Minute Pulmonary Meningothelial-like Nodules : A Case Report

Kazusa SUGIURA[1)2)], Satoshi KAWAKAMI[2)]*, Mina MATSUSHITA[2)], Keisuke TODOROKI[2)]
Takashi EGUCHI[3)], Takeshi UEHARA[4)] and Yasunari FUJINAGA[2)]

1) *Department of Radiology, Nagano Municipal Hospital*
2) *Department of Radiology, Shinshu University School of Medicine*
3) *Department of General Thoracic Surgery, Shinshu University School of Medicine*
4) *Department of Pathology, Shinshu University School of Medicine*

Minute pulmonary meningothelial-like nodules (MPMNs) are traditionally identified incidentally as solitary or multiple nodules with a size of 0.1-3 mm in autopsied or resected lungs. Recently, there have been several reports of MPMNs identified as ground-glass nodules (GGNs) on computed tomography (CT), leading to surgical intervention. Here, we present a case of MPMN with a brief overview of the literature.

A 73-year-old female patient underwent CT for the evaluation of aspergilloma, and multiple GGNs were identified in the lower lobes of both lungs. One of the GGNs, as well as the aspergilloma, was resected for pathological examination and was subsequently diagnosed as MPMN. Differential diagnoses for multiple GGNs include atypical adenomatous hyperplasia, multifocal micronodular pneumocyte hyperplasia, and metastatic lung tumors. In MPMN, GGNs exhibiting ring-like structures with a central lucency are sometimes observed, which may be a characteristic feature to differentiate MPMN from other diseases. *Shinshu Med J 73 : 37—41, 2025*

(Received for publication August 27, 2024 ; accepted in revised form November 29, 2024)

Key words : minute pulmonary meningothelial-like nodules, ground-glass nodule, multiple nodules, lung, computed tomography

Ⅰ Introduction

Minute pulmonary meningothelial-like nodules (MPMNs) are small benign lesions that are incidentally found in surgical or autopsy specimens of the lung[1)]. Although their pathological features resemble that of meningothelial epithelial cells, the etiology and pathogenesis of MPMNs remain unclear. MPMNs can appear as solitary or multiple pure ground-glass nodules (GGNs) on CT, often rendering the differentiation between MPMNs and lung cancer problematic. In this report, we present a case with multiple GGNs that were incidentally detected on a chest computed tomography (CT) scan, leading to a pathological diagnosis of MPMN.

* Corresponding author : Satoshi Kawakami
Department of Radiology, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto, Nagano 390-8621, Japan
E-mail : kawasato@shinshu-u.ac.jp

Ⅱ Case Presentation

A 73-year-old female patient was referred to our institution for detailed examination of an abnormal shadow on a chest X-ray detected by her family doctor. The patient had a history of hypertension, dyslipidemia, and surgery for appendicitis and uterine fibroids. She had no respiratory symptoms and no history of smoking nor exposure to dust. Laboratory examinations showed that serum Carcinoembryonic Antigen (CEA) was 4.2 ng/mL, Sialyl Lewis-x antigen (SLX) was 40 U/mL, Pro-gastrin-releasing peptide (Pro-GRP) was 66.9 pg/mL, Squamous Cell Carcinoma antigen was 1.0 ng/mL, cytokeratin 19 fragment (CYFRA) was 1.6 ng/mL, and β-D glucan was 10.2 pg/mL, all within normal ranges.

Subsequent evaluation with chest CT revealed a cavitary mass in the segment S^3 of the right lung. The mass was suggestive of a fungus ball, while the

