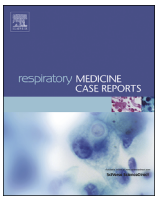
Respiratory Medicine Case Reports 45 (2023) 101887

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr



Case Report

Lung cancer resembling allergic bronchopulmonary mycosis with an asthma-like presentation

Yoshiro Kai [a, *], Ryosuke Kataoka [a], Kentaro Suzuki [a], Masato Takano [b], Shigeo Muro [c]

[a] Department of Respiratory Medicine, Minami-Nara General Medical Center, 8-1 Fukugami, Oyodo-cho, Yoshino-gun, Nara, 638-8551, Japan
[b] Department of Diagnostic Pathology, Minami-Nara General Medical Center, 8-1 Fukugami, Oyodo-cho, Yoshino-gun, Nara, 638-8551, Japan
[c] Department of Respiratory Medicine, Nara Medical University, 840 Shijo-cho, Kashihara City, Nara, 634-8522, Japan

ARTICLE INFO

Keywords:
ABPA
ABPM
Bronchial asthma
Bronchoscopy
Lung cancer

ABSTRACT

Allergic bronchopulmonary aspergillosis (ABPA) is a lung disorder caused by a hypersensitivity reaction to antigens of the *Aspergillus species*. Recently, allergic bronchopulmonary mycosis (ABPM) caused by fungi other than *Aspergillus species* but with the same symptoms has been described. ABPM commonly affects patients with allergic diseases including bronchial asthma. ABPM is characterized by radiographic appearance, with the most common findings being proximal bronchiectasis and signs of mucoid impaction. However, the differentiation of ABPM is often necessary to enable accurate diagnosis of lung cancer. A 73-year-old man visited the outpatient clinic with symptoms of exertional dyspnea. He was diagnosed with ABPM due to suspicious bronchiectasis and mucoid impaction observed in computed tomography (CT) of his chest. After 3 months, he visited our hospital with continued exertional dyspnea and suspicion of a possible tumor in his lung. Marked eosinophilia and high-attenuation mucus impaction were not taken into consideration as diagnosis was conducted as per clinical diagnostic criteria for ABPA/ABPM. We hereby report a case of lung cancer in a patient initially evaluated for suspected ABPM of the right lung. The diagnosis of lung cancer was established using bronchoscopy. If any definitive diagnosis is not achieved by following the clinical diagnostic criteria for ABPM, physicians should achieve a histological diagnosis by performing a prompt bronchoscopy.

Abbreviations

ABPA	Allergic bronchopulmonary aspergillosis
ABPM	Allergic bronchopulmonary mycosis
CT	Computed tomography
FeNO	Fractional exhaled nitric oxide
IgE	Immunoglobulin E
FEV1	Forced expiratory volume in 1 s
LABA	Long-acting β2-agonist
SITT	Single inhaler triple therapy

* Corresponding author.
E-mail address: y-kai@eco.ocn.ne.jp (Y. Kai).

https://doi.org/10.1016/j.rmcr.2023.101887
Received 2 May 2023; Received in revised form 4 June 2023; Accepted 19 June 2023
Available online 19 June 2023

PET	Positron emission tomography
FDG	Fluorodeoxyglucose
ROS-1	C-ros oncogene1
BRAF	V-raf murine sarcoma viral oncogene homolog B1
RET	Rearranged during transfection
PD-L1	Programmed death ligand-1
HRCT	High-resolution computed tomography
HAM	High-attenuation mucus

1. Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a disease characterized by asthma, eosinophilia, and pulmonary infiltrates caused by a hypersensitivity reaction to *Aspergillus species* [1]. Recently, fungi other than *Aspergillus species* have been reported to cause similar pathologies, altogether known as allergic bronchopulmonary mycosis (ABPM) [2]. ABPM is characterized based on the presence of proximal bronchiectasis and signs of mucoid impaction, which can be detected radiographically [3]. ABPM was diagnosed according to the clinical diagnostic criteria for ABPM [2]. The diagnosis of ABPM is supported by the clinical examination and radiological imaging [2,4]. However, the patients with ABPM are often misdiagnosed [5]. Our patient was misdiagnosed with ABPM due to radiological imaging and asthma-like presentation. Finally, 4 months later, he was diagnosed with non-small cell carcinoma by bronchoscopy. Here, we describe a case of lung cancer mimicking ABPM. We require the differentiation of ABPM from lung cancer. If the definitive diagnosis was not obtained by the clinical diagnostic criteria for ABPM, we must perform bronchoscopy for accurate diagnosis of lung cancer.

