Invasive Mucinous Adenocarcinoma Mimicking Organizing Pneumonia Associated with Mycobacterium fortuitum Infection

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Abstract

We herein report the case of a 68-year-old man diagnosed with invasive mucinous adenocarcinoma of the lungs. Chest computed tomography showed subpleural ground-glass opacity and small nodules with cavitation. A culture of the bronchoalveolar lavage fluid resulted in the detection of Mycobacterium fortuitum. The patient’s lung consolidation rapidly progressed; however, repeated bronchoscopy showed no atypical cells, thus suggesting a diagnosis of organizing pneumonia associated with M. fortuitum infection. However, the surgical biopsy specimen was diagnostic for adenocarcinoma, with no mycobacterial infection. Invasive mucinous adenocarcinoma should not be excluded in the differential diagnosis of patients with clinical features of organizing pneumonia and nontuberculous mycobacterium infection, even if a transbronchial biopsy confirms the absence of malignancy.

Key words: mucinous adenocarcinoma, organizing pneumonia, pulmonary nontuberculosis, Mycobacterium fortuitum

(Intern Med 53: 2795-2799, 2014)
( DOI: 10.2169/internalmedicine.53.2783)

Introduction

Lung cancer is one of the leading contributors to malignancy-related death worldwide. Although diagnostic procedures for detecting lung cancer have significantly improved, diagnosing adenocarcinoma with lepidic growth - i.e., invasive mucinous carcinoma, particularly that formerly classified as mucinous bronchioloalveolar carcinoma (BAC) - can be time consuming (1, 2). The most frequent symptoms of mucinous adenocarcinoma are sputum production, coughing, shortness of breath and fever. The findings of computed tomography (CT) usually include ground-glass opacity (GGO) and consolidation (3, 4). These clinical and radiographic features sometimes resemble those of bacterial pneumonia; therefore, a careful clinical and radiologic evaluation must be followed by the selection of an optimal procedure for obtaining diagnostic tissue.

We herein report a case of invasive mucinous adenocarcinoma with clinical features that mimicked organizing pneumonia in association with pulmonary Mycobacterium fortuitum infection in which repeated transbronchial biopsies showed no malignant findings, thereby resulting in a major diagnostic challenge.

Case Report

A 68-year-old man was admitted with a two-month history of coughing and sputum production. Five years earlier, he had been suspected of having interstitial pneumonia due to the detection of subpleural pure GGO in the right lower lobe with bilateral subpleural reticular opacity. At the time...
of referral to our hospital, the patient’s chest radiographs and CT scans showed subpleural consolidation with surrounding GGO in the right lower lobe (Fig. 1). He had a 10 pack-year smoking history from 20 to 30 years of age and a history of localized scleroderma, which had remained stable without treatment for many years. Upon presentation, his fingers were swollen without redness or pain due to localized scleroderma. Fine crackles were heard in the lung bases during the late inspiratory phase. The laboratory findings revealed that the Krebs von den Lungen-6 (KL-6) and surfactant protein D levels were slightly increased at 574 U/mL and 211 ng/mL, respectively. In addition, serum tumor markers were slightly elevated, with cytokeratin 19 fragment and pro-gastrin-releasing peptide levels of 4.3 ng/mL and 211 ng/mL, respectively. In addition, serum tumor markers were slightly increased, with cytokeratin 19 fragment and pro-gastrin-releasing peptide levels of 4.3 ng/mL and 211 ng/mL, respectively.

Radiologically, the lobar consolidation with ground-glass attenuation in the right lower lobe progressed. Fiberoptic bronchoscopy was therefore performed to evaluate the consolidation. A transbronchial lung biopsy (TBLB) with endobronchial ultrasonography using a guide sheath showed nonspecific findings, and a smear examination of the bronchoalveolar lavage (BAL) fluid in the right B’ segment was negative for AFB. PCR performed to detect Mycobacterium tuberculosis and Mycobacterium avium complex was also negative. Isolating M. fortuitum using a liquid mycobacterium growth indicator tube took five weeks. During this five-week period, the patient’s coughing and sputum production increased, and the subpleural, nonsegmental consolidation radiographically progressed in both lungs, from the upper to the lower lobes (Fig. 2A). Repeat bronchoscopy was thus performed in order to make a definitive diagnosis. TBLB showed many macrophages in the normal structure of the alveoli, with no granulomatous changes, fibrotic changes or atypical cells. BAL of the right B’ segment was subsequently performed because a new area of consolidation was observed in right S’. The differential cell count in the BAL fluid showed a total cell count of $3.1\times10^3$/mL, with neutrophils, lymphocytes and macrophages accounting for 3%, 16% and 81%, respectively. An examination for AFB was negative. The chest CT findings and lymphocytosis in the BAL fluid suggested a diagnosis of organizing pneumonia. M. fortuitum was considered to be a contaminant, as it was cultured at only one time point and the CT findings were not typical of pulmonary nontuberculous mycobacterium (NTM) infection at that time.

