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【 CASE REPORT 】

A Rare Case of Diffuse Bilateral Minute Pulmonary Meningothelial-like Nodules Increasing over the Short Term and Resembling Metastatic Lung Cancer

Daiki Murata[1], Yoshiaki Zaizen[1,2], Saeko Tokisawa[1], Goushi Matama[1], Tomonori Chikasue[3], Yuuya Nishii[1], Shuuhei Ohno[1], Kenji Tsumura[1], Masaki Tominaga[1], Junya Fukuoka[2], Kiminori Fujimoto[3] and Tomoaki Hoshino[1]

Abstract:
A 54-year-old woman was referred to our hospital because computed tomography (CT) revealed multiple lung nodules during a health checkup. The nodules were up to 5 mm in diameter and randomly distributed in both lungs, appearing ring-shaped. No clinical symptoms were present. However, the nodes proliferated, and multiple lung metastases could not be ruled out, so a biopsy was performed to establish a diagnosis. She was diagnosed with minute pulmonary meningothelial-like nodules (MPMNs), and her condition had not deteriorated at the latest follow-up. Although rare, MPMNs can proliferate for a short time, but a biopsy to exclude malignant causes is essential.

Key words: minute pulmonary meningothelial-like nodules, pulmonary chemodectoma, increasing nodules, mimicking metastatic lung cancer

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Introduction

Minute pulmonary meningothelial-like nodules (MPMNs) are rare pulmonary nodules that are histologically composed of small nests of spindle cells with eosinophilic cytoplasm located within the interstitium of the lung (1-5). Conventionally, the nodules are usually found incidentally at autopsy or in surgical specimens, but recently, they have been found on radiological examinations with the increased use of thin-section computed tomography (CT) (1, 6). The lesions are most often single or few, and diffuse bilateral lesions are extremely rare (1, 6).

The clinical course of MPMNs is benign, and the number of nodules usually does not increase (1, 7, 8). However, it is often clinically important to distinguish diffuse bilateral cases from malignant disease, since radiographic findings mimic metastatic lung cancer (1, 7-9).

We herein report a case of diffuse bilateral MPMNs, in which the number of nodules increased in the short term.

Case Report

A 54-year-old woman was referred to our hospital for the investigation of multiple lung nodules on CT that were incidentally found during a medical checkup. The patient had a very short smoking history (only one year) and was never involved in any work that required her to inhale dust. The patient had cholelithiasis and hypercholesterolemia, but denied any other symptoms. Other physical examination results did not reveal any abnormalities. The patient had no respiratory failure during the pulmonary function test. Biochemical examination results were normal, including tumor markers and indications for collagen disease (Table). Chest

[1]Division of Respirology, Neurology and Rheumatology, Department of Medicine, Kurume University School of Medicine, Japan, [2]Department of Pathology Informatics, Nagasaki University Graduate School of Biomedical Sciences, Japan and [3]Department of Radiology, Kurume University School of Medicine, Japan
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Correspondence to Yoshiaki Zaizen, zaizen_yoshiaki@med.kurume-u.ac.jp

Table. **Blood Test**

WBC	6.8×10^3 /μL
Neut	70.6 %
Ly	22.7 %
Eo	2.9 %
Baso	0.3 %
Mono	3.5 %
RBC	5.08×10^6 /μL
Hb	14.4 g/dL
Plt	312×10^3 /μL
Na	141 mEq/L
K	4.1 mEq/L
Cl	102 mEq/L
AST	25 U/L
ALT	29 U/L
LDH	210 U/L
T-Bil	0.6 mg/dL
BUN	9 mg/dL
Cre	0.51 mg/dL
UA	4.8 mg/dL
TP	8.2 g/dL
Alb	4.7 g/dL
CRP	0.14 mg/dL
ANA	40 nX
Anti-Scl70	1.6 U/mL
Anti-SSA	<1.0 U/mL
Anti-SSB	<1.0 U/mL
Anti-ARS	<1.0 U/mL
Anti-CCP	<5.0 U/mL
RF	7 IU/mL
MPO-ANCA	<1.0 U/mL
PR3-ANCA	<1.0 U/mL
IGRA	Negative

WBC: white blood cell, Neut: neutrophil, Ly: lymphocytes, Eo: eosinophils, Baso: basophils, Mono: monocytes, RBC: red blood cells, Hb: hemoglobin, Plt: platelet, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, T-bil: total bilirubin, BUN: blood urea nitrogen, Cre: creatinine, UA: uric acid, TP: total protein, Alb: albumin, CRP: C-reactive protein, ANA: antinuclear antibody, anti-Scl70: anti scleroderma 70 antibodies, anti-ARS: anti aminoacyl-tRNA synthetase antibodies, anti-SSA: anti Sjögren syndrome A antibodies, anti-SSB: anti Sjögren syndrome B antibodies, anti-CCP: anti cyclic citrullinated peptide antibodies, RF: rheumatoid factor, MPO-ANCA: myeloperoxidase-antineutrophil cytoplasmic antibody, PR3-ANCA: proteinase-3-antineutrophil cytoplasmic antibody

radiography revealed no evidence of abnormalities.