2. Case presentation

A 73-year-old man who was a regular smoker, with a history of consuming 79.5 packs of cigarettes/year, consulted the clinic with a complaint of exertional dyspnea in September 2022. His history was insignificant, and he had no complaints of any allergic diseases in the past. In computed tomography (CT) of his chest, proximal bronchiectasis and mucoid impaction were suspected (Fig. 1A–C). Furthermore, emphysematous changes were detected. A diagnosis of pneumonia or ABPM with bronchial asthma was made in the outpatient clinic. He was treated with antibiotics (clarithromycin), an antitussive, and an expectorant. Despite these medications, his symptoms persisted. Three months later, his symptoms worsened. Therefore, he was suspected of having ABPM with bronchial asthma and was referred to our hospital in December 2022. He presented with persistent cough and shortness of breath. A wheeze could be confirmed in the right lung field. Laboratory findings revealed a normal white blood cell count of 6200/μL with 1.0% eosinophils. The bronchial inflammatory marker, fractional exhaled nitric oxide (FeNO), was normal (12 ppb). Total serum immunoglobulin E (IgE) level was also normal (37.1 IU/mL). Serological test results for Aspergillus-specific IgE and antibody test against Aspergillus were negative. Pulmonary function showed a forced expiratory volume of 920 mL in 1 s (FEV_1) (% predicted; 35.7%) and ratio of FEV1 and forced vital capacity of 44.7%. This result indicated an obstructive disorder.

The peripheral blood eosinophil count of the patient did not elevate; however, the chest CT findings from 30th September 2022 and due to the presence of other symptoms, such as persistent cough, wheeze, and obstructive disorder, he was suspected to be suffering from a combination of bronchial asthma and ABPA. Furthermore, on the first visit, bronchoscopy was scheduled after 2 weeks because of the definitive diagnosis of ABPM and the possibility of lung cancer.

He was treated with a triple regimen of inhaled corticosteroid, long-acting β2-agonist (LABA), and long-acting muscarinic antagonist delivered using a single inhaler triple therapy (fluticasone furoate 200 μg/umeclidinium 62.5 μg/vilanterol 25 μg). However, his symptoms did not improve. Chest CT was performed upon referral and the tumor, which was suspected mucoid impaction was remarkably enlarged from 59 cm × 28 cm–79 cm × 37 cm and emphysematous changes were detected (Fig. 1D–F). Positron emission tomography (PET)/CT scan with 18F-labeled fluorodeoxyglucose (FDG) revealed abnormal accumulation of FDG in the right lower tumor and hilar/mediastinal lymph nodes (Fig. 1G and H). Basis on these results, he was suspected of having lung cancer. Bronchoscopy was performed for a confirmed diagnosis. Bronchoscopy examination revealed a pedunculated endobronchial tumor covered with a white surface obstructing the distal portion of the right bronchus intermedius (Fig. 1I). Pathologic examination of the tumor biopsy revealed poorly differentiated non-small cell carcinoma, suggesting squamous cell carcinoma (Fig. 1J, K, L, M). He was diagnosed with lung non-small cell carcinoma (cT4N2M0, stage IIIB), which was negative for epidermal growth factor receptor mutation, anaplastic lymphoma kinase fusion, c-ros oncogene1(ROS-1) fusion, v-raf murine sarcoma viral oncogene homolog B1 (BRAF) mutation, and rearranged during transfection (RET) fusion. Programmed death ligand-1 (PD-L1) expression with a tumor proportion score of $<1\%$ (negative) was confirmed via immunohistochemistry with a 22c3 antibody. Because of poor respiratory function and advanced stage, surgery was not recommended. He is currently undergoing treatment with chemoradiotherapy.