Based on the presumptive diagnosis of organizing pneumonia, the patient received steroid therapy with prednisolone at a dose of 60 mg/day for two weeks. However, the bilateral areas of consolidation on chest CT continued to increase. Furthermore, small cavities in the right middle lobe and centrilobular nodules appeared, compatible with a pulmonary NTM infection (Fig. 2B). These findings suggested a pulmonary M. fortuitum infection coexistent with organizing pneumonia. Therefore, the patient received combination therapy with corticosteroids and antibiotics for pulmonary M. fortuitum infection, including imipenem cilastatin, amikacin and levofloxacin. However, this treatment regimen was ineffective. According to the laboratory findings, the serum cytokeratin 19 fragment level increased to 122.6 ng/mL, and positron emission tomography (PET)-CT revealed a diffuse increase in the $^{18}$F-fluorodeoxyglucose uptake in the bilateral areas of lung consolidation (Fig. 2C, D).

In order to confirm the diagnosis, a surgical lung biopsy of the right S’ was performed because a surgical approach via the emphysematous and fibrotic right lower lobe, in which lung cancer was most suspected, had the potential to induce pulmonary fistula formation. The histopathological findings showed tall columnar tumor cells with basally lo-

![Figure 1. Radiological findings on admission. (A) A chest radiograph shows ground-glass opacity in the right lower lung field. (B) Chest CT shows consolidation with surrounding ground-glass opacity in the right lower lobe and bilateral subpleural reticular opacity.](image-url)
cated nuclei and abundant apical cytoplasmic mucin growing in a lepidic pattern along the surface of the alveolar wall. The tumor cells had infiltrated the areas of stromal fibrosis in some locations (Fig. 3). However, no evidence of mycobacterium infection was observed. Finally, the patient was diagnosed with pulmonary adenocarcinoma cT4N0M1a, cStage IV. Systemic chemotherapy with carboplatin AUC5 and pemetrexed was subsequently administered. However, due to this regimen’s poor effect, bevacizumab was co-administered in the second cycle. After two cycles of chemotherapy, the patient’s symptoms improved, and CT demonstrated that all of the areas of bilateral consolidation had regressed dramatically (Fig. 4).

Discussion

The histological diagnosis of invasive mucinous adenocarcinoma, formerly classified as mucinous BAC, is based on the detection of established pathologic features. The entire tumor is composed of tall columnar cells with basally located nuclei and abundant apical cytoplasmic mucin growing in a lepidic pattern along the surface of the alveolar wall. The tumor, which contains an invasive area, is diagnosed as invasive mucinous adenocarcinoma (5).

The CT findings of invasive mucinous adenocarcinoma vary widely, including consolidation, air bronchograms, and masses, which are commonly observed with lower lobe predominance. Multifocal and, sometimes, multilobar solid and subsolid nodules, which tend to be centrilobular or bronchocentric, are often observed (7, 8). The radiographic findings

![Figure 2. Chest CT and PET CT findings prior to the second bronchoscopy procedure. Chest CT shows subpleural patchy consolidation with air bronchograms spreading throughout the bilateral lungs (A), with bilateral enlarged consolidation, small cavitation and centrilobular nodules (B). PET-CT reveals a diffusely increased $^{18}$F-fluorodeoxy glucose uptake in the bilateral areas of lung consolidation (C, D).](image-url)
of organizing pneumonia also include consolidation with nonsegmental distribution, occasionally with rapid expansion (9). In the present case, the patient rapidly developed peripheral and subpleural patchy consolidation in both lungs, a finding compatible with a diagnosis of organizing pneumonia (9), but not mucinous adenocarcinoma. The mechanisms underlying how the consolidation of invasive mucinous carcinoma progressed rapidly in the present case remain unclear.

In the current case, the positive smear of sputum AFB for Gaffky 2 and the detection of \textit{M. fortuitum} in a culture of BAL fluid suggested pulmonary \textit{M. fortuitum} infection. According to the American Thoracic Society guidelines, a positive culture and specific chest CT findings are required to diagnose pulmonary NTM infection (10). The chest CT findings of pulmonary \textit{M. fortuitum} infection have been reported to be similar to those of other pulmonary NTM infections (11). In the present case, the diagnosis of active \textit{M. fortuitum} infection was inconclusive; however, nodular shadows with cavitation appeared and increased in size following corticosteroid treatment, suggesting active NTM infection. Therefore, we started treatment for \textit{M. fortuitum} infection; however, the patient did not respond to this therapy, and the surgical biopsy specimens showed no active NTM infection. Instead, most of the abnormal shadows, including the small nodules and nodules with cavitation, ultimately regressed after chemotherapy. Therefore, the findings for the right middle lobe reflected invasive mucinous carcinoma alone, not active NTM infection. These clinical features also made it difficult to make a diagnosis of invasive mucinous carcinoma.

The present case suggests that invasive mucinous carcinoma can present with findings that are clinically similar to those of organizing pneumonia as well as \textit{M. fortuitum} infection and that obtaining a definitive diagnosis using a transbronchial biopsy can be difficult in such cases. These diseases behave aggressively, and a definitive diagnosis must be established as soon as possible. Therefore, awareness of the variable symptoms and radiographic features of invasive mucinous carcinoma and the difficulty in diagnosing the condition using small biopsy specimens, with the consequent need for a careful morphologic examination, is criti-
Figure 4. Chest CT findings before and after two cycles of chemotherapy. Chest CT performed before chemotherapy shows bilateral subpleural consolidation at the level of the tracheal bifurcation (A), cardiac ventricle (B) and lower lobe (C). Chest CT performed after two cycles of chemotherapy (D-F) shows that all of the areas of bilateral consolidation had regressed.

Author’s disclosure of potential Conflicts of Interest (COI).
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References

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