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Pneumonic-type mucinous lung adenocarcinoma diagnosed by transbronchial cryobiopsy

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Abstract

Primary lung adenocarcinoma with lepidic growth can mimic diffuse pulmonary parenchymal processes like infectious pneumonia or idiopathic inflammatory pneumonitis. We report a case of subacute pneumonitis refractory to antibiotic therapy and empirical corticosteroids, proven to be diffuse mucinous adenocarcinoma with lepidic growth on transbronchial cryobiopsy.

Introduction

Rapidly progressive diffuse parenchymal lung disease not caused by an infectious organism represents a diagnostic challenge, particularly when severe hypoxemia ensues. The differential diagnosis is broad, and diagnostic tissue procurement is not always feasible. We report a case in which transbronchial cryobiopsy was used for diagnosis.

Case Report

A 68-year-old Filipina who was previously healthy presented with dyspnoea, productive cough, right-sided pleuritic chest pain, and bilateral pulmonary infiltrates that progressed over three months. She had never smoked cigarettes or had any occupational exposures associated with lung disease. Outpatient treatment with oral antibiotics, including levofloxacin and doxycycline, had been ineffective, and she had become progressively hypoxemic, requiring hospitalization. A CT scan of the chest revealed patchy bilateral pulmonary infiltrates, some with ground glass appearance and others with dense consolidation, without effusions or lymphadenopathy (Fig. 1). Bronchoscopy had shown normal airways, lymphocytic predominance of bronchoalveolar lavage fluid, and no evidence of alveolar haemorrhage. Lavage was negative for AFB and fungi but grew *Moraxella spp* for which she was treated with ampicillin/clavulanate intravenously without improvement. An autoimmune panel, including ANA, ANCA, Scl-70, anti-RNP, anti-SSA/SSB, and myositis autoantibodies, was negative. Urine antigen assays for *Legionella*, pneumococcus, and *Histoplasma* were negative. Serum cryptococcal antigen, beta-D-glucan assay, and fungal antibodies for endemic mycoses were negative. Due to progressive hypoxemia and respiratory distress, empirical treatment with intravenous methylprednisolone (1 g daily) was started for presumed steroid-responsive pneumonitis/interstitial lung disease, without clinical improvement after 7 days. She was transferred to our institution to undergo a diagnostic procedure. Upon initial evaluation, she was in respiratory distress with a respiratory rate of 30/min and an oxygen saturation of 94% on high-flow nasal cannula on an inspired fraction of oxygen of 0.7. She was deemed too ill to undergo thoracoscopic lung biopsy. We decided to perform bedside transbronchial cryobiopsies, for which the patient was electively

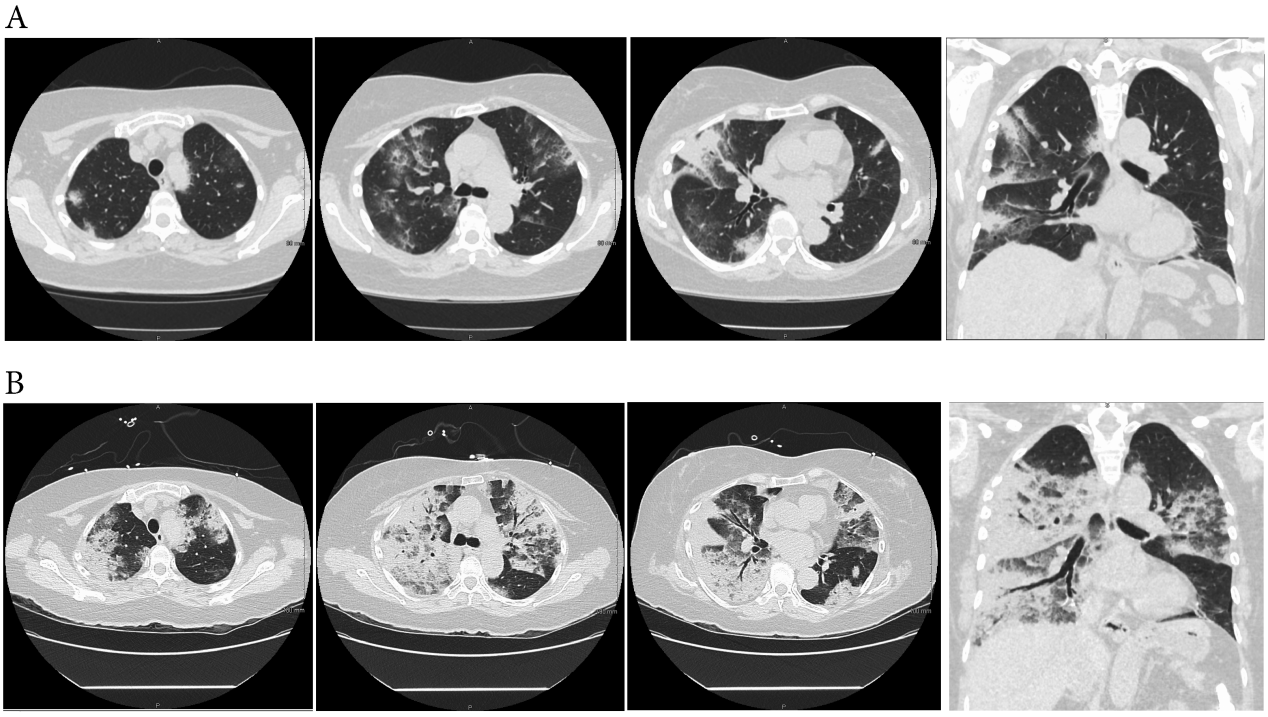

Figure 1. Computed tomographic scans of the chest obtained at the onset of symptoms (A) and three months later (B). There are multifocal patchy ground glass pulmonary infiltrates that progress, evolving into large consolidated areas with air bronchograms.

