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Case Report

A Case of Pneumothorax Complicated by Multiple Large Pulmonary Nodules Due to *Mycobacterium Kansasii* Infection

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Abstract: We report a rare case of pulmonary infection with *Mycobacterium kansasii* complicated by pneumothorax and multiple large nodules in both lungs. A 68-year-old man presented with sudden right chest pain and dyspnea. He was diagnosed with pneumothorax on the right side and immediately treated by insertion of a chest tube and drainage. After admission, the pneumothorax was cured, but a high fever continued. A chest x-ray and computed tomography scan showed multiple large nodules with and without cavities in both lungs. We suspected malignant disease, inflammatory granulomatosis, or pneumomycosis and subsequently performed bronchofiberscopy. The results of a transbronchial lung biopsy indicated caceous necrosis surrounded by epithelioid cells, without forming distinct granulomas on histology, and the results of acid-fast bacilli smear tests were positive. *Mycobacterium* could not be detected by polymerase chain reaction. Because the patient's condition was poor, we started him on anti-*Mycobacterium* therapy: rifampin, isoniazid, and ethambutol. His condition subsequently improved. Bacterial culture confirmed the presence of *M. kansasii*, so the antibiotic therapy was continued. The patient's temperature decreased to below 37°C, and the nodules in his lungs reduced in size. In this atypical case of *M. kansasii* infection, the patient presented with severe symptoms. Bronchofiberscopy enabled prompt diagnosis and early treatment.

Key words: bronchofiberscopy, large pulmonary nodules, *Mycobacterium kansasii*, nontuberculous mycobacteria, pneumothorax

Introduction

Mycobacterium kansasii is the second most common cause of nontuberculous mycobacteria (NTM) infection in Japan. The radiographic features of *M. kansasii* infection are similar to those of other NTM infections and include multifocal bronchiectasis with clusters of small nodules and cavities. These clinical features, along with the appropriate exclusion of other diagnoses,

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Table 1. Laboratory data on admission

Peripheral blood		Blood chemistry and serology	
White blood cell count	13,750 /μl	Total protein	6.4 g/dl
Neutrophils	84.1%	Albumin	2.2 g/dl
Lymphocytes	8.8%	Blood urea nitrogen	10.6 mg/dl
Eosinophils	0.7%	Creatinine	0.69 mg/dl
Monocytes	6.3%	Glucose	81 mg/dl
Basophils	0.1%	Total cholesterol	108 mg/dl
Red blood cell count	437×10^4 /μl	Total bilirubin	1.0 mg/dl
Hemoglobin	12.7 g/dl	Lactate dehydrogenase	228 IU/l
Hematocrit	38.9%	Aspartate aminotransferase	47 IU/l
Platelets	2.8×10^4 /μl	Alanine aminotransferase	67 IU/l
Glycated hemoglobin	6.6%	Creatine kinase	85 IU/l
		Sodium	34 mEq/l
		Potassium	4.2 mEq/l
		Chloride	97 mEq/l
		C-reactive protein	28.85 mg/dl

are required for the diagnosis of *M. kansasii* infection[1, 2].

In this article, we describe a patient who was admitted to hospital with right pneumothorax and respiratory failure. This case was complicated by multiple large nodules in both lungs and severe symptoms, including high fever and exhaustion. While this was an atypical case of NTM infection, we diagnosed the patient with *M. kansasii* infection using bronchofiberscopy.

Case report

A 68-year-old man presented to our hospital with a history of several hours of acute-onset right chest pain and dyspnea. He had no relevant medical history and was a current smoker of 50 pack-years. He had been employed as a plumber.

Physical examination

The patient's body temperature was 40.5°C, blood pressure was 130/70 mmHg, and resting oxygen saturation was 87% on room air. There was no lymphadenopathy in the neck or supraclavicular regions. Chest examination revealed respiratory sound attenuation on the right side. There were no findings of note on examination of the extremities, abdomen, skin, and nerves.

