

[CASE REPORT]

Pulmonary Hyalinizing Granuloma Mimicking Primary Lung Cancer

Shigeo Kawase¹, Rie Matsumoto², Shigeo Imai², Kentaro Kawaguchi¹, Yusuke Hata¹,
Naokatsu Horita¹ and Yutaro Shiota¹

Abstract:

We herein report a case of pulmonary hyalinizing granuloma (PHG), which is a rare pulmonary mass. A 69-year-old man with no symptoms presented to our hospital because of the appearance of an abnormal shadow on chest X-ray. Computed tomography revealed a right middle-lobe mass with spicula and infiltration into the upper lobe. Since a bronchofiberscopic examination showed no malignant cells in the specimen, the patient underwent thoracoscopic surgery, which revealed PHG. Spiculation and interlobar infiltration, which comprise the characteristic features of primary lung cancer, are uncommon presentations of this rare entity.

Key words: pulmonary hyalinizing granuloma, lung cancer, bronchofiberscopy, PET-CT

(Intern Med 57: 3615-3617, 2018)

(DOI: 10.2169/internalmedicine.1277-18)

Introduction

Pulmonary hyalinizing granuloma (PHG) is a rare disease characterized by hyalinized lamellar collagen bundles, usually surrounded by plasma cells, lymphocytes, and histiocytes (1). Although an immune response to the antigenic stimulation by bacterial infection or autoimmune response has been suggested as a cause of this disease, its etiology remains unknown. Most of its lesions are reported as single or multiple pulmonary round nodules (2). Furthermore, its radiological findings indicate the possibility of metastatic lung cancer. However, the presence of a single nodular lesion with parenchymal and interlobar infiltration, indicating the possibility of primary lung cancer, is very rare in this disease.

We herein report an interesting case of PHG mimicking primary lung cancer.

Case Report

A 69-year-old man was referred to our hospital for the further evaluation of an abnormal shadow on chest X-ray. He had no symptoms. His medical history included hypertension, hyperlipidemia, diabetes mellitus, hyperuricemia,

nephrotic syndrome, and renal failure. He also had a history of smoking 5 cigarettes per day for 29 years and had quit smoking 20 years ago. He was a maintenance worker of a building management company.

On presentation, his blood pressure was 174/92 mmHg, pulse rate 80 beats per minute, and respiratory rate 16 breaths per minute with an O₂ saturation of 99% on room air. The cardiovascular examination findings were normal, his lungs were clear on auscultation, and no subcutaneous edema was observed. Laboratory examinations revealed elevated levels of blood urea nitrogen (27.9 mg/dL) and creatinine (2.93 mg/dL). Although carcinoembryonic antigen (2.8 ng/mL) and cytokeratin 19 fragment (1.6 ng/mL) levels were not elevated, an increased level of progastrin-releasing peptide (83.5 pg/mL) was found because of renal failure. The results of the pulmonary function tests were within normal limits.

A chest radiograph revealed a tumorous shadow on the right middle-lobe field (Fig. 1). Computed tomography (CT) revealed an abnormal mass with spicula on the right middle lobe that had infiltrated the right upper lobe (Fig. 2A-C). Fluorodeoxyglucose positron emission tomography (FDG-PET) indicated a low uptake of FDG (maximum standardized uptake value, 1.9) in this lesion (Fig. 2D).

In light of these findings, bronchofiberscopy was per-

¹Department of Respiratory Medicine, Kure Kyosai Hospital, Japan and ²Department of Thoracic Surgery, Kure Kyosai Hospital, Japan
Received: March 27, 2018; Accepted: May 10, 2018; Advance Publication by J-STAGE: August 10, 2018
Correspondence to Dr. Shigeo Kawase, s-kawase@kure-kyosai.jp

formed. A transbronchial biopsy from the right B⁴b using radial endobronchial ultrasonography with a guide sheath revealed no malignant cells in the specimen. A second attempt of bronchofiberscopy revealed the same result. To establish a definite diagnosis, the patient underwent video-assisted thoracoscopic surgery. An elastic hard tumor in the right middle lobe and its infiltration and adhesion into the right upper lobe was identified. Therefore, resection of the right middle lobe and part of the right upper lobe was performed.

The postoperative course was uneventful, and the patient was discharged. A histological analysis demonstrated com-

plicated proliferation of thick collagen fibers surrounded by lymphoplasmacytic infiltrate (Fig. 3). No atypical epithelial cells were found. Amyloid was not detected with Congo red stain. These histopathological findings led to the diagnosis of PHG. The patient received no specific subsequent treatment and remained asymptomatic.