intubated and placed on mechanical ventilation. The bronchoscopic exam was only remarkable for copious clear secretions in all airways. Using a 2.4-mm ERBE cryoprobe (Turbingen, Germany), two biopsies were obtained from the right upper lobe and right lower lobe, respectively; each piece was approximately 50 mm in size. A bronchoalveolar lavage was obtained from the right middle lobe with a cloudy non-bloody return. The procedure was complicated by a right pneumothorax requiring chest tube thoracotomy with good lung re-expansion. Both lung biopsies revealed mucinous adenocarcinoma of lung origin, without any other findings to suggest a

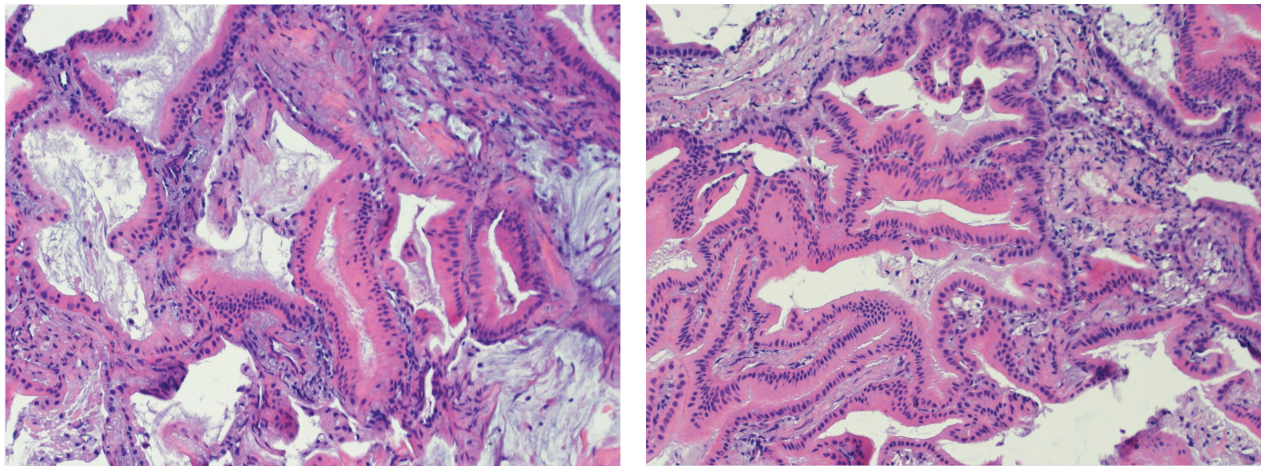

Figure 2. Transbronchial lung cryobiopsy, haematoxylin, and eosin stain, showing irregular back-to-back glands with columnar lining epithelium and mucin, diagnostic of mucinous adenocarcinoma with lepidic growth. Also note the alveoli filled with mucin.

concomitant interstitial lung disease (Fig. 2). Molecular testing was positive for KRAS mutation and negative for EGFR, ALK, and ROS1. Respiratory cultures grew *Enterobacter cloacae*, for which she received appropriate antibiotics. The patient was started on chemotherapy with paclitaxel and carboplatin with good response. Her oxygen requirements decreased markedly, and she was successfully extubated after 6 days on mechanical ventilation. She was discharged to a rehabilitation facility after 28 days.

Discussion

We describe a case of primary lung adenocarcinoma presenting as subacute pneumonia and progressing to the development of respiratory distress. Given our suspicion of interstitial lung disease, with our top two diagnoses being acute interstitial pneumonitis (AIP) and cryptogenic organizing pneumonia (COP), we chose to obtain transbronchial cryobiopsies that provide larger tissue samples and have a higher diagnostic yield compared to conventional forceps biopsies [1–7]. The diagnostic yield of transbronchial cryobiopsy is widely variable depending on the technique used and has been reported to be 51–80% [2,3,6,8]. The overall diagnostic yield at our institution using a two-scope technique is 84–89% (Cooley J, Sriprasart T, Benzaquen S, unpublished data).

Primary lung adenocarcinoma with lepidic growth mimicking pneumonia has been described extensively [9–12]. This type of malignancy has also been associated with a concomitant organizing pneumonia pattern [10].

What makes our case unique is the diagnostic use of transbronchial cryobiopsy in a patient who was too ill to undergo thoracoscopic biopsy, which is considered the standard of care for presumed interstitial lung disease [13]. Cryobiopsy specimens are large, (usually 4–8 mm) permitting the adequate evaluation of parenchymal architecture, immunohistochemical staining, and testing for molecular markers of lung cancer. Although bronchoalveolar lavage cytology has been reported to have a diagnostic yield of up to 93% in this type of lung cancer [14], our patient had negative cytology.

The extensive multilobar involvement and the mucinous histology in this case are poor prognostic indicators [15]. The median survival time after diagnosis was 10.5 months (range 1–150 months) in one large series of pneumonic-type lung adenocarcinoma [12]. Mucinous histology has been associated with a high prevalence of KRAS mutation and the absence of favourable EGFR mutations, rendering these tumours not amenable to therapy with tyrosine kinase inhibitors [16].

It is important to consider adenocarcinoma with lepidic growth in the differential diagnosis of non-resolving pneumonia. Although the yield of conventional transbronchial forceps biopsy is high in this condition, transbronchial cryobiopsy is a better option as it provides a larger tissue sample, allowing the evaluation of interstitial lung disease.

Disclosure Statements

No conflicts of interest declared.
Appropriate written informed consent was obtained for the publication of this case report and accompanying images.

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