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Case Report

Diffuse pulmonary meningotheliomatosis: A case report

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ABSTRACT

A 57-year-old female presented with chest discomfort and exertional dyspnea but no other respiratory symptoms or history of malignancy. Chest CT revealed multifocal centrilobular nodules with ground-glass opacity in both lungs. Thoracoscopic wedge resection was done, and histological examination confirmed interstitial meningothelial-like nodules, consistent with diffuse meningotheliomatosis. The patient was discharged without complications and showed no disease progression on follow-up CT at 3 months, maintaining stability during 6 months of outpatient observation. Diffuse pulmonary meningotheliomatosis is an exceedingly rare condition, but this may be one of the causative etiologies in patients with diffuse bilateral pulmonary nodules.

1. Introduction

Diffuse pulmonary nodules present a wide range of diagnoses, spanning multiple benign tumors, malignancies, autoimmune diseases, and infections. Among these possibilities, diffuse pulmonary meningotheliomatosis (DPM) stands out as extremely rare, characterized by the presence of multiple minute meningothelial-like nodules (MPMNs) in both lungs. Here, we have meticulously examined the clinical course and diagnostic process of the DPM case, aiming to shed light on considerations relevant in actual clinical settings. Furthermore, by demonstrating the feasibility of surgical diagnosis and reviewing existing literature, we endeavor to contribute to enhancing understanding of this rare condition.

2. Case report

A 57-year-old female patient without underlying disease, except for dyslipidemia and no history of malignancy, presented to the clinic complaining of chest discomfort that had begun several months prior. The patient reported mild dyspnea on exertion corresponding to mMRC grade 1 but denied other respiratory symptoms such as coughing or producing sputum. There was no history of TB or any known exposure to TB patients. Also, there was no recent history of aspiration. She had never smoked and had no occupational or environmental exposures that could predispose her to respiratory disease.

On physical examination, vital signs including temperature were within normal limits, and the oxygen saturation on room air was 99 %. Basic blood tests including complete blood count (CBC), C-reactive protein (CRP), and electrolytes were all within normal ranges, and serologic markers for autoimmune diseases including antinuclear antibody (ANA), anti-neutrophil cytoplasmic antibody (ANCA), and rheumatoid factor (RF) were negative. PPD skin test was negative. Pulmonary function tests demonstrated normal

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spirometry with a forced vital capacity (FVC) of 2.8L(88 % predicted) and forced expiratory volume in 1 s (FEV1) of 2.28L (93 % predicted). The diffusion capacity was also 101 % of the predicted value, at 18.1 ml/min/mmHg.

On chest CT scans, ill-defined multifocal centrilobular nodules with ground-glass opacity (GGO) were observed in both lungs (Fig. 1). The distribution was irregular, but predominantly located in the dependent portion and peripheral areas, with nodule sizes ranging from 1 to 7mm. There was no significant enlargement of lymph nodes in the mediastinum or hilum. Except for this diffuse lesion, no other remarkable findings suggestive of inflammatory conditions, infections, or malignancies were observed on the chest CT and abdominal-pelvic CT.

A video-assisted thoracoscopic surgery(VATS) wedge resection of the right upper lobe (RUL) and right lower lobe (RLL) was performed for histological examination. In the pathology examination, the presence of interstitial meningothelial-like nodules was noted (Fig. 2). Additionally, immunohistochemical staining showed positivity for epithelial membrane antigen (EMA) and progesterone receptor (PR), as well as membranous staining for Pan-TRK, while CK (cytokeratin), CD1a, and HMB45 showed negativity. Based on these findings, a diagnosis of diffuse meningotheliomatosis was established.

The patient was discharged without complications on post-operation day 4. Follow-up observation via chest CT three months later revealed no evidence of disease progression (Fig. 3). The patient has been undergoing outpatient follow-up for six months without any clinical symptom changes or disease progression, without any specific treatments administered.

This study was reviewed and approved by the institutional review board of Inha University Hospital, and the requirement for informed consent was waived (IRB no.2024-03-030).

