)-guided transbronchial lung cryobiopsy and computed tomography-guided biopsy for a pathological diagnosis. The pathology reports of bilateral lungs disclosed mucinous adenocarcinoma. After tumor staging and mutation testing, the patient received chemotherapy with pemetrexed and cisplatin. The bilateral lung lesions subsided after four cycles of first-line chemotherapy. Patients with CTD and lung involvement may be diagnosed with CTD-ILD. Although histopathological results are not mandatory for ILD diagnosis, EBUS-guided transbronchial lung biopsy or lung cryobiopsy should be considered when ILD has atypical or unexplained features.

Keywords: Connective tissue disease, endobronchial ultrasound, transbronchial lung cryobiopsy

INTRODUCTION

Connective tissue disease-associated interstitial lung disease (CTD-ILD) is not rare and presents in patients with systemic sclerosis, inflammatory myositis, rheumatoid arthritis, Sjögren's syndrome, and systemic lupus erythematosus.^[1] The diagnosis of CTD-ILD is usually made by clinical presentation, serologic testing, high-resolution computed tomography (HRCT), and pulmonary function tests. However, lung biopsy is not mandatory for the diagnosis of CTD-ILD.^[2] We present a case of systemic sclerosis with unexpected findings after transbronchial lung cryobiopsy (TBLC).

CASE REPORT

A 64-year-old woman was diagnosed with systemic sclerosis with an initial presentation of cutaneous sclerosis 3 years ago. She received prednisolone and hydroxychloroquine sulfate to control her disease. The patient had never smoked. She underwent an examination by chest HRCT due to a

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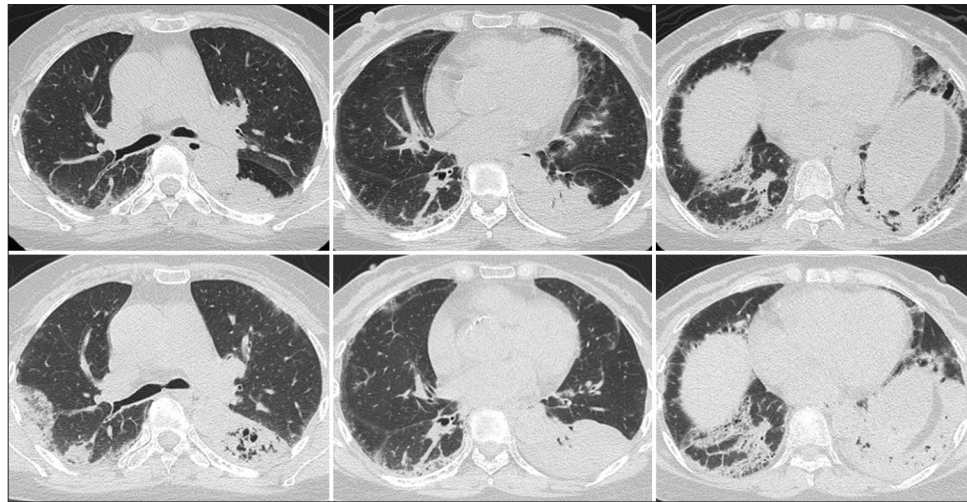


Figure 1: Transverse thin-section lung computed tomography at the level of the main bronchi, left atrium, and lower lung zone from left to right. The initial scan (top row) showed predominantly subpleural and lower lobe reticulation and ground-glass opacities with immediate subpleural sparing in the right lung. Consolidations are seen in the dependent part of the left lower lobe and traction bronchiectasis in the anterior and posterior basal left lower lungs. Follow-up scans (bottom row) 1 year later showed an increase in the extent of reticulation and consolidation. New peripheral consolidations with surrounding ground-glass opacities in the posterior right upper lobe and progressive consolidations in the left lower lobe were biopsy-proven mucinous adenocarcinomas

