

[ CASE REPORT ]

## Lung Metastases from Bile Duct Adenocarcinoma Mimicking Chronic Airway Infection and Causing Diagnostic Difficulty

Mitsuo Sato<sup>1</sup>, Shotaro Okachi<sup>1</sup>, Jun Fukihara<sup>1</sup>, Yoshie Shimoyama<sup>2</sup>, Keiko Wakahara<sup>1</sup>,  
Toshihiro Sakakibara<sup>1</sup>, Tetsunari Hase<sup>1</sup>, Yasuharu Onishi<sup>3</sup>, Yasuhiro Ogura<sup>3</sup>,  
Osamu Maeda<sup>4</sup> and Yoshinori Hasegawa<sup>1</sup>

### Abstract:

We herein report a case of lung metastases with unusual radiological appearances that mimicked those of chronic airway infection, causing diagnostic difficulty. A 60-year-old woman who underwent liver transplantation from a living donor was incidentally diagnosed with bile duct adenocarcinoma after a histopathological analysis of her explanted liver. Six months later, chest computed tomography (CT) revealed bilateral bronchogenic dissemination that had gradually worsened, suggesting chronic airway infection. A biopsy with bronchoscopy from a mass lesion beyond a segmental bronchus revealed adenocarcinoma identical to that of her bile duct adenocarcinoma, leading to the diagnosis of multiple lung metastases from bile duct adenocarcinoma.

**Key words:** bronchoscopy, bile duct neoplasms, liver transplantation

(Intern Med 57: 1429-1432, 2018)

(DOI: 10.2169/internalmedicine.9718-17)

### Introduction

The lung is one of the most common sites of metastasis of extrapulmonary malignancy, as all the blood in the body is filtered through the lung, so circulating tumor cells are easily captured by the lung (1). It is usually not difficult to diagnose lung metastasis from extrapulmonary malignancy based on typical radiological findings, such as multiple round nodules randomly distributed in both lungs, along with coexisting uncontrolled, extrathoracic malignant tumors. Nevertheless, lung metastasis occasionally presents with an atypical radiological appearance, causing diagnostic difficulty (2).

We herein report a case of multiple lung metastases from bile duct adenocarcinoma whose radiological images mimicked those of airway infection, resulting in diagnostic diffi-

culty. This case may be considered a very rare subtype of endobronchial metastasis.