Laboratory data and imaging

The patient's white blood cell count was elevated at 13,750 cells/μl, with a differential of 84.1 % neutrophils, 8.8 % lymphocytes, 6.3 % monocytes, 0.7 % eosinophils, and 0.1 % basophils. His C-reactive protein level was elevated at 28.85 mg/dl. His hemoglobin level, platelet count, renal function, and urinalysis results were normal (Table 1). Chest radiography revealed a right pneumothorax (Fig. 1a). There was a cavity in the right upper lung and multiple large nodules

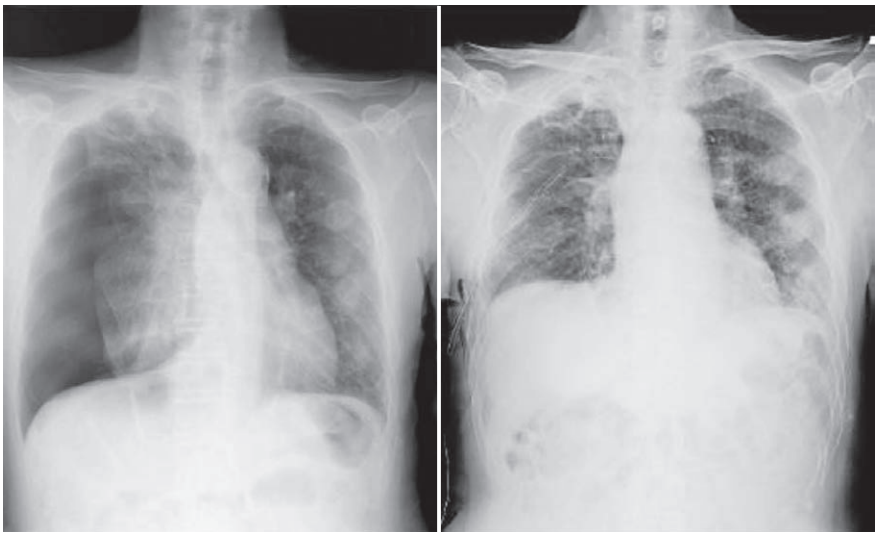

Fig. 1.
a : Chest radiography on admission showed pneumothorax, a cavity in the right lung, and large nodules in the left lung.
b : Chest radiography after drainage showed expansion of the right lung and bilateral nodules.

in the left lung. Results of chemistry studies were negative for human immunodeficiency virus (HIV), J-D-glucan, and tumor markers such as carcinoembryonic antigen, cytokeratin fragment, and pro-gastrin-releasing peptide. Results of QuantiFERON TB-2G tests were negative. Staining for acid-fast bacilli of the sputum produced a positive result (1+), but we could not detect the DNA of *M. tuberculosis* or *M. avium* complex (MAC) using polymerase chain reaction (PCR). Results of cytological examination of the sputum were negative (Table 2).

Hospital course

We placed a chest tube in the right thorax and expanded the right lung with drainage. A cavity in the right lung and multiple large nodules in both lungs were seen on the chest radiograph (Fig. 1b). We could not confirm any cavity in the nodules from the radiograph. After admission, we confirmed that there was no air leakage from the chest tube, and the tube was then removed. Computed tomography revealed cavities and multiple nodules ranging from 1 to 3 cm in diameter in both lungs (Fig. 2). Emphysematous changes were also observed in the upper lobes of the lungs, but no cysts were detected. The pneumothorax seemed to be cured, but the high fever continued and the patient felt exhausted. Broad-spectrum antibiotics — meropenem and clindamycin — were not effective. Pulmonary infection with an NTM other than MAC was possible according to the sputum test results. However, we needed a differential diagnosis from other diseases, such as granulomatosis with polyangiitis, malignant diseases including lung cancer, and pneumomycosis, because the radiological features of this case were not typical of NTM infection[1]. We performed bronchofiberscopy and analyzed the nodule in the left lung. Results of bronchofiberscopic assessment of the mucosa were normal. We then approached the

Table 2. Laboratory data on admission

Test	Result
Serology tests	
Anti-HIV antibody	Negative
Hepatitis B surface antigen	Negative
Hepatitis C virus antibody	Negative
Treponema pallidum particle agglutination	Negative
Carcinoembryonic antigen	2.3 ng/ml
Cytokeratin fragment	< 1.0 ng/ml
Pro-gastrin-releasing peptide	20.1 pg/ml
Antinuclear antibody	Negative
IgG	264.6 mg/ml
IgA	489.9 mg/ml
IgM	0.2 mg/ml
J-D-glucan	6.5 pg/ml
Blood test	
QuantiFERON TB-2G	Negative
Urine tests	
Streptococcus pneumoniae antigen	Negative
Legionella antigen	Negative
Sputum tests	
Cytology	Negative
Bacteria	Normal flora
Acid-fast bacilli	
Smear	1+(Gaffky 2)
PCR for tuberculosis	Negative
PCR for *Mycobacterium avium* complex	Negative