Discussion

First reported by Benfield et al. in 1964 (3) and characterized by Engleman et al. in 1977 (1), PHG is a rare benign condition. The etiology and pathogenesis of this tumor remain unknown. PHG has been previously reported to be associated with immune disorders, such as sclerosing mediastinitis, rheumatoid arthritis, multiple sclerosis, Sjögren syndrome, granulomatosis with polyangiitis, primary biliary cirrhosis, and membranous glomerulonephritis (4, 5). Although our patient developed renal failure, the findings for antinuclear antibody, antineutrophil cytoplasmic antibody, and other autoantibodies were negative. Furthermore, no evidence of arthralgia, erythema, or other signs of collagen vascular diseases was noted. The differential diagnosis of PHG includes infectious diseases, such as tuberculosis, histoplasmosis, and fungal infections (2, 4). In this case, bronchial wash fluid for bacterial infection, including *Mycobacterium tuberculosis*, was negative.

PHG tumors often exist in the subpleural pulmonary parenchyma. Histopathologically, hyalinized lamellar collagen bundles are found in the central area surrounded by lympho-

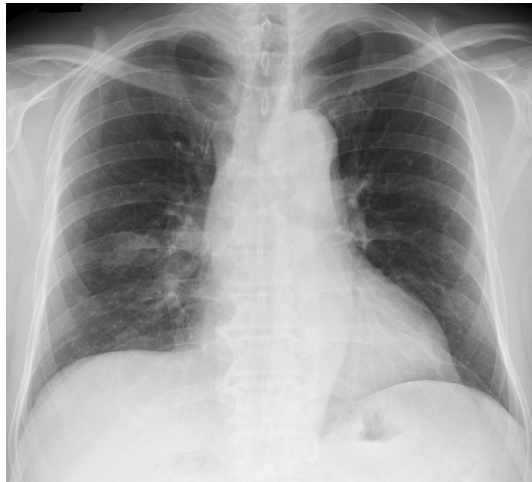


Figure 1. Chest radiograph showing nodular opacity in the right middle field.

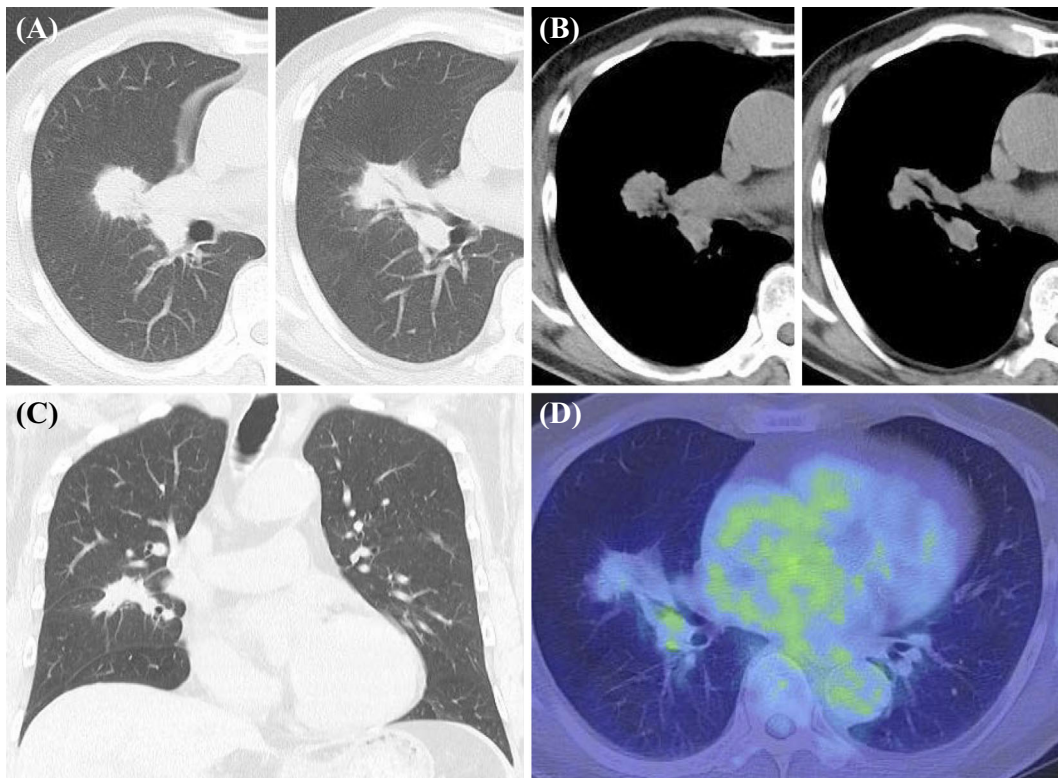


Figure 2. (A-C) Chest CT without contrast showing a nodular lesion with spicula and infiltration into the upper lobe. (D) PET-CT showing the slight uptake of FDG (SUVmax 1.9).