Thin-section chest CT confirmed the presence of innumerable disseminated minute nodules measuring up to 5 mm in diameter. The nodules were randomly distributed throughout both lungs, and there were no significant differences between the lobes. Some of the nodules showed central lucency and appeared ring-shaped (Fig. 1).

Although contrast-enhanced CT of the head and abdomen showed no evidence of malignancy, we were unable to completely rule out metastatic lung cancer of unknown primary lesions. To exclude metastatic neoplasms and make a definitive diagnosis, the patient underwent a transbronchial lung biopsy. Bronchoscopy revealed no visible airway abnormalities, and the collected lung specimens revealed no malignant cells. Although no definitive diagnosis was made, the patient was followed up considering the possibility of benign disease.

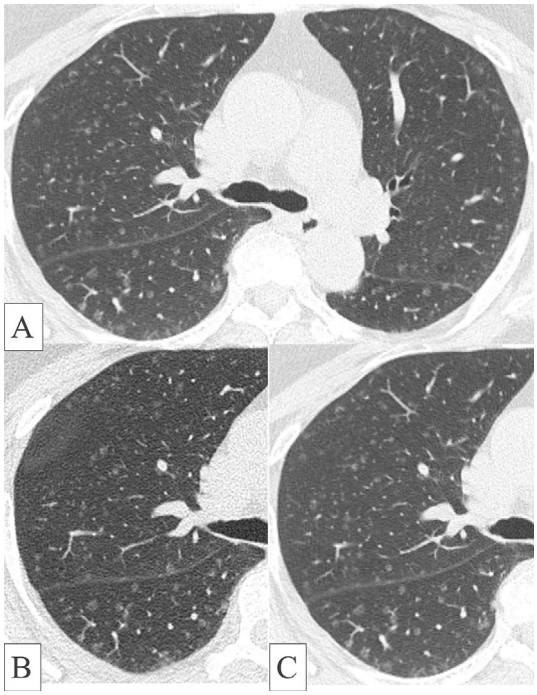

Figure 1. **Chest computed tomography (CT) showed diffuse bilateral minute ground-glass opacities on initial consultation. The nodules were randomly distributed, measuring up to 5 mm in diameter, and some had central lucency (A, B). The number of nodules increased four months later (C).**

Four months after the first visit, she did not show any symptoms, and her condition was generally stable. Her chest radiograph and spirometry results were unchanged. However, the number of nodules further increased on follow-up chest thin-section CT. Numerous new ground-glass nodules appeared throughout the lungs, and the diameter of the new nodules was less than 5 mm, but many of them were smaller than the pre-existing lesions. Pre-existing nodules showed no remarkable changes in size or morphology. Metastatic lung cancer was strongly suspected because of the increase in the number of nodules over a short period. A multidisciplinary discussion was held, and tissue confirmation was considered necessary for a definitive diagnosis. Therefore, the patient underwent a surgical lung biopsy. Surgical lung biopsies were performed from the right middle lobe S4 and right lower lobe S6.

Histological findings showed spindle-shaped cells with lightly acidic vesicles, and round nuclei proliferated along the alveolar septum. Immunohistochemical staining of the cells was negative for cytokeratin AE1/AE3 and positive for vimentin and progesterone receptors (Fig. 2). Based on these histopathological findings, the patient was diagnosed with MPMNs.

