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Micropapillary Lung Adenocarcinoma with Aerogenous Spread

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We experienced a case of micropapillary lung adenocarcinoma with aerogenous spread in a patient who was suspected of having interstitial pneumonia. To our knowledge, our case has not been described in the Korean literature. Our case indicates that clinicians cannot rule out the possibility of micropapillary lung adenocarcinoma with aerogenous spread in patients with a persistent presence of lesions in the lower left lung.

Key Words: Adenocarcinoma, Lung, Papillary, Pneumonia

Introduction

According to the 2011 International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society (IASLC/ATS/ERS) lung adenocarcinoma classification, based on the stages of lung adenocarcinoma, it is classified into preinvasive, minimally invasive and invasive one [1]. Moreover, it is pathologically classified into lepidic, acinar, papillary and solid lung adenocarcinoma. Then, according to the new IASLC/ATS/ERS lung adenocarcinoma classification, micropapillary adenocarcinoma was added as a new subtype [1, 2].

As compared with traditional papillary adenocarcinoma and bronchioloalveolar carcinoma, micropapillary growth patterns have been associated with an aggressive clinical course [3,4]. Micropapillary adenocarcinoma often manifests at a high stage in nonsmokers, and frequently metastasizes to the contralateral lung, mediastinal lymph nodes, bone and adrenal glands, with high mortality [3-5]. Recently, the micropapillary pattern has been reported to have worse outcomes in breast, colon, urinary tract, ovary, salivary gland and lung cancer.

Moreover, micropapillary lung adenocarcinoma has been reported to show a poor prognosis [3-5].

To date, there are few clinical and pathological reports about Korean cases of micropapillary lung adenocarcinoma with aerogenous spread. We experienced a case of micropapillary lung adenocarcinoma with aerogenous spread in a patient who was suspected of having interstitial pneumonia.

Case Report

A 66-year-old man visited us with chief complaints of cough, sputum and shortness of breath. Prior to outpatient visit, the patient had a 5-year-history of diagnosis of chronic obstructive pulmonary disease (COPD), but did not receive any treatments. In addition, the patient had a 1/3 pack/day smoking history of 30 years. But the patient had no other notable findings than hypertension on family history.

On admission, the patient presented with an acute ill-looking appearance, showing no notable findings on vital signs. On cardiac auscultation, despite normal heart sound, the patient had fine crackles in the left lower lung (LLL). In addition, the patient had no abdominal tenderness and hepatosplenomegaly.

On complete blood counts and serum biochemistry, the patient had no notable findings. On post-bronchodilator pulmonary function test, the patient had a forced expiratory volume in 1 second (FEV1)/forced vital capacity of 52% and an FEV1 of 75% (1.89 L).

On plain chest radiography, the patient had a reticular opacity with an ill-defined margin in the LLL. But the patient had no other abnormal findings such as cardiomegaly (Fig. 1A). On chest computed tomography (CT) scans, the patient had enlargements of bilateral hilar and mediastinal lymph nodes (Fig. 1B) with fibrobronchiectatic lesions in both upper lobes (Fig. 1C). This was accompanied by ground-glass opacity and multifocal lung parenchymal consolidation mainly in the LLL concurrently with multifocal emphysema with a honeycombing appearance (Fig. 1D). Based on these radiological findings, the patient was suspected of having acute exacerbation of pulmonary fibrosis accompanied by emphysema.

On mycobacterial and blood culture test, no specific pathogens were detected. But the patient was orally given antibiotics and corticosteroid (prednisone® 40 mg) based on the current tentative diagnosis. On week 1, on plain chest radiography, the patient achieved improvement in the LLL, which was accompanied by that in symptoms. The patient was discharged and followed up at the outpatient desk.

Despite continual improvements in cough and sputum, the patient did not achieve improvement in shortness of breath. On month 3, on chest CT scans, the patient had a persistent presence of honeycomb lesions in the lung periphery, accompanied by the emphysema and mediastinal lymphadenopathy (Fig. 2A&B). The patient also had a concurrent presence of increased ground-glass opacity and pulmonary consolidation mainly in the LLL (Fig. 2C&D). This was accompanied by bilateral bronchial anthracosis and right-sided bronchial stenosis on fiberoptic bronchoscopy, for which we performed bronchoalveolar lavage (BAL) fluid analysis in the posterobasal bronchus of the LLL. Thus, we detected adenocarcinoma cells from the BAL fluid. The patient therefore underwent wedge resection for the posterobasal segment of the LLL using a video-assisted thoracoscopic surgery. Intraoperatively, there was a cluster of adenocarcinoma cells with aerogenous spread showing micropapillary pattern across the posterior basal segment of the LLL (Fig. 3). Despite a lack of solid mass, desquamative interstitial pneumonia and multifocal calcification were identified in the surrounding benign tissues.