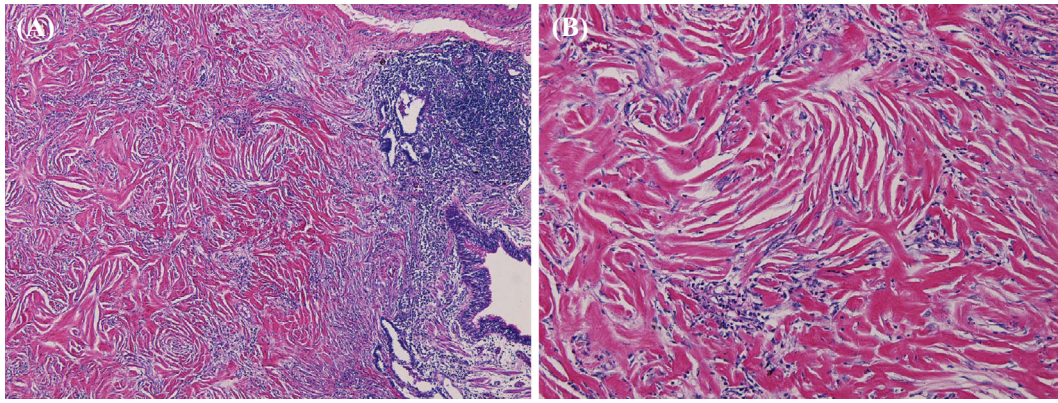


Figure 3. (A, B) Histopathology of the resected tumor in the right middle lobe with part of the upper lobe (Hematoxylin and Eosin staining, A: $\times 40$, B: $\times 400$). Complicated proliferations of thick collagen fibers were found in association with surrounded lymphocyte infiltration. No atypical epithelial cells were found.

cyte and plasma cell infiltrates. Bronchoalveolar lavage and a transbronchial biopsy reportedly do not permit the diagnosis of PHG (2). A bronchoscopic biopsy might fail to make an accurate diagnosis because this tumor comprises a central hard and peripheral soft lesion. Therefore, a CT-guided percutaneous biopsy or surgical resection should be considered to confirm the diagnosis.

In the literature review, isolated or multiple nodular lesions were the most frequent findings, sometimes with excavation and/or calcification (2, 5-8), and parenchymal infiltration and condensation were rare conditions. In this case, the tumor was initially suspected to be primary lung cancer. It was radiologically observed to be spiculated and to have infiltrated into another pulmonary lobe, and this feature was quite similar to those of primary lung neoplasm. To our knowledge, there have been no reports of PHG cases with infiltration into the adjacent lobe. It is difficult to distinguish between PHG and lung cancer by radiological findings alone. Both PHG and lung cancer radiologically appear to be solitary or multiple nodules with well-defined or irregular borders. A histopathological evaluation is therefore very important for making an accurate diagnosis. A 3-mm-diameter hyalinizing nodule with anthracosis near the resected tumor was noted, and silicate crystals were found using polarized light microscopy. Although the resected tumor showed no silicotic nodules, silicosis may have affected the development of PHG in this case.

The prognosis of PHG is generally favorable. A single nodule can be cured by surgical resection, whereas multiple nodules cannot. Some publications recommend glucocorticoid treatment for PHG (2, 9); however, the efficacy of this approach remains unclear. No effective treatment has yet been established for multiple nodules of PHG.

In conclusion, this case should remind clinicians to consider PHG as a possible cause of pulmonary tumor found on imaging. Furthermore, histological examinations with proper

specimens are required to make an accurate diagnosis of PHG.

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

Acknowledgement

We thank Dr. Naomi Sasaki for conducting the pathological studies.

References

- Engleman P, Liebow AA, Gmelich J, Friedman PJ. Pulmonary hyalinizing granuloma. *Am Rev Respir Dis* **115**: 997-1008, 1977.
- Lhote R, Haroche J, Duron L, et al. Pulmonary hyalinizing granuloma: a multicenter study of 5 new cases and review of the 135 cases of the literature. *Immunol Res* **65**: 375-385, 2017.
- Benfield JR, Harrison RW, Moulder PV, Lyon ES, Graff PW. Bilateral nodular pulmonary granulomas and retroperitoneal fibrosis. *JAMA* **182**: 579-581, 1962.
- Yousem SA, Hochholzer L. Pulmonary hyalinizing granuloma. *Am J Clin Pathol* **87**: 1-6, 1987.
- Ussavarungsi K, Khoor A, Jolles HI, Mira-Avendano I. A 40-year-old woman with multiple pulmonary nodules. *Chest* **146**: e198-e203, 2014.
- Na KJ, Song SY, Kim JH, Kim YC. Subpleural pulmonary hyalinizing granuloma presenting as a solitary pulmonary nodule. *J Thorac Oncol* **2**: 777-779, 2007.
- Patel Y, Ishikawa S, MacDonnell KF. Pulmonary hyalinizing granuloma presenting as multiple cavitory calcified nodules. *Chest* **100**: 1720-1721, 1991.
- Düzgün N, Kurtipek E, Esmé H, Eren Karanis Mİ, Tolu İ. Pulmonary hyalinizing granuloma mimicking metastatic lung cancer. *Case Rep Pulmonol* **2015**: 610417, 2015.
- Shinohara T, Kaneko T, Miyazawa N, et al. Pulmonary hyalinizing granuloma with laryngeal and subcutaneous involvement: report of a case successfully treated with glucocorticoids. *Intern Med* **43**: 69-73, 2004.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).