3. Discussion

ABPM is a disease caused by hypersensitivity to antigens of various fungi [1]. ABPM usually develops in patients suffering from asthma [4]. The diagnosis of ABPM is based on a combination of radiological manifestations, clinical, biological, and diagnosis criteria [2]. In 2021, Asano et al. put forth their diagnostic criteria for the diagnosis of ABPM. Clinical diagnostic criteria for ABPA/ABPM

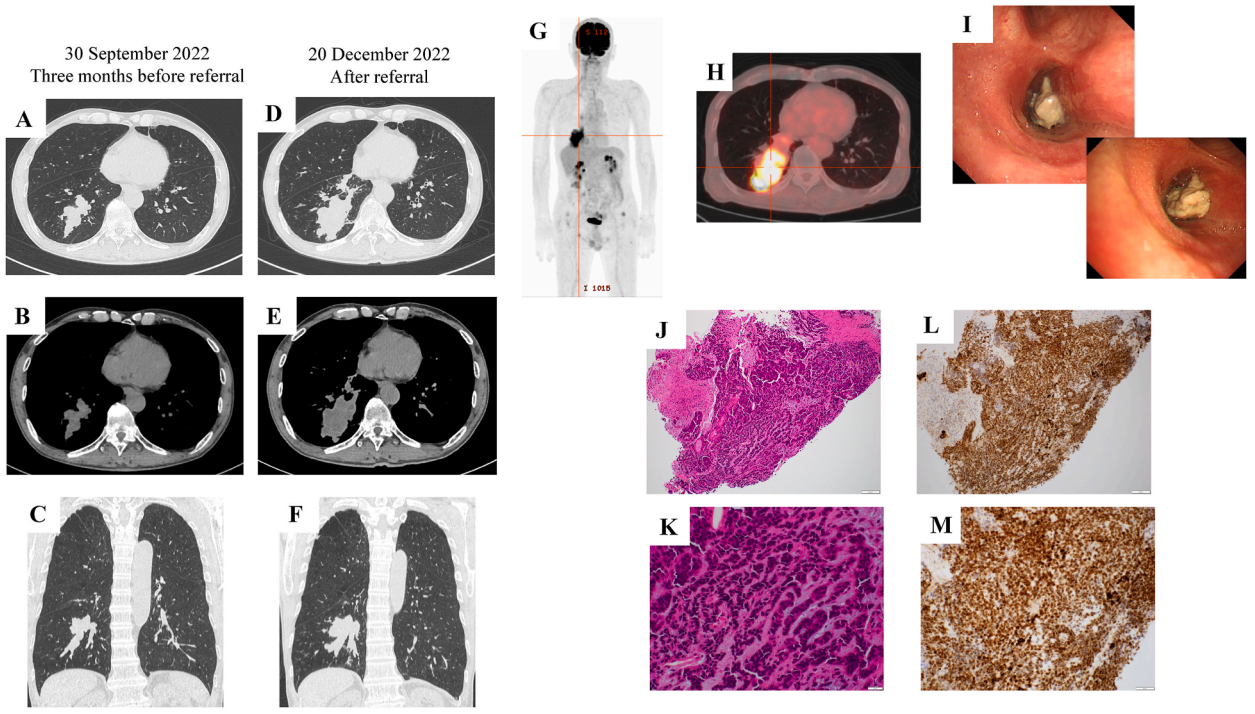


Fig. 1. Chest computed tomography (CT) findings showing mucoid impaction-like tumor in the right lower lobe in 30 September 2022 (A–C). CT findings showing an enlarged tumor in 20 December 2022 at the time of referral (D–F). Coronal image of whole-body positron emission tomography (PET) revealed abnormal accumulation of 18F-labeled fluorodeoxyglucose (FDG) in the right lower tumor and hilar/mediastinal lymph nodes (G). PET-CT image revealed abnormal accumulation of FDG in the tumor in the right lower lobe (H). Bronchoscopy revealed an endobronchial tumor covered with a whitish surface narrowing of the truncus intermedius (I). Pathological examination of the specimen obtained from transbronchial lung biopsy. Hematoxylin and eosin staining showing poorly differentiated non-small cell carcinoma. [(J) × 100, (K) × 400]. Immunohistochemistry revealed that the tumor cell was positive for p63 expression. The tumor was immunohistochemically suspected to be squamous cell carcinoma. [(L) × 100, (M) × 200].

include (1) current or previous history of asthma or asthmatic symptoms, (2) peripheral blood eosinophilia (≧500 cells/mm^3), (3) elevated total serum IgE levels (≧417 IU/mL), (4) immediate cutaneous hypersensitivity or specific IgE for filamentous fungi, (5) presence of precipitins or specific IgG for filamentous fungi, (6) filamentous fungal growth in sputum cultures or bronchial lavage fluid, (7) presence of fungal hyphae in bronchial mucus plugs, (8) central bronchiectasis on CT, (9) presence of mucus plugs in central bronchi, based on CT/bronchoscopy or mucus plug expectoration history, and (10) high-attenuation mucus in the bronchi on CT [2]. Filamentous fungi in criteria 4 to 6 should be identical. Patients that met 6 or more of these criteria were said to be diagnosed with ABPM. In this case, we observed that criteria (1), (7), and (8) were positive. Accordingly, this case could not be diagnosed with ABPM.