On immunohistochemistry, the patient was

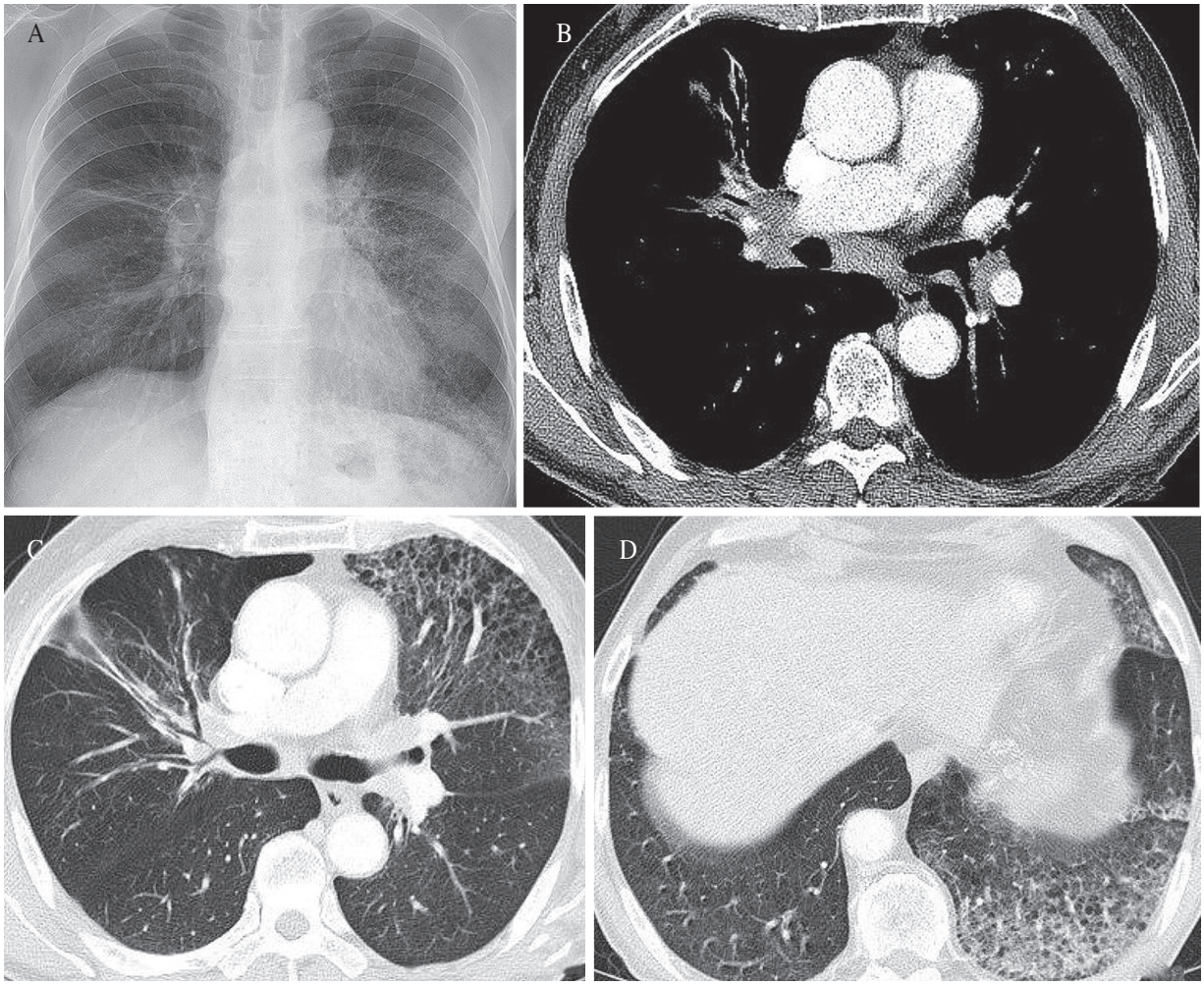

Fig. 1. (A) On plain chest radiography, the patient had a reticular opacity with an ill-defined margin in the left lower lobe (LLL). But the patient had no other abnormal findings such as cardiomegaly. (B) On chest computed tomography (CT) scans, the patient had enlargements of bilateral hilar and mediastinal lymph nodes (C) with fibrobronchiectatic lesions in both upper lobes. (D) This was accompanied by ground-glass opacity and multifocal lung parenchymal consolidation mainly in the LLL concurrently with multifocal emphysema with a honeycombing appearance.

