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Case report

Pulmonary *Mycobacterium kyorinense* infection secondary to cavitary pulmonary tuberculosis

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ABSTRACT

Mycobacterium kyorinense (*M. kyorinense*) was first reported in patients with pulmonary infection or lymphadenitis in 2009. To date, fewer than 20 cases of pulmonary or extra-pulmonary infections have been reported with the bacterium, and the clinical features remain unclear. We report a case of pulmonary *M. kyorinense* infection in a 45-year-old man who had a history of cavitary pulmonary tuberculosis seven years ago. The patient visited a hospital due to hemosputum and a prolonged productive cough. Chest computed tomography revealed large and thick-walled cavities, with surrounding parenchymal infiltration in the right upper and lower lung lobes. The microbiological diagnosis of *M. kyorinense* was based on positive culture results from multiple respiratory tract specimens. The patient's treatment started with antimycobacterial medicines, clarithromycin, moxifloxacin, and intravenous amikacin, in accordance with the drug susceptibility profile and previous case reports. The treatment stabilized the patient's symptoms and improved the thoracic imaging. In addition, the sputum culture was negative after the treatment. We reviewed the literature and summarized the clinical features of *M. kyorinense* infection in 18 patients. All patients with extrapulmonary infections were immunocompromised. In contrast, pulmonary infection occurred in immunocompetent patients who often had a predisposing lung disease. Cavitary lesions were observed at diagnosis only in patients with prior cystic or cavitary lung disease, including pulmonary tuberculosis. This study contributes to the body of case knowledge of *M. kyorinense* infection and summarizes the clinical features in the literature.

1. Introduction

Mycobacterium kyorinense (*M. kyorinense*) is a non-pigmented, slow-growing mycobacterium that was first reported in 2009 [1]. To date, less than 20 cases of isolation of this bacterium have been reported in respiratory and extra-respiratory samples, predominately in Japan [1–9]. The clinical features of this rare nontuberculous mycobacterial (NTM) infection remain unclear. This study describes a case of pulmonary *M. kyorinense* infection in an immunocompetent patient with a history of cavitary pulmonary tuberculosis. We reviewed the literature and summarized the clinical features of this rare infection.

2. Case

A 45-year-old man presented with hemosputum, following a persistent productive cough and serous sputum for five months. The patient had a history of cavitary pulmonary tuberculosis that was successfully treated with rifampicin, isoniazid, ethambutol, and pyrazinamide seven years ago. The patient was slightly lean (body mass index 20.3) and smoked ten cigarettes a day. Otherwise, he was immunocompetent and without diabetes mellitus, human immunodeficiency virus infection, malnutrition, or alcohol abuse. Chest computed tomography (CT) imaging revealed large cavitary lesions with thick walls and surrounding parenchymal infiltrations in the right upper and lower lung lobes (Fig. 1A, D, and G). No parenchymal lung disease was observed in the other lungs. Unfortunately, comparable radiological images were unavailable during the prior pulmonary tuberculosis, but the medical records revealed extended pulmonary cavities. Acid-fast smear and polymerase chain reaction (PCR) tests for *Mycobacterium tuberculosis* (*M. tuberculosis*) and *Mycobacterium avium/intracellular* (*M. avium/intracellular*) in the sputum were negative. The lavage fluid obtained from a cavity in the