High-resolution computed tomography (HRCT), a promising tool of investigating ABPM, of the chest was performed. However, the diagnosis of ABPM purely by radiological method is difficult. In our case, central bronchiectasis and mucus plugs were suspected in chest HRCT; hence, the diagnosis of ABPM was made without the using of clinical criteria.

In the diagnostic criteria described by Asano et al., central bronchiectasis and mucus impaction were included [2]. Mucoid impaction and central bronchiectasis are the characteristic features of ABPM [3]. According to Kaur M et al., ABPM is characterized by the tubular branching opacities forming a gloved-finger appearance, which was visible in this case [3]. Further, bronchoscopy of the chest was performed to evaluate the lung opacity. The opacity was mistaken to be a mucoid impaction. The non-small cell carcinoma was diagnosed because of the transbronchial biopsy. Mucoid impaction is filling of the dilated airways via mucoid secretions. The mucus plug in ABPM is generally hypodense. High-attenuation mucus (HAM) is detected in 36% of patients with ABPM [3,6]. Here, opacity was hypodense; however, HAM was not detected. According to the new clinical diagnostic criteria for ABPA/ABPM, this case could not be diagnosed with ABPM. ABPM is often difficult to distinguish from lung cancer and causes delayed diagnosis or misdiagnosis of lung cancer [5,7]. Zou et al. have reported the clinical features and reasons for missed diagnosis of ABPM [8]. In this retrospective study, of 46 patients suffering from ABPM, only 2 patients were accurately diagnosed at the first visit, and the remaining 44 were misdiagnosed with asthma, bronchiectasis, pneumonia, pulmonary tuberculosis, and lung cancer (4 cases, 8.7%) [8]. This paper described that ABPM is characterized by recurrent episodes of wheezing, lung opacities, and bronchiectasis. The main reasons for misdiagnosis in patients with ABPM are atypical symptoms and early atypical imaging changes. Common symptoms of 46 patients with ABPM included wheezing; 35 cases (76.1%) had obstructive ventilation dysfunction. In chest CT, 28 cases (60.9%) showed bronchiectasis and 8 cases (17.4%) manifested mucus plugs, and among them, 4 cases were with high-attenuations [8]. Asano's criteria included current or previous history of asthma or asthmatic symptoms [4]. This case was misdiagnosed because of symptoms of wheezing, obstructive ventilation dysfunction, and chest imaging. The symptoms of wheezing and lung function tests indicated obstructive disorder. FeNO was normal and the patient was a known heavy smoker. Furthermore, the bronchoscopy revealed narrowing of the

truncus intermedius by mass. These results indicated chronic obstructive pulmonary disease and not bronchial asthma. PET/CT scan with FDG revealed abnormal accumulation of FDG in the entire right lower tumor. Furthermore, the tumor in the right lower lobe, which was suspected mucoid impaction in September 2022 was remarkably enlarged for only 3 months. These results were atypical for ABPM and lung cancer was suspected. Finally, the diagnosis was confirmed using bronchoscopy. Bronchoscopy is useful to evaluate the diagnostic procedure for patients with suspected ABPM [9]. Based on the symptoms and further tests, the patient was diagnosed with lung cancer.

Bronchoscopic examination revealed a tumor and obstruction in the distal portion of the right bronchus intermedius. Pathologically, the tumor was diagnosed as poorly differentiated squamous cell carcinoma and showed intrabronchial branching growth into the peripheral site of the right lower lobe. The bronchus was impacted by the squamous cell carcinoma. Meanwhile, the tumor in his right lung had grown. He was not fit for surgery and is now undergoing chemotherapy. A diagnosis of ABPM was made because of the wheezing and imaging results but it has also been misdiagnosed due to overlapping symptoms with asthma. Bronchoscopy led to a more accurate diagnosis of lung cancer. Therefore, it is advisable that the physicians should perform a histological diagnosis by bronchoscopy as soon as possible in such cases.