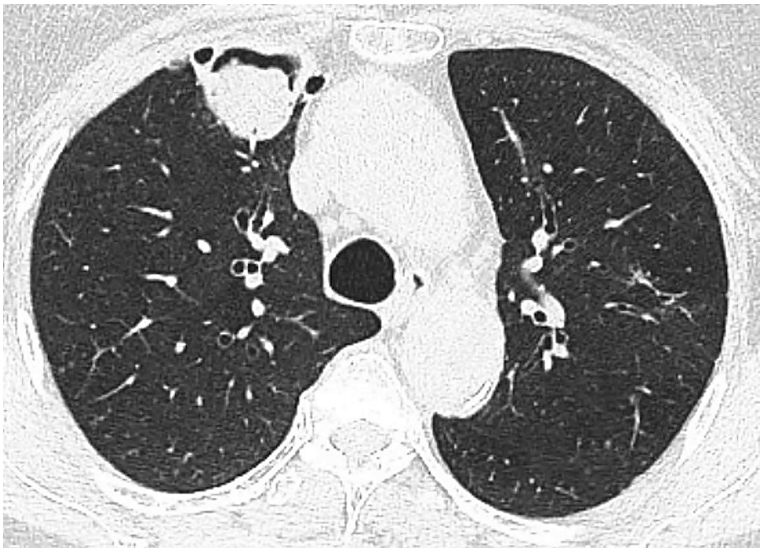

Fig. 1 Chest CT
A cavitary mass was observed in the right lung S^3.
A structure suggestive of a fungal ball was identified inside, and the meniscus sign was positive. The preoperative imaging diagnosis was aspergilloma.

meniscus sign was suggestive of aspergilloma **(Fig. 1)**. Additionally, a large number of GGNs, ranging from 2 to 5 mm in size, were identified predominantly in the lower lobes of bilateral lungs, more pronounced dorsally than ventrally, and distributed in the subpleural area. As shown in **Fig. 2**, some of these lesions exhibited central lucency.

As a result, we surgically resected the cavitary mass in the right upper lobe with a suspicion of aspergilloma. Simultaneously, we partially resected the right lower lobe to extract pathological information of the multiple GGNs, due to suspicion of atypical adenomatous hyperplasia, carcinoma in situ, or multifocal micronodular pneumocyte hyperplasia (MMPH).

The cavitary mass of the right upper lobe was macroscopically found to contain a fungus ball. Histopathologically, Grocott-stain showed Y-shaped branching hyphae stained to black, consistent with Aspergillus, thereby confirming our initial diagnosis of aspergilloma. The partial resection specimen from the right lower lobe macroscopically showed a 3-mm white nodule, and the subsequent histopathological examination revealed a proliferation of short spindle-shaped cells within the alveolar septal stroma, with no nuclear atypia nor mitosis. Although the lesion had no encapsulation, it was relatively well-defined. Immunohistochemical staining was negative for cytokeratin AE1/AE3, smooth muscle actin, desmin, synaptophysin, chromogranin A, HMB45, and MART1; weakly positive for epithelial membrane antigen; and positive for progesterone receptor (PgR). Consequently, our findings led to the diagnosis of MPMN **(Fig. 3)**.

Ⅲ Discussion

MPMNs are considered benign proliferative lesions resembling meningothelial epithelial cells occurring in the pulmonary interstitial tissue. In 1960, Korn initially reported these lesions as pulmonary chemodectomas resembling pulmonary chemoreceptors[2]. Subsequent immunohistochemical and electron microscopic studies by Gaffey in 1988 identified similarities with meningothelial cells, thereby explaining their definition as "meningothelial-like nodules"[3]. Although these lesions are speculated to arise from pluripotent cells or heterotopic remnants of meningothelial cells, the exact etiology and pathogenesis still remain unclear. Niho's clonality analysis of 11 MPMN lesions suggested that MPMNs are multiclonal cellular aggregates, indicating their reactive rather than neoplastic nature[4].

MPMNs predominantly affect women in their 60s to 70s[1)5)]. These lesions are progesterone receptor-positive, potentially implicating hormonal involvement in their higher incidence among females. Our patient was 73 years old, which is a common age of MPMN onset.

MPMNs have been reported as very small lesions (0.1-3 mm) incidentally found in surgically resected lungs or autopsy lungs. The frequency of these le-