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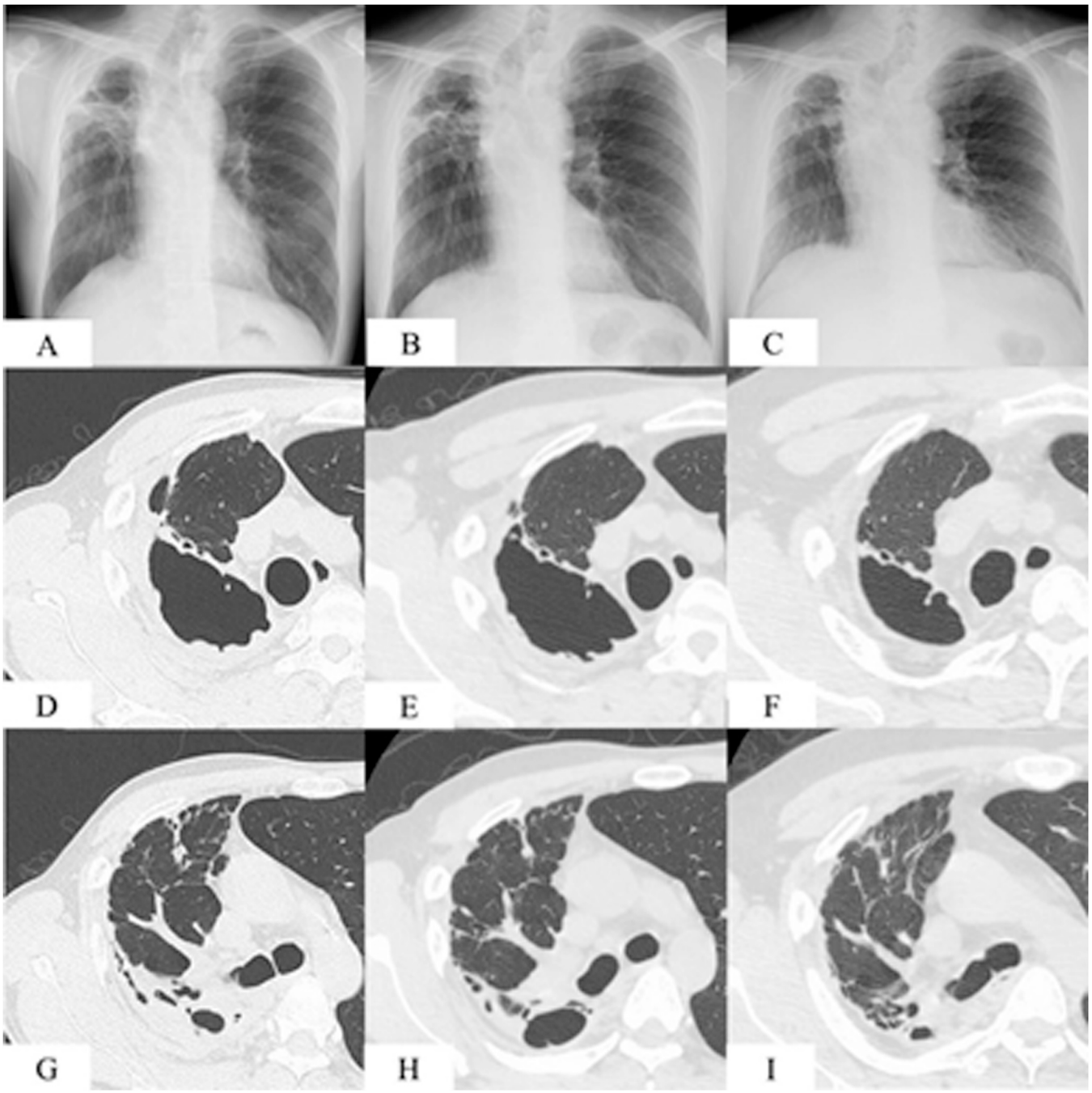

Fig. 1. Radiological findings at diagnosis and during treatment. Chest radiography (A) and computed tomography (D, G) at the time of diagnosis showed large cavitary lesions with thick walls in the right upper and lower lung lobes. Peri-cavitary parenchymal infiltration was noted in the lower lung lobe (G). Following the treatment, the lower lung initiation was attenuated on chest radiography (B) and CT (H), while the cavity sizes were not significantly reduced (E, H) in four months. The cavity was reduced in size, with thinner walls, and the parenchymal infiltration near completely disappeared on the chest radiography (C) and CT (F, I) at twenty-four months.

right upper lobe using a bronchoscope was positive for the acid-fast bacillus smear, but was negative for PCR tests for *M. tuberculosis* or *M. avium/intracellular.* These findings suggest that the patient was infected with an NTM other than *M. avium/intracellular*. Later, the acid-fast bacillus culture was positive in the bronchial lavage fluid and two separate sputa, and *M. kyorinense* was identified by mass spectrometry. The patient met the microbiological criteria for pulmonary NTM infection based on the American Thoracic Society guidelines [10].