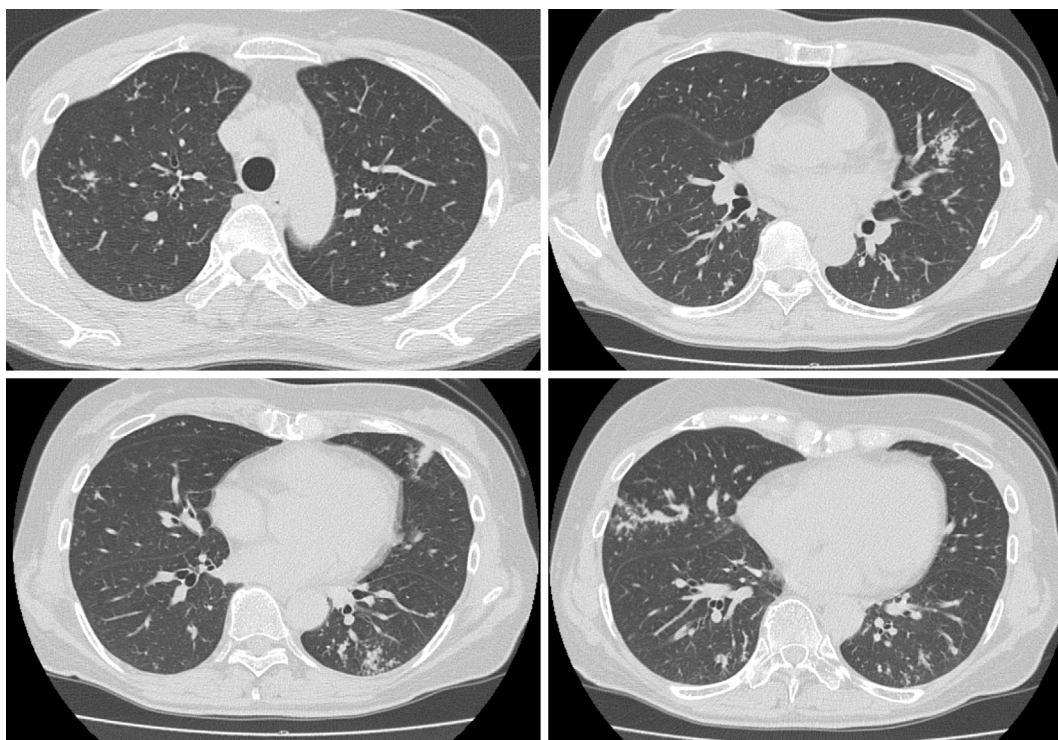
### Case Report

A 60-year-old woman who complained of a dry cough persisting for >2 months and had abnormal chest computed tomography (CT) findings consulted the Department of Respiratory Medicine from the Department of Transplantation Surgery. She had undergone liver transplantation from a living donor for primary sclerosing cholangitis six months earlier. She was incidentally diagnosed with bile duct adenocarcinoma by a histopathological analysis of her explanted liver, despite the results of a preoperative bile duct biopsy being negative and repeated bile juice cytologies. Because the blood type combination between the donor and recipient was ABO-incompatible, chimeric anti-CD20 monoclonal an-

<sup>1</sup>Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Japan, <sup>2</sup>Department of Pathology, Nagoya University Graduate School of Medicine, Japan, <sup>3</sup>Department of Transplantation Surgery, Nagoya University Hospital, Japan and <sup>4</sup>Department of Clinical Chemotherapy and Pharmacology, Nagoya University Graduate School of Medicine, Japan

Received: June 28, 2017; Accepted: September 26, 2017; Advance Publication by J-STAGE: December 27, 2017

Correspondence to Dr. Mitsuo Sato, msato@med.nagoya-u.ac.jp



**Figure 1.** Chest CT at the initial presentation showing bilateral bronchogenic dissemination in several segments, including the right middle and left lingual segments, suggestive of airway infection, specifically non-tuberculosis mycobacteriosis.

tibody (rituximab) had been administered two weeks prior to the scheduled liver transplantation. After the transplantation, she had been treated with immunosuppressants (oral tacrolimus and mycophenolate mofetil) in addition to one-week methylprednisolone administration via portal vein catheter, which was followed by oral prednisolone according to our ABO-incompatible immunosuppression protocol.

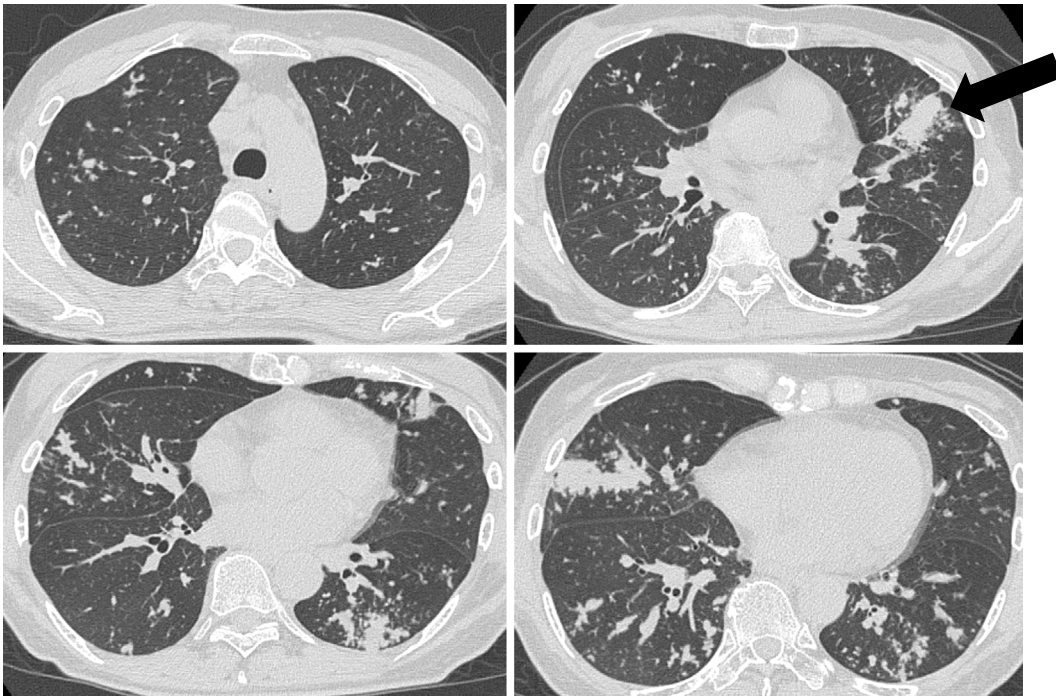
At the initial presentation, chest auscultation was normal, and chest computed tomography revealed bilateral bronchogenic dissemination in several segments (Fig. 1). These radiological findings suggested that the most likely diagnosis was chronic airway infection, specifically non-tuberculosis mycobacteriosis. We therefore first tested her expectorated or induced sputum several times for the isolation of microorganisms. However, despite repeated tests, the results were negative. In addition, serological tests of T-spot and anti-*Mycobacterium avium* complex antibody were negative. We therefore performed bronchoscopy, but neither signs of infection nor malignancy were noted. As her coughing symptoms were mild and not worsening, we decided to follow the patient conservatively.