PCR=polymerase chain reaction.

nodule in the left lung through the bronchus of the left B3a and performed lavage, brushing, and transbronchial lung biopsy (TBLB). We selected this nodule for biopsy because the risk of pneumothorax was thought to be lower on the left side.

Histological analysis of the TBLB specimen revealed a caseous necrosis surrounded by epithelioid cells, without forming distinct granulomas. There were no findings suggestive of malignant disease. Smears from the TBLB specimen tested positive for acid-fast bacilli; however, no *M. tuberculosis* DNA or MAC DNA was detected by PCR (Table 3).

Based on these results, we diagnosed the patient with NTM infection other than MAC. We suspected that the patient might have an *M. kansasii* infection because this species has been reported to have a high prevalence, similar to that of MAC, in Japan. Thus, we started treatment with rifampin (RFP), isoniazid (INH), and ethambutol (EB) at 13 days after the patient was admitted[1, 2]. The patient's condition improved after initiation of treatment — the high fever, cough, dyspnea, and general fatigue subsided. *M. kansasii* was identified from the culture of the patient's TBLB specimen 56 days after admission. We confirmed that our diagnosis was

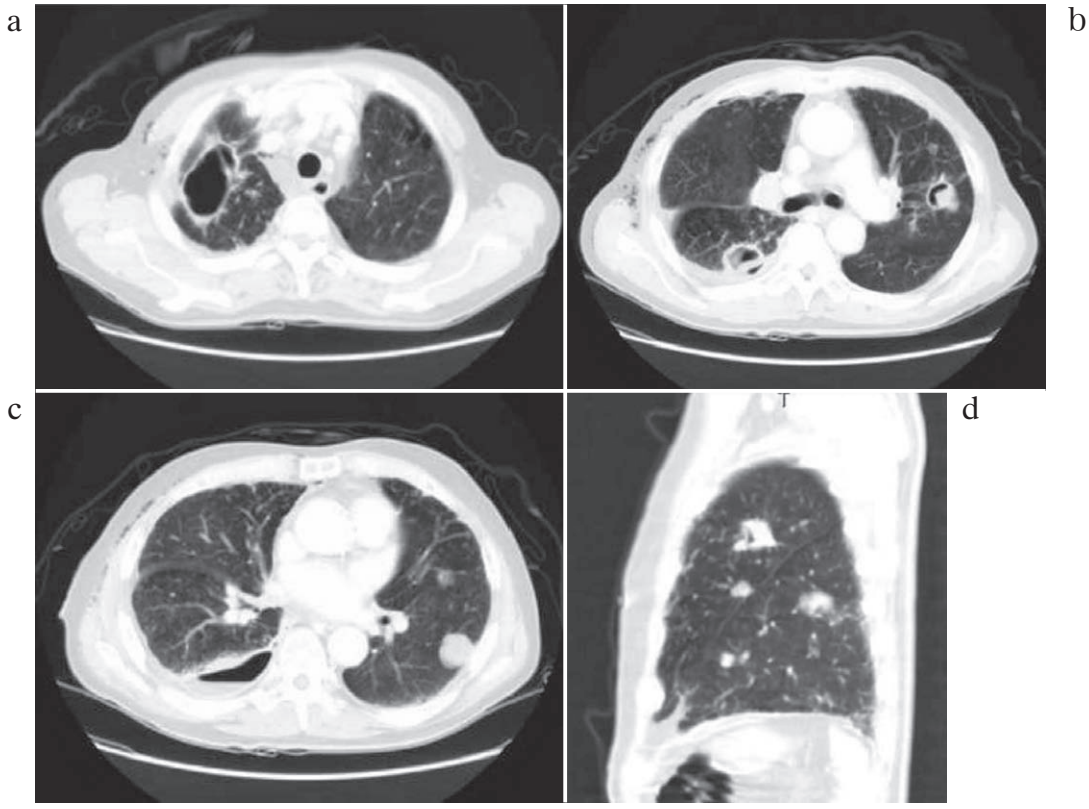

Fig. 2.
a, b, c, d : Chest computed tomography showed a cavity in the right upper lobe, and multiple bilateral nodules with and without cavities. Emphysematous changes were also observed in the upper lobes of the lungs.