The patient was referred to our hospital for subsequent care. While an optimal regimen for the treatment of *M. kyorinense* has not been established in the guidelines, favorable outcomes have been previously reported with a combination therapy of macrolides, aminoglycosides, and fluoroquinolones, based on drug susceptibility profiles [2,4,5]. The drug susceptibility profile in the present case was similar to those reported previously: low minimum inhibitory concentrations (MICs) for amikacin, clarithromycin, and levofloxacin, and high MICs for rifampicin and ethambutol. Antimycobacterial medications were prescribed with clarithromycin (800 mg daily), moxifloxacin (400 mg daily), and intravenous amikacin (800 mg three times a week). Following the treatment, symptoms improved and the lung infiltration was attenuated on CT at four months (Fig. 1B, E, and H). In addition, the sputum culture results were converted to negative in four weeks or later following

Table 1
Summary of reported cases.

Respiratory tract infection						
Age, sex	Country	Pulmonary comorbidity	Extra-pulmonary comorbidity	Sample	Comments	Ref
89, M	Japan	COPD, Pulmonary tuberculosis	Bladder carcinoma, Prostate carcinoma	Sputum		1
70, M	Japan	–	–	Sputum		1, 2
81, M	Japan	–	–	BALF		2
67, M	Japan	–	–	BALF		2
72, M	Japan	–	–	Sputum		2
66, M	Japan	–	–	Sputum		2
60, M	Japan	–	–	Sputum		2
26, M	Brazil	Lung fibrotic lesion	–	Sputum		3
63, M	Japan	Lung cancer, COPD	–	Sputum	Cavity (at *a* diagnosis)	4
66, M	Japan	–	Weight loss, Gastric ulcer	Sputum	Cavity (after *a* diagnosis)	5
85, M	Japan	Lung resection	–	Sputum	Cavity (after *a* diagnosis)	6
46, F	Australia	Post pleurodesis (pneumothorax)	Anxiety disorder	Sputum, BALF	Cavity (at *a* diagnosis)	7
55, F	Indian	Pulmonary tuberculosis	DCM, IHD, HTN, Weight loss	Sputum	Cavity (at *a* diagnosis)	8
40, M	Japan	Pulmonary tuberculosis	–	Sputum, BALF	Cavity (at *a* diagnosis)	Present
Extra-pulmonary infection						
Age, sex	Country	Pulmonary comorbidity	Extra-pulmonary comorbidity	Sample	Comments	Ref
64, F	Japan	–	Brest cancer	LN drainage		1, 2
50, M	Japan	–	MDS	LN drainage		2
48, F	Japan	–	RA, SLE	Synovial fluid		2
48, M	Japan	–	Follicular lymphoma, Post BMT, GVHD	Pleural effusion		9

BALF, bronchoalveolar lavage fluid; BMT, bone marrow transplantation; COPD, chronic obstructive lung disease; DCM, dilated cardiomyopathy; GVHD, graft *versus* host disease; HTN, hypertension; IHD, ischemic heart disease; LN, lymph node; MDS, myelodysplastic syndrome; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

the treatment. Amikacin was stopped at the end of four months, and clarithromycin and moxifloxacin were maintained for twenty-four months. The patient was in good health and his radiological findings improved, with reduced cavity sizes, thinner walls, and further attenuated infiltration (Fig. 1C, F, and I). Surgical resection of the residual cavities was an option, but might require pneumonectomy; therefore, the patient refused the treatment.

3. Discussion

We report a case of pulmonary *M. kyorinense* infection in an immunocompetent patient with a history of cavitary pulmonary tuberculosis. The patient had large cavities with thick walls, and *M. kyorinense* was isolated. Combination therapy with clarithromycin, moxifloxacin, and amikacin resulted in a favorable outcome.