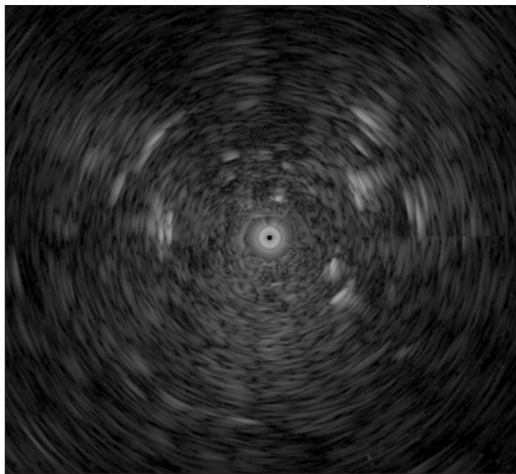


Figure 2: The radial probe EBUS showed heterogeneous echogenicity along with linear-discrete air bronchogram. The probe was within the lung lesion over the left lower lung. EBUS: Endobronchial ultrasound

chronic cough for months. The HRCT showed subpleural, peribronchovascular interstitial thickening, and ground-glass opacities in the bilateral lungs. One year later, the followed-up HRCT revealed progressive consolidations in the bilateral lungs [Figure 1].

The patient underwent endobronchial ultrasound (EBUS)-guided TBLC over the left lower lung. Radial probe EBUS showed heterogeneous echogenicity along with a linear-discrete air bronchogram, and the probe was within the lung lesion over the left lower lung [Figure 2]. The pathologic report of the left lower lung through bronchoscopic cryobiopsy showed wild-type mucinous adenocarcinoma [Figure 3]. The computed tomography (CT)-guided biopsy of her right lower lung was performed, and the pathology report was

also mucinous adenocarcinoma. Brain magnetic resonance imaging and positron emission tomography revealed no distant metastasis. The patient was diagnosed with Stage IV mucinous adenocarcinoma. Molecular testing for epidermal growth factor receptor (EGFR) mutations, anaplastic lymphoma kinase, and programmed death ligand-1 expression were negative [Figure 4]. She received four cycles of first-line chemotherapy with pemetrexed and cisplatin. After treatment, the follow-up CT scan showed disease in partial remission with a decrease in the size of the right lower lung lesion and the left lower lung solid component subsided.

The present study was approved by the Institutional Review Board of Chang Gung Memorial Foundation (IRB No.: 202100222B0). Owing to the retrospective study design, informed consent was not required and the Institutional Review Board approved the waiver in our institution.

DISCUSSION AND CONCLUSIONS

We demonstrated that lung biopsy might be indicated in patients with CTD-ILD when lung lesions progressively deteriorate. Mucinous adenocarcinoma lesions vary on CT scans, and CT findings are classified as solitary or pneumonic type.^[3] The solid mass had a clear margin on CT. The pneumonic lesion showed alveolar consolidations, which are often confused with pneumonia. Mucinous adenocarcinomas originate from mucus-containing cells presenting a goblet or columnar cell morphology with intracytoplasmic mucin. The involved alveoli are typically filled with mucin.

Previous studies showed that 3.5% to 7% of patients with pulmonary mucinous adenocarcinoma presented with EGFR mutations.^[4,5] Kirsten rat sarcoma viral oncogene homolog amino acid changes were the most frequent driver

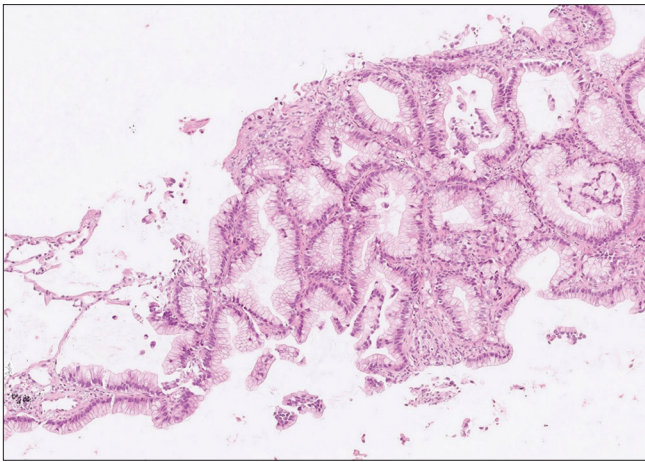


Figure 3: Left lower lung tumor cells with mucinous cytoplasm growing along the alveolar wall (lepidic pattern, and left side) or in an acinar pattern (right side) (hematoxylin and eosin stain, $\times 20$)