During eight months of follow-up, the radiological appearance progressed with an increase in mucoid impaction and bronchogenic dissemination (Fig. 2), and blood tests revealed increased carcinoembryonic antigen (CEA) levels from 8.7 ng/mL to 37.2 ng/mL. We therefore strongly suspected malignancy and performed bronchoscopy again. No endobronchial tumors were visible even with a thin bronchoscope, as several subsegmental and segmental bronchi were

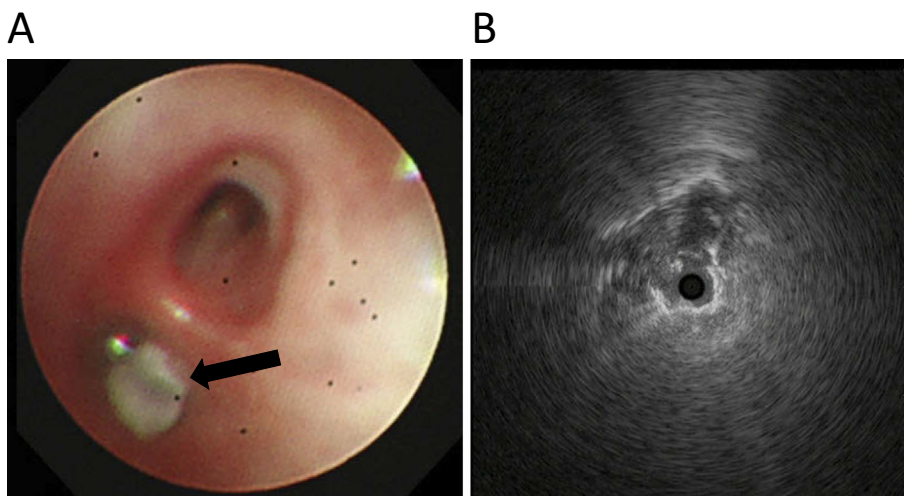
occluded with viscous sputum. By performing a biopsy using endobronchial ultrasonography (EBUS) with a guide sheath (EBUS-GS) through the left B4 (superior lingular segment) bronchus occluded with sputum (Fig. 3A), we were able to obtain echo images suggestive of a mass lesion and biopsied it (Fig. 3B). A histopathological examination revealed adenocarcinoma identical to her bile duct adenocarcinoma (Fig. 4A and B), leading to the diagnosis of lung metastases from bile duct adenocarcinoma. No microorganisms, including fungi and non-tuberculous mycobacteria, were isolated from any bronchial lavage, excluding the possibility of co-existing respiratory infection. Simultaneously, she was suspected of having bone metastasis of L4. This bone lesion was also biopsied, and a histopathological examination revealed metastasis from bile duct adenocarcinoma (Fig. 4C). Based on these results, she was diagnosed with metastatic recurrence of bile duct adenocarcinoma and thus was treated with systemic chemotherapy.

## Discussion

The frequency of endobronchial metastasis is highly variable, ranging from 2% to 50%, in part because of the different definitions used for endobronchial metastasis (3, 4). Kiryu et al. proposed a definition of endobronchial metastasis of, “documented nonpulmonary neoplasms metastatic to the subsegmental or more proximal central bronchus, in a bronchoscopically visible range” (3). In the present case, we were unable to directly visualize any tumors by broncho-



**Figure 2.** Chest CT at eight months after the initial presentation showing progression of the non-tuberculosis mycobacteriosis-like appearance in both lungs. An EBUS-GS-guided biopsy was performed to target the mass lesion in the left S4 segment (arrow).