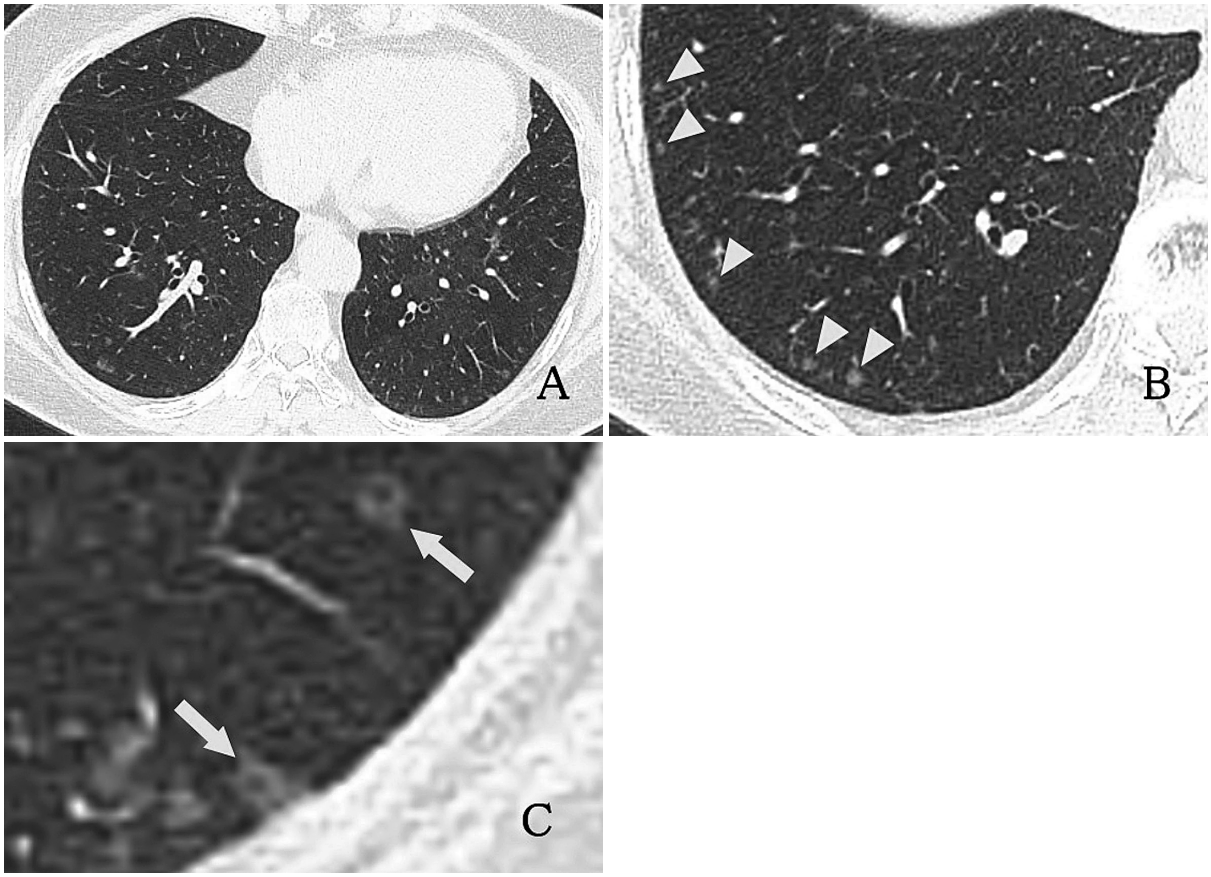

Fig. 2　Chest CT

Multiple 2–5 mm GGNs were observed (A) predominantly in the lower lobes of both lungs. These nodules were more prevalent dorsally than ventrally, with a notable subpleural distribution (B, arrow heads). Some of the lesions exhibited ring-like structures with a central lucency (C, arrows).

sions varies in the literature, ranging from 0.3 %–0.5 % in autopsy lungs and 1.1 %–9.5 % in surgically resected lungs. A previous study examining 1,724 cases of surgical lung resections reported an incidence of 7 % for MPMN[1]. The difference in frequency between autopsy and surgically resected lungs is attributed to underlying disease differences. It has been noted that MPMNs are significantly more common in patients with lung malignancies compared to benign conditions, particularly in lung adenocarcinomas. MPMNs often accompanies chronic respiratory diseases such as pulmonary embolism, interstitial pneumonia, and chronic bronchitis[6]. In our case, coexistence with aspergilloma suggested the possible involvement of chronic inflammation in the development of MPMN, although the exact association remains unclear.

Recent advances in high-resolution CT have led to an increase in the incidental detection of MPMNs. On chest CT, MPMNs appear as solitary or multiple pure GGNs. The number of nodules varies widely, ranging from a few to over a hundred, whereas their size typically ranges from 2–5 mm, rarely exceeding 1 cm. Although the distribution of these nodules does not show any significant differences between lung lobes, they are more commonly found subpleurally[5], and ring-like structures with a central lucency can sometimes be observed within the lesions[7][8].