positive for cytokeratin (CK)7, CK19, thyroid transcription factor-1 (TTF-1) and napsin A but negative for CK 20, CDX-2 and thyroglobulin. This led to a diagnosis of primary lung adenocarcinoma. The patient was also negative for both epidermal growth factor receptor (EGFR) and K-Ras mutation.

We also performed a positron emission tomography (PET)-CT. This showed an increased multifocal fluorodeoxyglucose (FDG) uptake in both mediastinal lymph nodes (Fig. 4A&B). But there were no remarkable findings or significant increase in FDG uptake, both of which are suggestive of malignancy, in the diffuse LLL lesions (Fig. 4C&D). In addition, there was no bone metastasis on the bone scan. The patient was finally diagnosed with micropapillary lung adenocarcinoma with aerogenous spread of

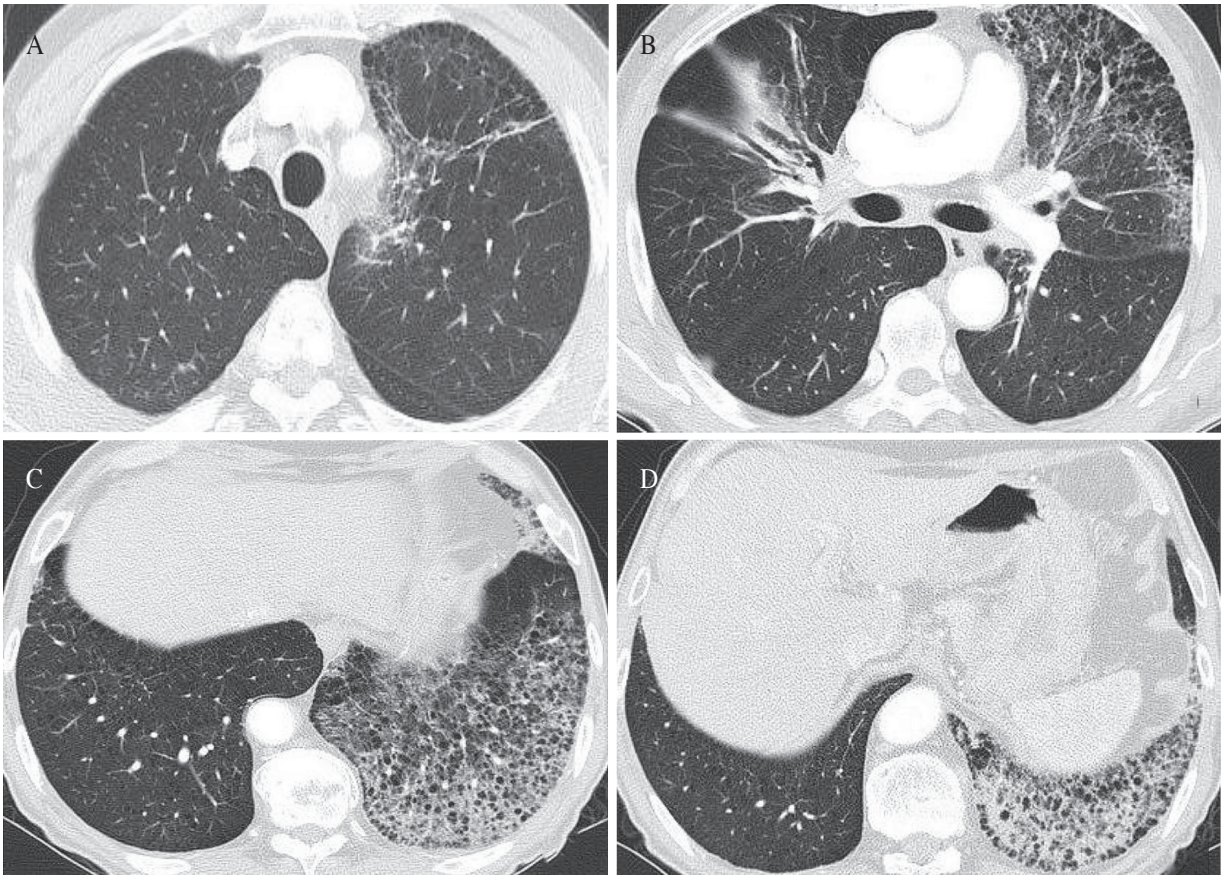

Fig. 2. On month 3, on chest CT scans, the patient had a persistent presence of honeycomb lesions in the lung periphery, accompanied by the emphysema and mediastinal lymphadenopathy (A&B). The patient also had a concurrent presence of increased ground-glass opacity and pulmonary consolidation mainly in the left lower lobe (C&D).