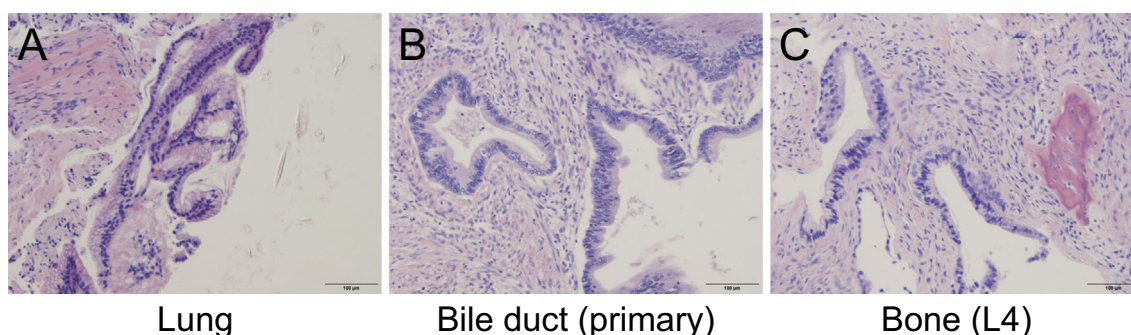
**Figure 3.** The left B4 (superior lingular segment) bronchus occluded with sputum (arrow) (A). An echo image obtained by EBUS-GS through the left B4 bronchus showing a mass lesion (B).

scopy; as such, this case cannot be considered endobronchial metastasis according to Kiryu's definition. However, we speculate that, in the present case, tumor cells directly metastasized to the peripheral bronchus or bronchi and may subsequently have spread in the lung through the airway. We suspect this for the following reasons: First, the CT findings showed a pattern of segmental distribution suggestive of dissemination through the tracheobronchial tree instead of random distribution, which implies dissemination via the pulmonary artery. Second, several mucus-occluded bronchi suggested the existence of multiple lesions in the peripheral bronchi. Third and most importantly, radiological, broncho-

scopic, and histopathological examinations revealed metastatic tumors in the lesion located beyond the segmental bronchus with the radiological appearance of mucoid impaction accompanying airway dissemination. Taken together, these findings suggest the occurrence of direct metastasis to the peripheral bronchus or bronchi followed by dissemination through the airway in the present case.

It is pathologically and molecularly still unknown precisely how tumor cells can metastasize to the bronchial wall. In the present case, tumor cells seemed to preferably metastasize to the peripheral bronchi instead of the proximal bronchi. We suspect that interaction between certain biologi-





**Figure 4.** Histopathology of specimens obtained by EBUS-GS through the left B4 bronchus (A) and needle-biopsy from L4 (C), both of which were identical to that of the primary bile duct adenocarcinoma (B), with characteristics of eosinophilic columnar cells with atypical nuclei eccentric to the basal membrane.

cal characteristics of tumor cells and the microenvironment in the peripheral bronchus may cause such a preference, based on the “seed and soil” hypothesis, a classical theory of tumor metastasis proposed by Paget (5). The pathology of the primary bile duct carcinoma showed that the tumor produces massive mucin. In addition, cytology of bronchial lavage revealed malignancy-suspected cells. These findings suggest that the characteristics of mucin production of tumor cells may have contributed to metastasis through the airway in the present case.

In conclusion, we herein report a case of lung metastases from bile duct adenocarcinoma that closely mimicked airway infection in radiological appearance, leading to diagnostic difficulty.

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

### References

1. Crow J, Slavin G, Kreel L. Pulmonary metastasis: a pathologic and radiologic study. *Cancer* **47**: 2595-2602, 1981.
2. Seo JB, Im JG, Goo JM, Chung MJ, Kim MY. Atypical pulmonary metastases: spectrum of radiologic findings. *Radiographics* **21**: 403-417, 2001.
3. Kiryu T, Hoshi H, Matsui E, et al. Endotracheal/endobronchial metastases: clinicopathologic study with special reference to developmental modes. *Chest* **119**: 768-775, 2001.
4. Lee SH, Jung JY, Kim DH, et al. Endobronchial metastases from extrathoracic malignancy. *Yonsei Med J* **54**: 403-409, 2013.
5. Mathot L, Steninger J. Behavior of seeds and soil in the mechanism of metastasis: a deeper understanding. *Cancer Sci* **103**: 626-631, 2012.

The Internal Medicine is an Open Access article 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/>).