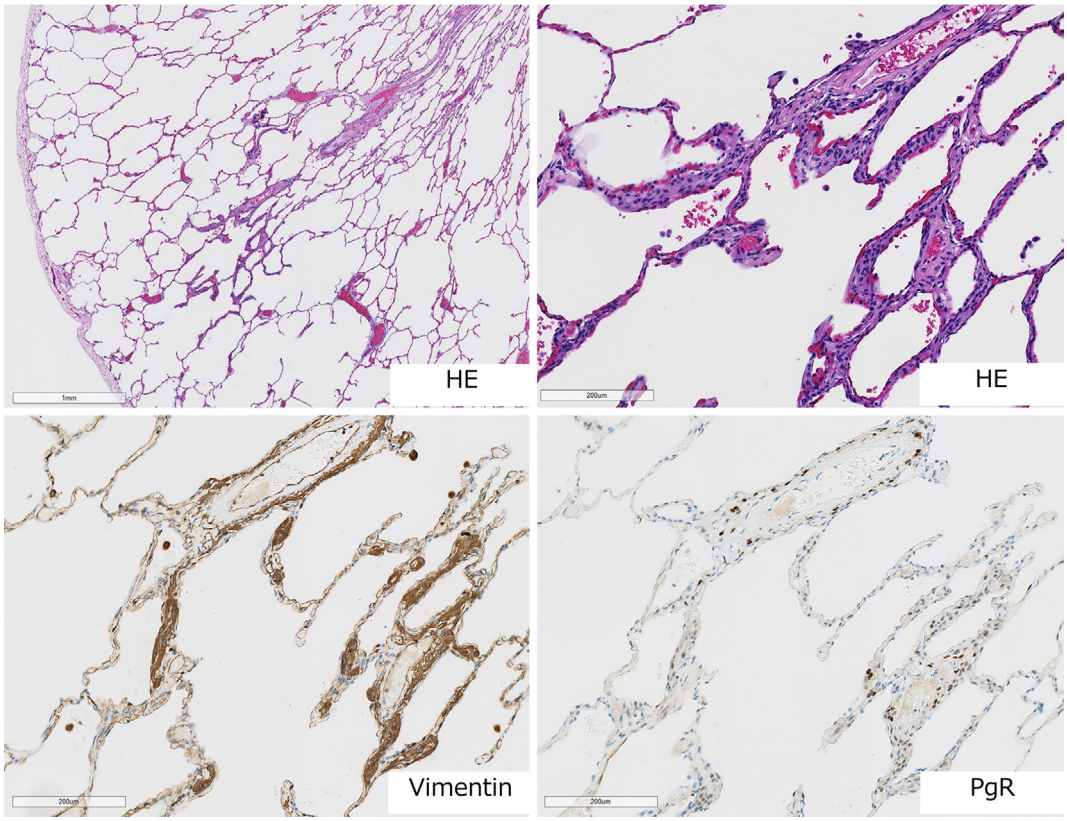

Figure 2. **Pathological findings. Spindle-shaped cells with lightly acidic vesicles and round nuclei proliferated along the alveolar septum. Immunohistochemical staining of the cells was positive for vimentin and progesterone receptors.**

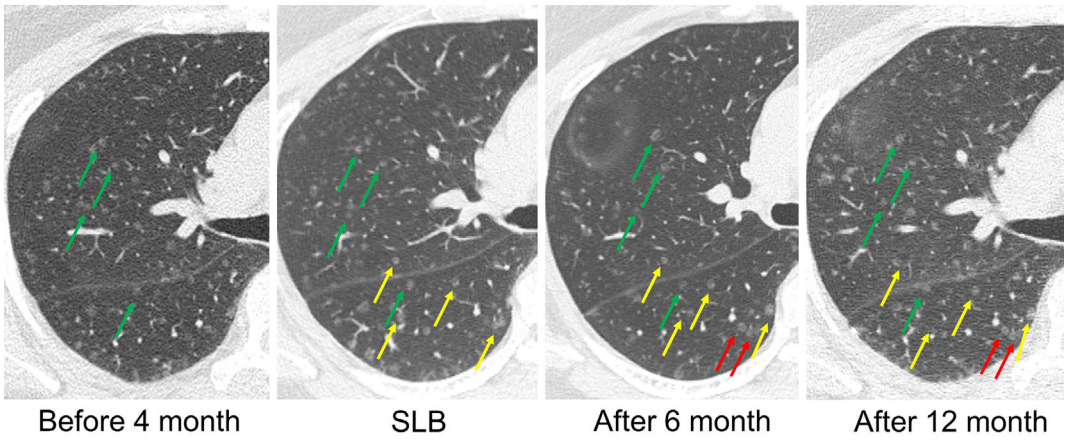

Figure 3. **Chest CT confirmed the presence of minute nodules four months prior to a surgical lung biopsy (SLB; green arrows). At the time of the SLB, an increased number (yellow arrows) and slight enlargement of some nodules (green arrows) were observed. Six months after the SLB, the size of the nodules remained unchanged (green and yellow arrows), but the number of nodules increased (red arrows). Twelve months after the SLB, there was no marked increase in the number or size of nodules (green, yellow and red arrows).**

At six months after the diagnosis, an increase in nodule numbers and slight enlargement of the relative sizes were observed on thin-section CT. Twelve months after the diagnosis, CT showed that the nodules were unchanged in number and size (Fig. 3). The patient remained asymptomatic, pulmonary function test results were normal, and no treatment was required.