4. Conclusion

- It is importance of proper diagnostic criteria for ABPM and lung cancer because the overlapping symptoms can lead to wrong diagnosis and adversely affect the patient's prognosis.
- Bronchoscopy leads to a more accurate diagnosis of lung cancer.
- There are several instances where ABPM has also been misdiagnosed due to overlapping symptoms with asthma, pulmonary tuberculosis, lung cancer, etc.

Authorship statement

All authors met the International Committee of Medical Journal Editors authorship criteria. YK wrote the manuscript. All authors contributed to the editing of the manuscript and approved the final version of the manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics approval and consent for publication

Written informed consent was obtained from the patient for the publication of this case report.

Declaration of competing interest

None

Acknowledgements

We would like to thank Enago (www.enago.jp) for English language editing.

References

[1] R. Agarwal, V. Muthu, I.S. Sehgal, S. Dhooria, K.T. Prasad, A.N. Aggarwal, Allergic bronchopulmonary aspergillosis, Clin. Chest Med. 43 (2022) 99–125, https://doi.org/10.1016/j.ccm.2021.12.002.

[2] K. Asano, A. Hebisawa, T. Ishiguro, N. Takayanagi, Y. Nakamura, J. Suzuki, N. Okada, J. Tanaka, Y. Fukutomi, S. Ueki, K. Fukunaga, S. Konno, H. Matsuse, K. Kamei, M. Taniguchi, T. Shimoda, T. Oguma, Japan ABPM Research Program, New clinical diagnostic criteria for allergic bronchopulmonary aspergillosis/mycosis and its validation, J. Allergy Clin. Immunol. 147 (2021) 1261–1268 https://doi.org/10.1016/j.jaci.2020.08.029, e5.

[3] M. Kaur, D.S. Sudan, Allergic bronchopulmonary aspergillosis (ABPA)-the high resolution computed tomography (HRCT) chest imaging scenario, J. Clin. Diagn. Res. 8 (2014) Rc05–Rc07, https://doi.org/10.7860/JCDR/2014/8255.4423.

[4] Y. Zeng, X. Xue, H. Cai, G. Zhu, M. Zhu, J. Wang, X. Song, Y. Mo, X. Gao, J. Zhou, L. Ye, M. Jin, Clinical characteristics and prognosis of allergic bronchopulmonary aspergillosis: a retrospective cohort study, J. Asthma Allergy 15 (2022) 53–62, https://doi.org/10.2147/JAA.S345427.

[5] H. Feng, P. Lv, X. Ren, H. Dai, T. Yang, Misinterpretation of allergic bronchopulmonary aspergillosis/allergic bronchopulmonary mycosis due to diverse characteristics in different clinical stages, J. Thorac. Dis. 11 (2019) 4484–4491, https://doi.org/10.21037/jtd.2019.10.78.

[6] S. Phuyal, M.K. Garg, R. Agarwal, P. Gupta, A. Chakrabarti, M.S. Sandhu, N. Khandelwal, High-attenuation mucus impaction in patients with allergic bronchopulmonary aspergillosis: objective criteria on high-resolution computed tomography and correlation with serologic parameters, Curr. Probl. Diagn. Radiol. 45 (2016) 168–173, https://doi.org/10.1067/j.cpradiol.2015.07.006.

[7] Y. Mou, L. Ye, M. Ye, D. Yang, M. Jin, A retrospective study of patients with a delayed diagnosis of allergic bronchopulmonary aspergillosis/allergic bronchopulmonary mycosis, Allergy Asthma Proc. 35 (2014) e21–e26, https://doi.org/10.2500/aap.2014.35.3731.

[8] M.F. Zou, S. Li, Y. Yang, L.L. Cao, Y. Pan, E.H. Sun, L. Dong, Clinical features and reasons for missed diagnosis of allergic bronchopulmonary aspergillosis, Zhonghua Yixue Zazhi 99 (2019) 1221–1225, https://doi.org/10.3760/cma.j.issn.0376-2491.2019.16.006.

[9] A. Tamura, A. Hebisawa, A. Kurashima, Y. Kawabe, K. Machida, H. Yotsumoto, M. Mori, The use of bronchofiberscopy for diagnosis of allergic bronchopulmonary aspergillosis, Intern. Med. 36 (1997) 865–869, https://doi.org/10.2169/internalmedicine.36.865.