Histopathologically, MPMNs can be characterized as round to spindle-shaped cells that proliferate in a small nest-like or spiral arrangement within the pulmonary interstitium, resembling the histopathological features of meningioma. Despite the fact that the existing alveolar structure is preserved, the thickening of the alveolar walls is believed to explain their

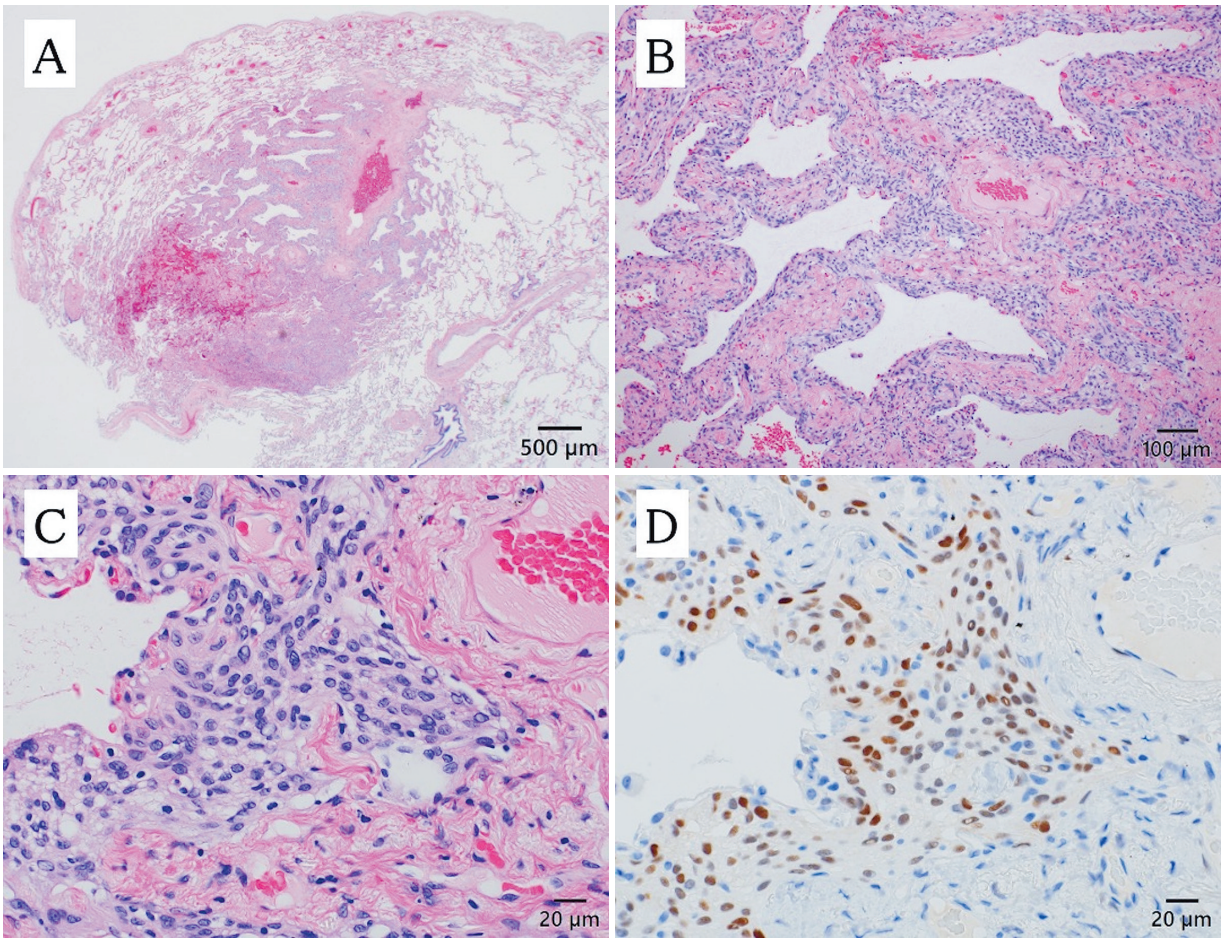

Fig. 3　A–C : Hematoxylin Eosin staining, D : Immunohistochemical staining
Although the lesion lacks a capsule structure, its boundary was relatively clear (A). Histopathologically, short spindle-shaped cells proliferated within the alveolar septal stroma with no nuclear atypia nor mitosis (B, C). Immunohistochemistry staining shows positive for PgR (D).

appearance as pure GGNs on CT. Expansion of adjacent alveoli and small bronchioles due to cellular proliferation in the interstitial space may contribute to the formation of the central lucency observed on CT[7].

Differential diagnoses for lesions presenting as pure GGNs include atypical adenomatous hyperplasia, adenocarcinoma in situ, minimally invasive adenocarcinoma, MMPH, and metastatic pulmonary tumors. However, it remains a challenging task to differentiate between these conditions based solely on imaging findings. Detailed clinical information, including findings associated with tuberous sclerosis and a history of malignancy, as well as long-term follow-up are necessary for accurate differentiation.