Discussion

MPMNs were initially described as pulmonary chemodectomas by Korn et al. in 1960 (2) and officially named

meningothelial-like nodules by Gaffey et al. in 1988 (3). The reported incidence varies in the literature and occurs in 0.07% to 9.5% of cases (2-4, 10). In recent reports with a relatively large number of cases, MPMNs were identified in 121 of 1,724 (7%) pulmonary resections by Mizutani et al. (6), 69 of 500 (13.8%) surgical biopsies, and 12 of 25 (48%) lobectomies by Mukhopadhyay et al. (5). Nodules are observed more frequently in women with underlying chronic lung disease than men (4, 6). Furthermore, 10% of patients have complicated lung adenocarcinoma (4, 6). Most patients are asymptomatic and do not require treatment (1, 5, 7). It should be noted that MPMNs are rare and benign diseases but are prone to being complicated with malignant tumors.

MPMNs have generally been reported to not increase the number of lesions (1), but in our case, chest thin-section CT showed that the number of nodules increased in a short period of three months. To our knowledge, only two cases with an increased number of nodules have been reported (9, 11). One particular case reported by Kuroki et al. showed an increase in nodules in the first six months, but the nodules had not increased on further CT performed six months later (9). These cases showed no other differences from previous reports, and the patients were asymptomatic and had a good prognosis. In our case, the pre-existing lesions showed few changes on imaging when new nodules appeared.

It has been suggested that female hormones (6, 12) and genetic background (12-14) may be involved in the development of MPMNs. Our case was a woman who was perimenopausal but not yet menopausal, so female hormonal fluctuations or genetic background may have been involved in the proliferation of MPMNs. Thus far, MPMNs have usually been found retrospectively during autopsy or in surgical specimens (2-6). Recently, with the development and increased use of CT, MPMNs have often become a clinical problem (2, 7-9, 11). The exclusion of malignant disease is important when encountering diffuse bilateral ground-glass nodules in both lung fields, and particularly in cases where lesions increase, biopsies should be performed to rule out malignant disease.

Imaging findings are important in patients with MPMNs because most are asymptomatic or present with non-specific symptoms, and a clinical examination is unremarkable (5, 7-9). Thin-section CT is especially important for patients with MPMNs, as lesions cannot always be detected by chest radiography, as in the present case (7). CT findings of MPMNs usually show single or multiple tiny nodules with ground-glass attenuation (1, 6, 8, 9, 11). Multiple cases account for 40% of MPMNs, but their average number of nodules is approximately 4, and diffuse bilateral cases are extremely rare (1, 6). Nodules can occur in all pulmonary lobes, and the frequency of incidence is not markedly different between lobes (6). Its distribution is centrilobular and tends to be peripheral, involving the outer third of the lung parenchyma (1, 5). The nodules usually measure approximately 5-10 mm in diameter (1). Some studies have reported that the lesions have central lucency, showing ring-shaped opacities (7, 8). The mechanisms causing these ring-shaped nodular forms are currently unclear, but it has been speculated that the extension of meningothelial cells along the alveolar septa may destroy the alveolar wall (8). The lesions show no changes in morphological characteristics (1).

In the present case, CT findings were important because the patient had no symptoms or chest radiographic findings. Thin-section CT revealed innumerable ground-glass nodules measuring up to 5 mm in diameter in both lung fields. The lesions were randomly distributed and predominantly peripheral to the lung parenchyma. There was no uneven distribution of nodules between lobes in this patient. Some of the nodules had central lucency and appeared ring-like in shape. These CT findings were typical and similar to those of previous reports. The only difference from previous reports was the increase in the number of nodules over time, which was the most important reason for excluding metastatic tumors.

We encountered a case of MPMNs that increased in number in the short term and was required to rule out metastatic lung cancers. Differentiation between metastatic lung cancers and diffuse bilateral MPMNs is extremely important for the treatment and prognosis of malignant tumors. Thus, clinicians should perform a lung biopsy to confirm a definitive diagnosis, especially if the number of pulmonary nodules increases.

The authors state that they have no Conflict of Interest (COI).

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