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Case Report

Coexistence of Multiple Pulmonary Sclerosing Pneumocytoma and Scleroderma–Rheumatoid Arthritis Overlap Syndrome: A Case Report

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Abstract

Pulmonary sclerosing pneumocytoma is a rare, low-grade pulmonary tumor observed as unilateral or bilateral multiple nodules at a rate of 4%-5%. Among the autoimmune connective tissue disorders, those most commonly associated with lung malignancies are scleroderma and rheumatoid arthritis. In this study, we report a rare case of a 55-year-old middle-aged Asian woman with slow-growing bilateral multiple pulmonary sclerosing pneumocytoma and scleroderma–rheumatoid arthritis overlap syndrome. The autoimmune disorders and pulmonary fibrosis of this case might have led to the development of PSP.

KEYWORDS: Pulmonary sclerosing pneumocytoma, bilateral multiple nodules, scleroderma-rheumatoid arthritis overlap syndrome
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INTRODUCTION

Pulmonary sclerosing pneumocytoma (PSP) defined as a rare, slow-growing, benign pulmonary tumor[1] is also known as sclerosing hemangioma, first discovered and named by Liebow and Hubbell in 1956.[2] Pulmonary sclerosing pneumocytoma is generally detected rather incidentally during routine follow-up examinations of individuals with current chronic diseases. It is observed on lung imagings as a well-circumscribed round or oval mass.[3] This tumor is mostly characterized by a homogenous and solitary nodule in a peripheral lung but unilateral or bilateral multiple nodules also appear in about 4%-5% of patients with this tumor.[4,5]

Available data suggest that scleroderma (SSc)[6] and rheumatoid arthritis (RA)[7] increase the risk of lung cancer. In the current report, a middle-aged female with bilateral multiple PSP and SSc-RA overlap syndrome is presented firstly in the literature.

CASE PRESENTATION

A 55-year-old female patient was referred to the pulmonology outpatient clinic for 3 suspicious pulmonary nodules by a rheumatologist. She had complaints of cough, sputum, and chest pain for 3 months. She was a non-smoker, but she had a 10-year biomass exposure to tandoori. Her family history was unremarkable. She had been diagnosed as SSc for 15 years and RA for 5 years and she was under hydroxychloroquine, azathioprine, salicylate for 15 years, and methotrexate for 5 years.

Also, she had been diagnosed with asthma and she was under bronchodilator and montelukast treatment. Laboratory findings showed C reactive protein of 4.2 mg/L (0-5) and a mildly decreased leukocyte count of 3.93 µL (4-10). Bilateral inspiratory rales on the lower areas of the back were auscultated.

Three nodules, the largest of which was 2.5 cm in the posterolateral right lower lobe (RLL), multiple mediastinal lymphadenopathies (LAP), and bilateral consolidations in both lower lobes were observed on the contrast-enhanced thoracic computed tomography (CT) ordered by a rheumatologist (Figure 1A, B, C). In another center, the cytopathological result of the CT-guided transthoracic core needle biopsy of the 2.5 cm nodule had been reported as a suspicious mucinous adenocarcinoma, but the pathologist suggested re-biopsy due to inadequate material.

Two years ago, the diameter of the RLL nodule was measured as 1.8 cm on CT in 2019, 2 cm 1 year ago, and it was enlarged to 2.5 cm on the final CT at admission. Additionally, a new juxtapleural nodule had been detected. Positron emission tomography (PET-CT) revealed hypermetabolic 3 nodules, bilateral consolidations, and ametabolic multiple mediastinal LAP (Figure 1D, E, F).