mutations (up to 63%).^[6] As primary pulmonary mucinous adenocarcinoma is uncommon, survival rate data are relatively limited. The 5-year survival rate for patients with mucinous and nonmucinous adenocarcinomas showed no significant difference.^[6]

CTD-ILD has various features of interstitial lung abnormalities on HRCT.^[7] A previous study showed that 48% of patients with rheumatoid arthritis and ILD had radiologic progression.^[8] Another study reported that 23% of patients with systemic sclerosis had progression of ILD.^[9] Mycophenolate, cyclophosphamide, or nintedanib is suggested to treat systemic sclerosis-associated ILD.

Some authors suggest that surgical lung biopsy is seldom used and rarely provides additional information on CTD-ILD.^[10] Even in cases of disease progression, surgical lung biopsy is usually not recommended. The current official clinical practice guideline has no recommendation for or against lung cryobiopsy for the diagnosis of idiopathic pulmonary fibrosis.^[11] Observational studies have reported that lung cancer risk increased in patients with ILD^[12,13] and CTD-ILD.^[14,15]

To exclude malignancy in ILD, transbronchial forceps biopsy using endobronchial ultrasonography is acceptable.^[16] However, the forceps biopsy specimen is relatively small to offer further information for ILD diagnosis. A randomized controlled trial showed that ILD diagnoses based on histopathological results from transbronchial cryobiopsy are reliable.^[17] We suggest that lung cryobiopsy can be performed when ILD has atypical or unexplained features. Although the risks of lung cryobiopsy are acceptable,^[18-20] an increased risk of bleeding is inevitable compared to transbronchial forceps biopsy.^[21-23] Therefore, EBUS-guided bronchoscopic cryobiopsy should be performed by experienced bronchoscopists.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her

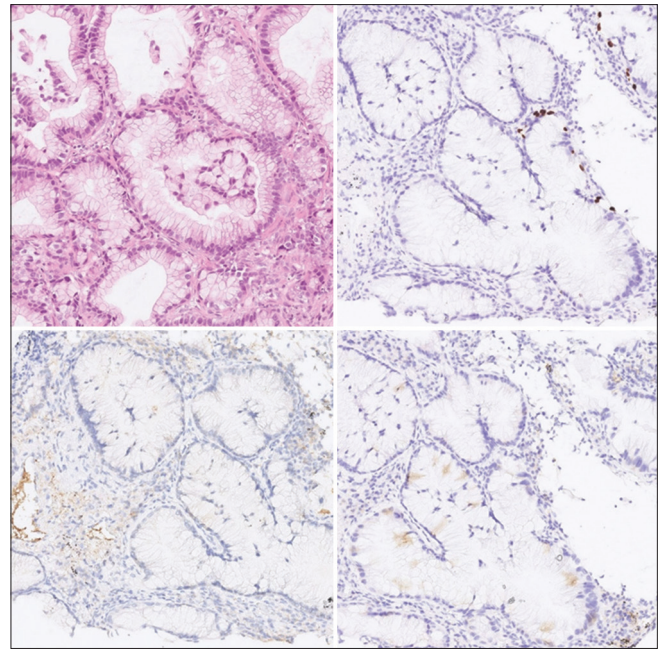


Figure 4: The left lower lung tumor cells showed mild-to-moderate nuclear atypia and abundant mucinous cytoplasm (top left). Tumor cells were negative for TTF1 immunostaining, whereas the residual alveolar epithelial cells were positive (top right). Tumor cells were negative for anaplastic lymphoma kinase (bottom left) and programmed death ligand-1 expression (bottom right) ($\times 40$). TTF1: Thyroid transcription factor-1

consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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