M. kyorinense was first described by Okazaki et al. in 2009 [1] and is currently classified as a non-pigmented, slow-growing NTM. So far, as few as 17 cases of isolation of this bacterium have been reported in 13 respiratory tract specimens, two lymph node drainages, one pleural effusion, and one synovial fluid [1–9]. The reported pulmonary (n = 14, including the present case) and extra-pulmonary (n = 4) infections are summarized in Table 1. The respective patient profiles were characterized by a male (14/18 cases, 77.8%) and Japanese (15/18 cases, 83.3%) predominance, with a wide age range (median: 63.5, 26–89-years-old). Patients with extra-pulmonary infections were relatively younger than those with pulmonary infections (median: 49 *vs* 66-years-old). It remains uncertain whether Japanese predominance was attributable to geographic differences or due to biases such as medical circumstances. Patients with pulmonary infection were mostly immunocompetent, whereas all patients with extra-pulmonary infection had comorbidities that potentially compromised their immune status, including hematological malignancies, breast cancer, or rheumatic disorder (Table 1). These findings suggest that immunocompromised status was associated with extra-pulmonary infections in *M. kyorinense*, similar to other NTMs [11,12]. Notably, predisposing lung diseases have been common in patients with pulmonary *M. kyorinense* infection; half of the patients had parenchymal diseases (n = 3), pulmonary tuberculosis (n = 3), lung resection (n = 2), or refractory pneumothorax requiring repeated pleurodesis (n = 1) (Table 1). Patients with pulmonary *M. kyorinense* infection but predisposing lung diseases (n = 7) were equal or over 60-years-old, implying that aging might influence disease susceptibility. Cavity formation was described in six cases, with four cases of cavity formation present at the time of diagnosis [4, 7, 8, and the present case] and the two after diagnosis [5,6]. All cases with cavity formation at the time of diagnosis had prior cystic or cavitary lung diseases, suggesting that secondary infection of the pre-existing cavities was common. In the present case, the medical records revealed extended cavities due to pulmonary tuberculosis seven years ago. Structural lung diseases or scarring related to prior pulmonary tuberculosis are known risk factors for secondary NTM infection [10]. A high prevalence of prior pulmonary tuberculosis has been reported in patients with NTM infection (34.4%) in the Singaporean population [13]. Nevertheless, it remains to be elucidated whether *M. kyorinense* preferentially infects the pre-existing pulmonary cavity or scarring.

As described above, an optimal regimen for *M. kyorinense* infection has not yet been established. The drug susceptibilities *in vitro* were more than comparable among the previous and present cases: low MICs to macrolide, fluoroquinolones, and aminoglycosides, and high MICs to rifampicin, ethambutol, and isoniazid. Interestingly, *M. kyorinense* has a unique sequence in *rpoB*, a gene linked to rifampicin resistance in *M. tuberculosis* [2]. It should be noted that the treatment strategy based on the susceptibility profile conferred excellent improvement to the patients in the previous [2,4,5] and the present studies. In contrast, Ohnishi et al. reported that all patients treated with rifampicin, ethambutol, and isoniazid presented resistance to *M. kyorinense in vitro*, which resulted in unfavorable outcomes [2].

In summary, we report a case of pulmonary *M. kyorinense* infection secondary to cavitary pulmonary tuberculosis. Based on the literature review, the present case demonstrated typical clinical features of pulmonary infection in an immunocompetent patient with pre-existing cavities. In addition, the literature review showed that the forms of infection were associated with the host immune status, predisposing lung conditions, and, possibly, aging. Drug susceptibilities *in vitro* were reliable when considering the treatment regimen.

Ethical approval

Not applicable

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CRediT authorship contribution statement

Genta Nagao worked on the manuscript preparation. **Shinichi Okuzumi** and **Tomoo Kakimoto** edited the manuscript. **Naoto Minematsu** worked on the clinical care of the patient and edited the manuscript.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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