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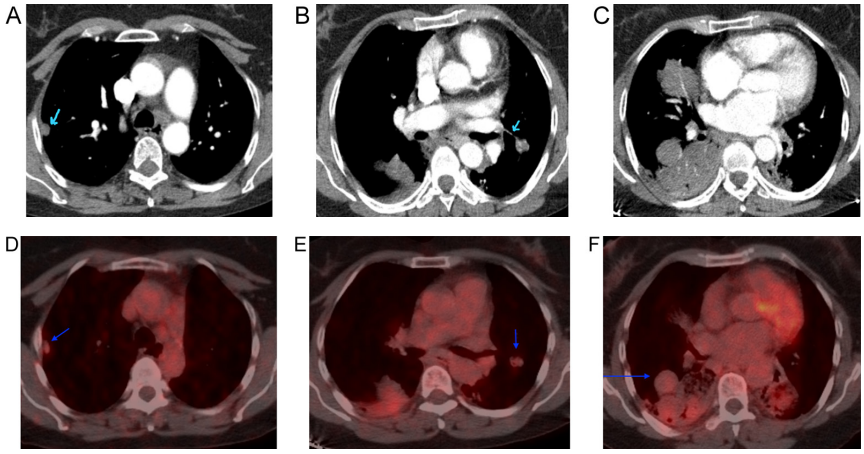


Figures 1. (A) Right lung apical juxtapleural 1.3 cm nodule (blue arrow); (B) Left lung hilar 1.5 cm nodule with overlying vessel sign (blue arrow); (C) Right lung lower lobe 2.5 cm nodule and right lung middle lobe, paracardiac, irregularly circumscribed 3 cm diameter consolidation and bilateral lung lower lobe consolidations on contrast-enhanced Thoracic CT (August 25, 2021); (D) Right apical, juxtapleural 1.3 cm nodule (blue arrow) (SUVmax:3.6); (E) Left hilar 1.5 cm nodule (blue arrow) (SUVmax:3.4); (F) Right lower lobe 2.5 cm nodule (SUVmax:4.9) (blue arrow) and right middle lobe, paracardiac, irregularly circumscribed 3 cm diameter consolidation and bilateral lower lobe consolidations (SUVmax:3.6) on PET-CT. PET, positron emission tomography; CT, computed tomography

For differential diagnosis, we re-performed CT-guided transthoracic fine-needle aspiration biopsy of the 2.5 cm nodule. Just after the procedure, the patient immediately developed hemoptysis of nearly 300-400 mL and she was hospitalized. Hemoptysis did not recur in the follow-up. Transthoracic fine-needle aspiration biopsy of the nodule's cytopathological result was reported as sclerosing pneumocytoma (see Figure 2A-B). Immune staining was positive with thyroid transcription factor-1 (TTF-1), and immune staining was negative with anti-P40 (Figure 2C). No microorganisms proliferated in the sputum culture. Acid-resistant bacillus staining and mycobacterial culture of the sputum were negative. The cytopathological results of subcarinal and right lower paratracheal lymph nodes' endo-bronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) biopsies were reported as epithelial cells, lymphocytes, macrophages, and blood elements. Polymerase chain reaction of EBUS-TBNA sample was negative for mycobacteria.

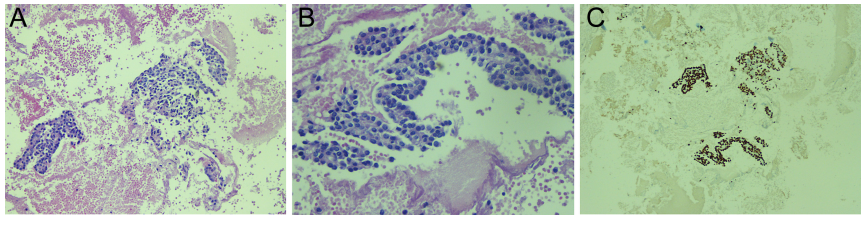
The case was discussed in the thoracic surgery council, and the nodular lesions in both lungs were decided to be operated on in 2 subsequent sessions. However, progressive bilateral infiltrative consolidations of both lungs despite antibiotic treatment were considered rheumatologic involvement, and the patient was referred to the rheumatology clinic in terms of treatment modification.

Informed consent was obtained from the patient for the use of scanning images and pathological materials included in this study.