compatible with the criteria in the American Thoracic Society and Infectious Diseases Society of America statement on diagnosis, treatment, and prevention of NTM diseases[1] and thus continued the treatment. The sizes of multiple large nodules were substantially reduced following treatment (Fig. 3) and the patient's temperature decreased to below 37°C. Air space was observed in the right lower lung, indicating that minor air leakage continued after a pneumothorax or cavity was newly formed in response to antibiotic therapy. All of the patient's symptoms resolved and laboratory data improved, and the patient was discharged 93 days after admission (Fig. 4).

Discussion

Our patient had a rare case of pulmonary infection with *M. kansasii* and *was* admitted with pneumothorax complicated by multiple large pulmonary nodules. The clinical characteristics were not typical of NTM infection ; however, histopathological and bacteriological assessment of the large nodule using bronchofiberscopy enabled us to make a differential diagnosis from other diseases characterized by multiple nodules. Diagnosis during the early stage of infection may improve the course of a patient's recovery from such severe symptoms.

Pneumothorax is generally considered to be a rare complication of pulmonary NTM infec-

Table 3. Results of bronchofiberscopy

Test	Result
Microscopic histopathology*	Caceous necrosis surrounded by epithelioid cells, without forming distinct granulomas; malignant findings were not observed
Cytology	Negative
Bacterial study	Normal flora
Acid-fast bacilli	
Smear	1+(Gaffky 2)
PCR for tuberculosis	Negative
PCR for *Mycobacterium avium* complex	Negative
Culture** for *Mycobacterium kansasii*	positive
Sensitivity against antibiotics***	
Isoniazid	0.2R, 1.0S
Rifampin	40S
Ethambutol	2.5S
Steptomycin	10R
PAS (paraaminosalicylic acid)	0.5R
Kanamycin	20R
Levofloxacin	1.0S
CS (cycloserine)	30S

PCR = polymerase chain reaction.

*Abnormal findings were not detected macroscopically; we performed transbronchial lung biopsy, brushing and lavage at the site of the nodule in the left upper lobe (left B3a).

**DNA-DNA hybridization.

***Antibiotic concentrations are expressed in μ g/ml; S: sensitive, R: resistant.

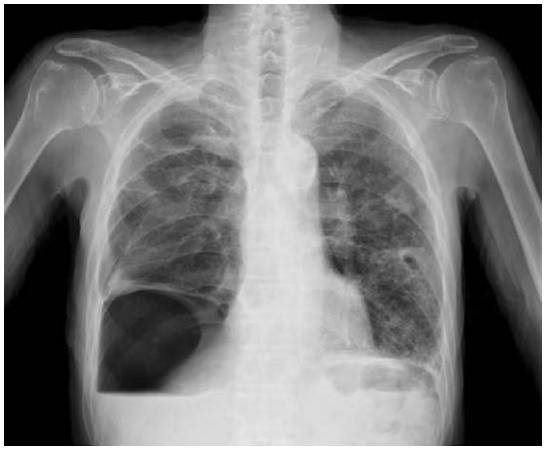

Fig. 3. Chest radiography on discharge showed fewer and smaller nodules in both lungs and airspace in the lower region of the right lung.

tion. However, recent reports have suggested that the rates of pneumothorax in patients with NTM infection range from 2.3% to 4.1%[3, 4], which is somewhat higher than expected. While the etiology of pneumothorax in NTM infection has not been clarified, this complication may arise from rupture of subpleural lesions formed by the infection, such as cavities or granulomas.