In the current case, multiple pure GGNs were observed predominantly in the lower lobes and subpleural areas of bilateral lungs, and central luecncy were observed in some lesions. Although these findings are consistent with previous reports, preoperative diagnosis based on imaging alone remains challenging, even when combined with clinical information. Observation was a possible option ; however, since surgical resection had to be conducted for the aspergilloma, the GGNs were also resected simultaneously for a definitive diagnosis.

MPMN is considered a benign lesion, typically asymptomatic, which does not affect life expectancy. Previous reports showed that these nodules could remain unchanged during follow-ups of up to 92 months[9]. It should be stated that in our current case, follow-up was not conducted at our hospital settings due to referral to a local clinic. Furthermore, previous studies

reported cases of MPMN with increased[10] or enlarged nodules[11], which were difficult to differentiate from lung metastases or adenocarcinoma. Additionally, there is a case report of MPMN with adenocarcinoma in which one nodule grew during follow-up[12]. The etiology, pathogenesis, and clinical management of MPMN remains unclear, and careful follow-up is advisable even after the diagnosis of MPMN. Although the duration of follow-up is not clearly specified, based on the recommendations of the Japan Society of CT Screening for the observation period of pure GGNs, a follow-up of 60 months is recommended.

Ⅳ Conclusion

The number of MPMN cases detected by chest CT screening has increased in recent years. Although definitive diagnosis of MPMN based on imaging findings alone is challenging, it is essential to consider MPMN during the differential diagnosis for lesions presenting as GGN. MPMNs are characterized by its predominance in women, minimal changes over time, multiple occurrences, and occasional appearance of central lucency.

References

1) Mizutani E, Tsuta K, Maeshima A, Asamura H, Mastuno Y : Minute pulmonary meningothelial-like nodules : clinicopathologic analysis of 121 patients. Hum Pathol 40 : 678-682, 2009
2) Korn D, Bensch K, Liebow AA, Castleman B : Multiple minute pulmonary tumors resembling chemodectomas. Am J Pathol 37 : 641-672, 1960
3) Gaffey MJ, Mills SE, Askin FB : Minute pulmonary meningothelial-like nodules. A clinicopathologic study of so-called minute pulmonary chemodectoma. Am J Surg Pathol 12 : 167-175, 1988
4) Niho S, Yokose T, Nishiwaki Y, Mukai K : Immunohistochemical and clonal analysis of minute pulmonary meningothelial-like nodules. Hum Pathol 30 : 425-429, 1999
5) Zhang Y, Wu J, Zhao Y, Zhang T, Xu H, Chen Y : Minute pulmonary meningothelial-like nodules : associations between computed tomography and pathology features. Quant Imag Med Surg 13 : 462-470, 2023
6) Mukhopadhyay S, El-Zammer OA, Katzenstein AL : Pulmonary meningothelial-like nodules : new insights into a common but poorly understand entity. Am J Surg Pathol 33 : 487-495, 2009
7) Zhang Y, Wu J, Zhang T, Zhang Q, Chen Y : Minute pulmonary meningothelial-like nodules : rare lesions appearing as a diffuse ground-glass nodules with cyst-like morphology. Quant Imag Med Surg 7 : 3355-3359, 2021
8) Harada M, Aono Y, Yasui H, et al : Minute Pulmonary Meningothelial-like Nodules Showing Multiple Ring-shaped Opacities. Intern Med 58 : 3149-3152, 2019
9) Suster S, Moran CA : Diffuse pulmonary meningotheliomatosis. Am J Surg Pathol 31 : 624-631, 2007
10) Murata D, Zaizen Y, Tokisawa S, et al : A Rare Case of Diffuse Bilateral Minute Pulmonary Meningothelial-like Nodules Increasing over the Short Term and Resembling Metastatic Lung Cancer. Intern Med 62 : 1207-1211, 2023
11) Ohashi T, Kawago M, Iguchi H, et al : Minute pulmonary meningothelial-like nodule that was difficult to differentiate from lung adenocarcinoma due to specific computed tomography findings changes : A case report. Respirology Case Reports 12 : e01263, 2023
12) Kondo M, Uyama N, Shinya T, Harada M : A case of multiple minute pulmonary meningothelial-like nodules combined with adenocarcinoma. Jpn J Clin Radiol 63 : 347-351, 2018

(2024. 8. 27 received ; 2024. 11. 29 accepted)