stage IIIB (TxN3M0). After four cycles of pemetrexed-cisplatin combination therapy followed by pemetrexed maintenance chemotherapy, the patient had a decrease in the diffuse ground-glass opacity and honeycombing appearance in the LLL on chest CT scans (Fig. 5). The patient was followed up under the pemetrexed maintenance chemotherapy.

Discussion

Micropapillary lung adenocarcinoma was first reported in 2002 by [4]. As compared with other subtypes, it and solid lung adenocarcinoma have been reported to show a poorer prognosis [5-7]. In addition, it is significantly related to the occurrence of lymph node metastasis, pleural invasion as well as lymphatic and vascular invasion [8]. Furthermore, it is also subdivided into aerogenous micropapillary component (tumor cells floating within the alveolar space) and stromal invasive one (those invading fibrous stroma) [9]. Lung adenocarcinoma cells survive independently within the alveolar space as they are shed from the basement membrane, while growing on it, which is accompanied by the initiation of aerogenous spread, and they can be detected in

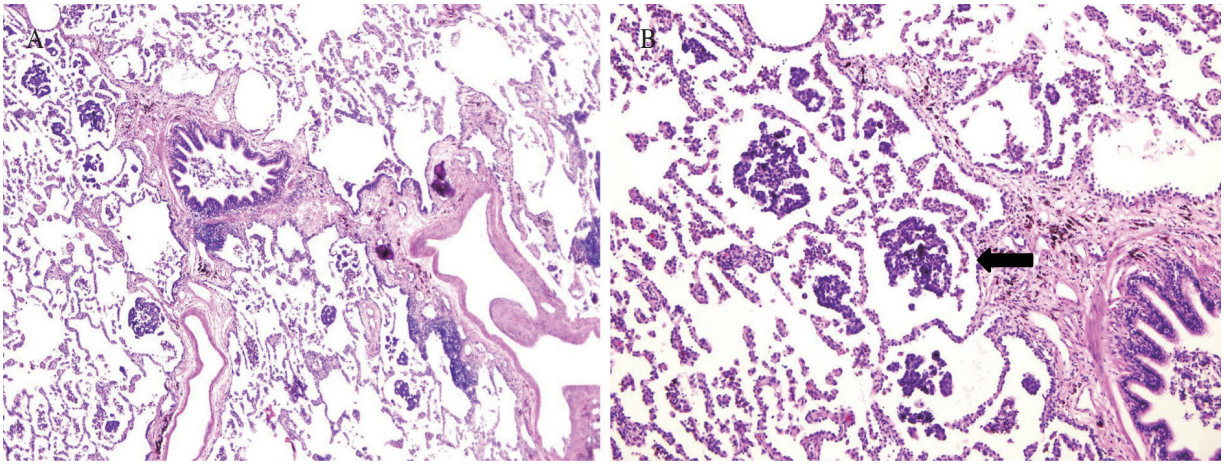

Fig. 3. (A) Micropapillary-predominant adenocarcinoma with notable aerogenous spread (A, H&E stain, × 40). (B) Aerogenous spread micropapillary-predominant adenocarcinoma characterized by floating tumor cells (black arrow) within the alveolar spaces (B, H&E stain, × 100).