DISCUSSION

Pulmonary sclerosing pneumocytoma generally occurs above the age of 50 and is observed 5-fold more frequently in women.[4] Asian women are particularly more vulnerable to the disease as the statistics show. Demographic features of the present case correspond to these characteristics. On CT, PSP nodule is often juxtapleural or juxtafissural in terms of location.[8] Right apical nodule of the case was juxtapleural. Although PSP is mostly asymptomatic, patients with at least 1 symptom (sputum, cough, hemoptysis, chest pain, or fever) were reported in the previous literature.[9]

Before, this tumor was considered to be originated from the vascular system. However, it is currently regarded as epithelial (pneumocyte type II) in origin and was entitled SP in the 2015 World Health Organization Classification of lung tumors.[10,11] While polygonal cells, erythrocytes, and foamy macrophages can be demonstrated in imprint or aspiration cytology, the components of solid, papillary, sclerosing, and hemorrhagic patterns can also be observed.[12] The cytological features of this tumor are suggestive of well-differentiated adenocarcinoma, which is considered to be the primary hazard in the cytological differential diagnosis of PSP. As in our case, adenocarcinoma and PSP can not be distinguished via the cytological findings. Whereas the presence of necrosis and more than 3 nuclei within single cells indicate adenocarcinoma, 2 different cellular components and the heterogeneous structure of the tumor indicate PSP.[13]



Figures 2. (A) Neoplastic epithelial cells lining around the fibrovascular core (H&E 10×10); (B) Neoplastic epithelial cells with columnar, eccentric core, eosinophilic cytoplasm around the fibrovascular core (H & E 40×10), C. Strong diffuse immune reaction in neoplastic epithelial cells with TTF-1 (20×10). H & E, hematoxylin and eosin; TTF-1, thyroid transcription factor-1.

Thyroid transcription factor-1 staining used for the immunohistochemical analysis of CT-guided transthoracic needle biopsy shows the most common positivity among vimentin, Cytokeratin 7 (CK7), Endomysial Antibody (EMA), a nuclear protein that expresses cell proliferation (Ki67).[14,15] A separate TTF-1 staining usually causes misdiagnosis because it is not specific and tends to also exist in adenocarcinomas, carcinoid tumors, and metastatic thyroid carcinomas.[16] Misdiagnosis risk may amplify in case of cytological atypia when one pattern is most prominent or where immunohistochemical analysis is uncertain due to inadequate material. Therefore, a combination of cytopathological and immunohistochemical analyses would reduce the rate of misdiagnosis, as observed in our case. Surgical enucleation and/or simple wedge resection are the main treatment approaches.[17]

It is suggested that autoimmune diseases may have a role in the carcinogenesis of the lung.[17] However, the association between autoimmune diseases and the development of cancer is still uncertain. Various hypotheses such as inflammatory processes, immunosuppressive agents, and paraneoplastic manifestations of autoimmune diseases have been proposed to define this association.[18,19] Among the connective tissue disorders, the most common association with lung malignancy is reported in SSc and RA. The incidences of malignancy in SSc are as follows, respectively: lung, bladder, hematologic, and non-melanoma skin cancers.[20] The overall pooled standardized incidence ratios of cancers in patients with RA are 3.21 (95% CI, 2.42-4.27) for Hodgkin disease, 2.46 (95% CI, 2.05-2.96) for malignant lymphoma, 2.26 (95% CI, 1.82-2.81) for non-Hodgkin lymphoma, 1.64 (95% CI, 1.51-1.79) for lung cancer and 1.23 (95% CI, 1.01-1.49) for melanoma.[21]

Scleroderma–rheumatoid arthritis overlap syndrome incidence is 4.6% in SSc patients.[22] Patients with SSc–RA overlap syndrome have long-term SSc with various organ involvement, further complicated by the development of RA, generally 1-16 years after the onset of SSc. In SSc-RA overlap syndrome, the most common conditions are: erosive polyarthritis (82%), pulmonary fibrosis (77%), esophageal involvement (55%), and cardiac manifestations (50%).[23] A 3- to 7-fold increased risk in interstitial lung disease, idiopathic pulmonary fibrosis, and the carcinogenesis of the lung have been found.[23,24] In the current case report, a rare, low-grade lung malignancy named PSP was presented. The individual presented here had the pre-condition of interstitial involvement complicated by the development of RA appearing 10 years after the onset of SSc.

In conclusion, patients with autoimmune diseases may have an increased risk of malignancy and low-grade potential malignant lesions. Patients with suspicious pulmonary nodules should be carefully evaluated, and biopsy materials should be reviewed via cytopathological and immunohistochemical analysis.

Informed Consent: Verbal informed consent was obtained from the patient who agreed to take part in the study.

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