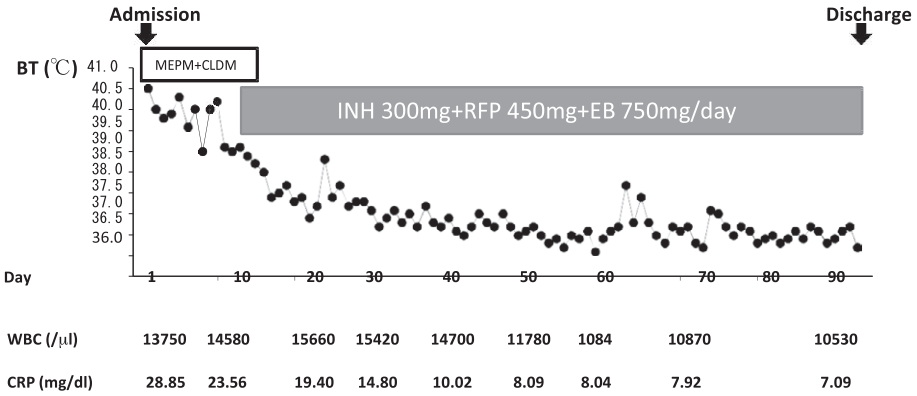

Fig. 4. The patient's clinical course : the patient had a high fever and elevated inflammatory responses on admission; initial treatment with meropenem (MEPM) and clindamycin (CLDM) were not effective ; the patient's elevated body temperature (BT), abnormal white blood cell (WBC) count, and abnormal C-reactive protein (CRP) levels resolved after initiation of antibiotic therapy with rifampin (RFP) 450 mg/day, isoniazid (INH) 300 mg/day, and ethambutol (EB) 750 mg/day ; and the patient was discharged 93 days after admission.

Rupture of the lesions could cause pneumothorax and subsequent pleuritis. In our patient, high fever and increased inflammatory responses may have been caused by underlying pleuritis, even though the pneumothorax was cured at an early stage. Unfortunately, we could not analyze the features of pleural effusion in this case.

Some investigators have indicated that when pneumothorax is a complication of NTM infection, it is incurable and has a high mortality rate[3, 4]. The present patient's condition was severe at admission, but improved after administration of antibiotics (INH, RFP, and EB). The sensitivity of *M. kansasii* to this therapy may have contributed to our ability to cure the patient. Although in vitro studies showed that the *M. kansasii* strain isolated from our patient was not completely sensitive to INH, combination therapy with INH, RFP, and EB was effective, in keeping with the guidelines we followed[1].

M. kansasii is a slow-growing photochromogenic mycobacterium classified as Runyon Group Ⅰ. It is the second most common NTM in Japan. While the radiological features of *M. kansasii* may not be very different from those of other NTM, Takahashi et al and Matveychuk et al reported that cavitation on the right upper lobe is characteristic of pulmonary infection with *M. kansasii*[5, 6]. In our patient, a cavity was also found in the right upper lobe. Thus, while this finding may be characteristic of *M. kansasii* infection, the other findings, such as the presence of multiple large nodules, were not typical. Inoue et al reported a rare case of NTM infection with multiple nodules measuring 1–2 cm in diameter in both lungs[7] ; the pathogen was *M. fortuitum*, which is classified as a Runyon Group Ⅳ bacterium. It is a rapidly growing NTM. In our case, the nodules were larger than 2 cm in diameter. Sekine et al also reported a case complicated by multiple large pulmonary nodules due to MAC, which is classified as Runyon Group Ⅲ — a slow-growing bacterium[8]. The differences between species may contribute to the characteristics of each NTM infection, but multiple nodules may occur for any NTM species.

The main reservoir of *M. kansasii* is thought to be tap water[1, 2]. Our patient had been working as a plumber and had been involved in construction of water supply structures for several decades. Therefore, it is possible that he had become infected with the bacteria at work. Chronic obstructive pulmonary disease and pulmonary emphysema have been shown to be associated with *M. kansasii* infection[5, 9]. We found that chronic obstructive pulmonary disease and smoking may have been be risk factors for *M. kansasii* infection in this patient because computed tomography imaging showed emphysematous changes, although the patient did not report signs of emphysema before admission.

In conclusion, we report an atypical case of *M. kansasii* infection complicated by pneumothorax and multiple large nodules in the lungs. Bronchofiberscopy was useful for early diagnosis and treatment.

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Conflict of interest disclosure

There are no conflicts of interest to declare.

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