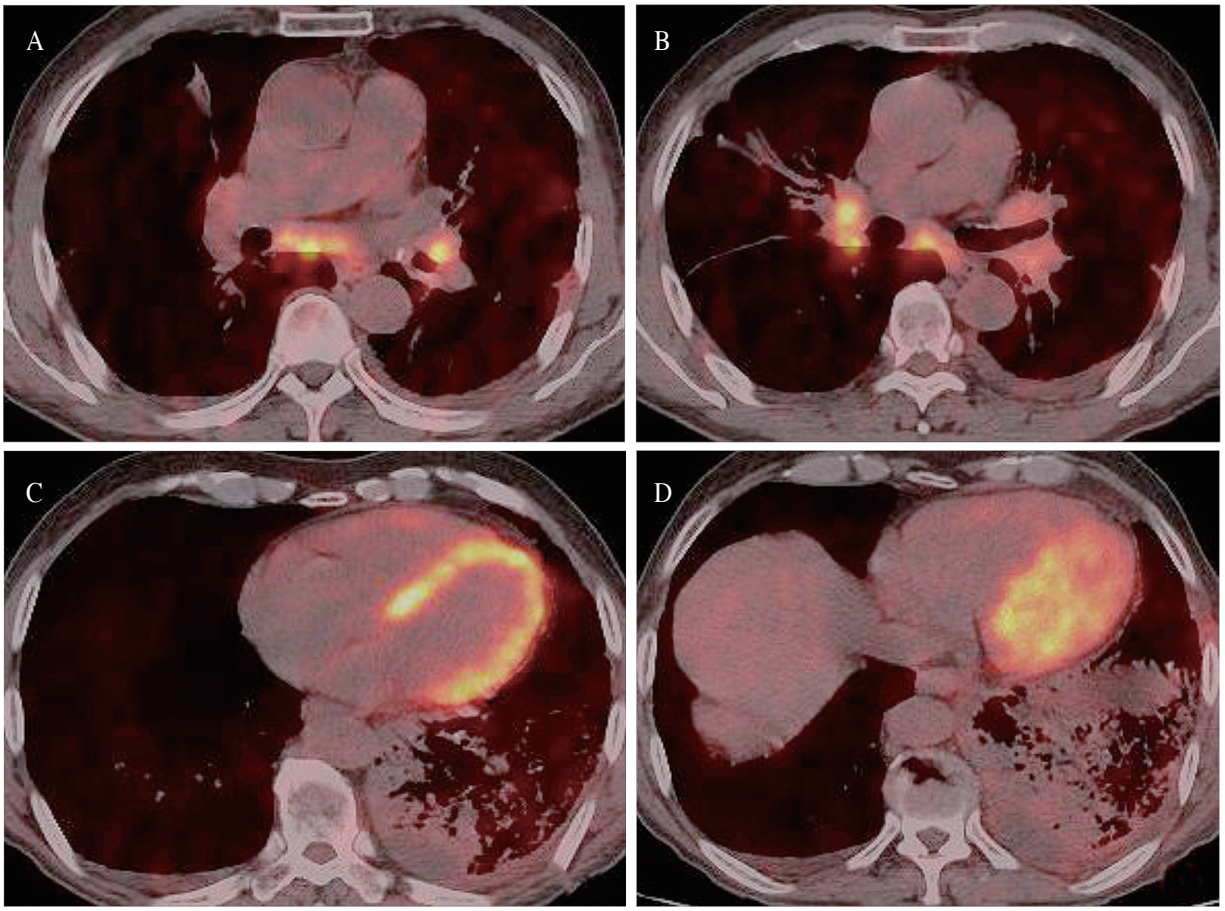

Fig. 4. A positron emission tomography (PET)-CT. This showed an increased multifocal fluorodeoxyglucose (FDG) uptake in both mediastinal lymph nodes (A&B). But there were no remarkable findings or significant increase in FDG uptake, both of which are suggestive of malignancy, in the diffuse left lower lobe lesions (C&D).