3. Discussion

Minute pulmonary meningothelial-like nodules (MPMNs) were first described in 1960 based on morphologic features as "Chemodectomas" [1]. Subsequent ultrastructural and immunohistochemical analyses revealed similarities with meningothelial cells, leading to their designation as MPMNs [2]. These are benign lesions primarily observed incidentally in surgically resected lung specimens, ei-

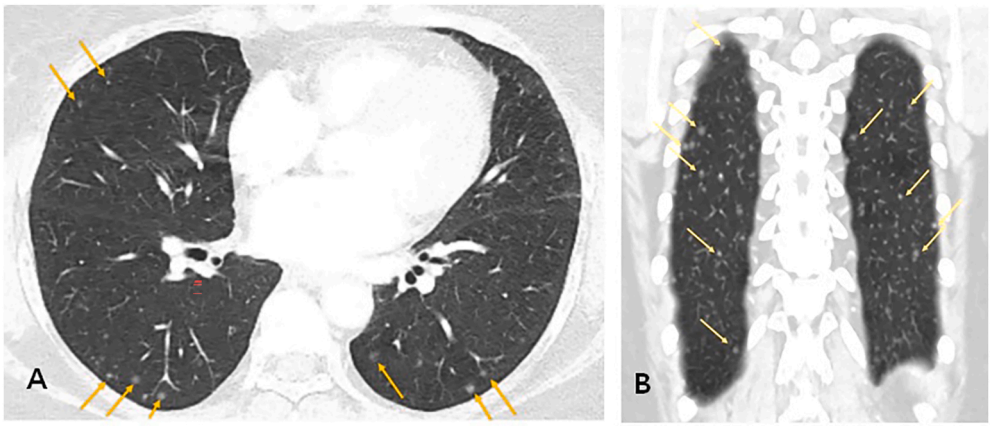

Fig. 1. Diffuse multifocal centrilobular nodules on Chest CT. (A: Axial view, B: Coronal view) Some nodules are indicated by yellow arrows. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

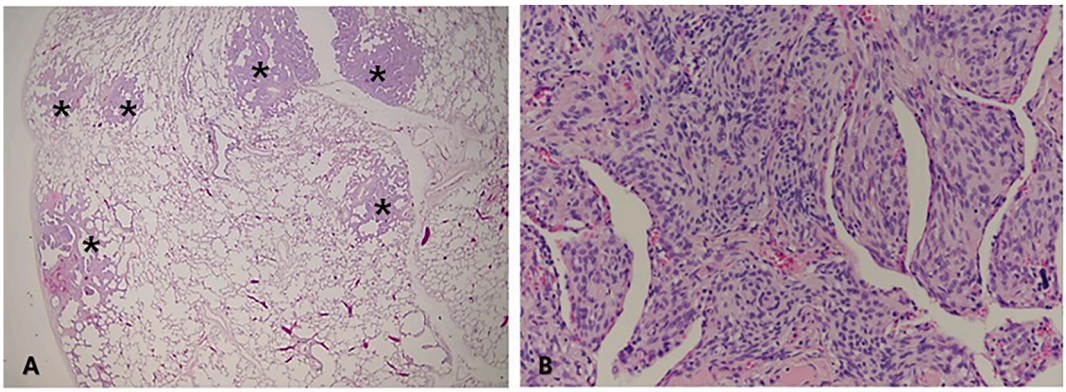

Fig. 2. A: Microscopic view at 12x magnification with HE (Hematoxylin and eosin) staining, ∗ indicates multiple meningothelial-like nodules. B: Microscopic view at 200x magnification with HE staining.

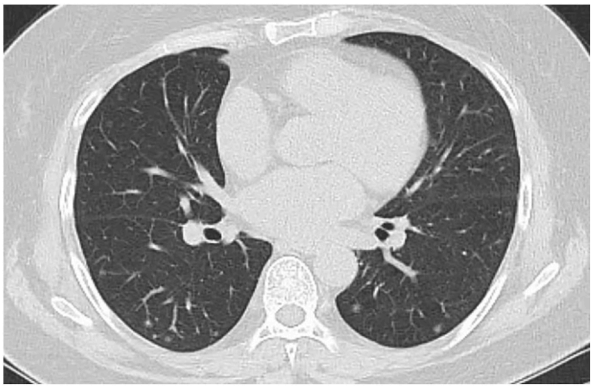

Fig. 3. Chest CT follow-up at 3 months, Diffuse multifocal nodules without significant change.

ther as single or multiple nodules [3]. Among them, the diffuse spread of MPMNs in bilateral lung constitutes a rare condition known as DPM [3,4].