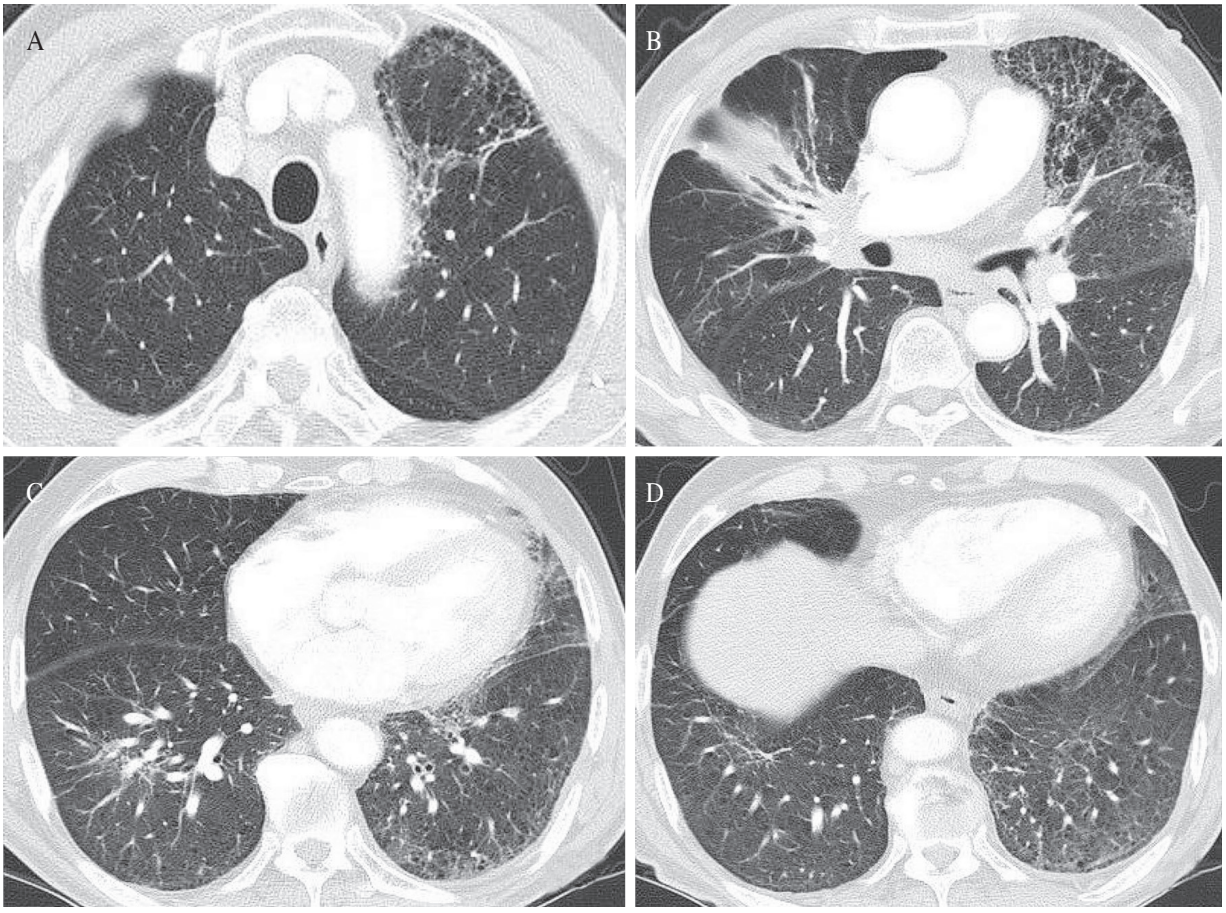

Fig. 5. After four cycles of pemetrexed-cisplatin combination therapy followed by pemetrexed maintenance chemotherapy, the patient had a decrease in the diffuse ground-glass opacity and honeycombing appearance in the left lower lobe on chest CT scans (A-D).

the BAL [10]. Even the PET-CT may fail to adequately visualize the micropapillary component with highly relevant prognostic value. It would therefore be mandatory to identify the presence of micropapillary components on preoperative or intraoperative histopathology or cytology. This may potentially have future treatment implications, as adjuvant or neoadjuvant chemotherapy may be of relevance, even in the early stages of the disease [11]. In the current case, the patient had no significant FDG uptake on PET-CT scans although there was a wide presence of tumor cells in the pulmonary parenchyma through aerogenous spread. This implies that the stage of micropapillary lung adenocarcinoma tends to be underestimated owing to insufficient visualization of tumor invasion on PET-CT scans in determining the disease stage based on FDG uptake [12].

The patient presented with symptoms such as cough and sputum, which are suggestive of pneumonia on chest radiography. On initial CT scans, the patient had pulmonary emphysema and ground-glass opacity spread across the LLL with pulmonary consolidation. With the improvement of symptoms and radiological findings, the patient was discharged after one week course of antibiotics and steroids. But the patient had a persistent presence of parenchymal

abnormalities on follow-up chest radiography. The patient therefore underwent bronchoscopy and tissue biopsy. This led to a diagnosis of micropapillary lung adenocarcinoma. Because the micropapillary component of lung adenocarcinoma may be more likely to metastasize, its presence should alert the clinician to search more carefully for metastases and have a closer follow-up on these patients. It is also important to recognize this component in evaluating a metastasis from an unknown primary site [4].

In conclusion, clinicians cannot rule out the possibility of micropapillary lung adenocarcinoma with aerogenous spread in patients with a persistent presence of the LLL lesions.

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