DPM is an extremely rare condition, and its pathophysiology remains unclear. Based on several case reports and literature reviews, it appears to be more prevalent in females. Symptoms are typically nonspecific or asymptomatic, such as mild dyspnea or cough, as observed in this case. There is no specific treatment documented in the literature, and all reported patients have survived during the follow-up period, maintaining a stable condition [4–10].

The diagnosis of this condition typically begins with identifying bilateral micronodules on chest CT scans and excluding other diseases through differential diagnosis. In this case, the patient showed no elevation in infection markers on blood tests, indicating a very low likelihood of acute bacterial infection. Miliary TB was considered, but the absence of typical symptoms such as fever, anorexia, and weight loss made this diagnosis less likely. Blood tests for autoantibodies, including ANCA, were conducted to rule out vasculitis and other autoimmune diseases, all of which returned negative results. Pulmonary toxocariasis, another potential cause of nodular lung lesions, was also considered but deemed unlikely due to negative blood test results and no changes observed on CT scans performed two months apart. Considering the possibility of malignancy, such as lung metastasis, chest CT and abdominal-pelvic CT scans were performed, but no primary malignancy was detected.

Based on these findings, a tissue biopsy was deemed necessary. Due to the small size of individual nodules and to ensure diagnostic accuracy, a surgical biopsy was chosen. While some studies have attempted transbronchial biopsy, the small and random distribution of lesions often leads to inconclusive results, necessitating subsequent surgical biopsy [10–13]. Definitive diagnosis is achieved through immunohistochemical staining of the obtained tissue. Advances in minimally invasive surgical techniques, such as video-assisted thoracoscopy, have lowered the barriers to surgery, making early consideration of surgical diagnostic methods appropriate for patients with low surgical risk profiles.

This study presents detailed clinical features and diagnostic processes of a case patient, which can aid in formulating diagnostic strategies in actual clinical scenarios. However, as a case report, there are limitations in generalizing the diagnosis and clinical symptoms of the disease. In this instance, the patient did not produce sputum, thus precluding tests that rely on sputum samples. However, if the patient had exhibited symptoms such as sputum production and anorexia, prioritizing differential diagnosis for TB through TB PCR or AFB smear tests would have been warranted. Additionally, depending on the patient's medical condition, less invasive procedures such as CT-guided biopsy might be considered, despite potentially lower diagnostic accuracy in cases with higher surgical risks.

In this study, the patient's pre-diagnostic screening included cerebral MRI, which excluded intracranial meningioma. Based on studies suggesting histological similarities and genetically similar mechanisms of occurrence between minute pulmonary meningothelial-like nodules (MPMNs) and CNS meningiomas, cerebral examination may be necessary. Melocchi et al. found unknown meningiomas in three out of four patients suspected of having DPM in their case series [4]. Therefore, consideration should be given to the differential diagnosis of metastatic meningioma with DPM features. However, uncertainties still remain regarding the pathogenesis of this entity and whether the likelihood of meningioma development is higher in patients with DPM.

So far, the prognosis of DPM has been reported as favorable [4]. However, Suster et al. pointed out in their paper reporting on five cases of DPM that three cases had a past medical history of cancer [5]. Cases of cancer co-occurring with DPM have also been reported in other case studies [8,11,14]. Although the reported cases are limited, making it difficult to study statistical correlations, Mizutani et al. suggested that considering the possible correlation between MPMNs and malignancy [15], further research is needed to investigate the co-occurrence or potential development of malignancy in DPM patients.

In conclusion, DPM may be one of the underlying conditions in patients with diffuse bilateral pulmonary nodules. Further research is necessary to explore its association with other malignancies or intracranial meningiomas, as well as to understand clinical symptom management.

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Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

IRB was approved by the institutional review board of Inha University Hospital, and the requirement for informed consent was waived (IRB no.2024-03-030)

Authorship

The International Committee of Medical Journal Editors (ICMJE) recommends that authorship be based on the following four criteria.

1 Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2 Drafting the work or revising it critically for important intellectual content; AND
3 Final approval of the version to be published; AND
4 Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

All listed authors meet all four criteria for authorshipReferences

CRediT authorship contribution statement

Su Ji Oh: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Jun Hyeok Lim:** Resources, Methodology, Investigation. **Lucia Kim:** Visualization, Resources, Methodology. **Young Sam Kim:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Formal analysis, Conceptualization.

Declaration of competing interest

No conflict of interest exists.

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