Pulmonary *Mycobacterium massiliense* Disease with Septicemia during Immunosuppressive Treatment

Yoshihiro Kobashi¹, Keiji Mouri¹, Yasushi Obase¹, Naoyuki Miyashita¹,
Kazue Nakanaga² and Mikio Oka¹

Abstract

A 75-year-old man with interstitial pneumonia due to ANCA-related vasculitis requiring immunosuppressive treatment was admitted to our hospital because of fever and rapidly progressive dyspnea. Chest CT showed diffuse ground-glass opacity with infiltration shadow in the bilateral lungs. We established a definitive diagnosis by isolating *Mycobacterium massiliense* on culture examination of acid-fast bacilli from peripheral blood and sputum. We began to administer CAM, LVFX, AMK, IPM/CS to this patient two weeks after admission. However, he died of respiratory failure and septic shock. There are few case reports of pulmonary lesion with septicemia due to *Mycobacterium massiliense*.

Key words: *Mycobacterium massiliense*, immunosuppressive treatment, septicemia

(Intern Med 50: 1069-1073, 2011)

(DOI: 10.2169/internalmedicine.50.4733)

Introduction

Rapidly growing mycobacterium infections are increasing in the United States (1), but the specific organisms are difficult to identify by conventional methods. *Mycobacterium massiliense* (*M. massiliense*) has been distinguished from *Mycobacterium abscessus* (*M. abscessus*) by sequencing of a 723-bp fragment of the RNA polymerase β subunit (*rpoB*) gene (2). Because this technique is available in relatively few clinical laboratories, cases of infection with *M. massiliense* may be mistakenly attributed to *M. abscessus*.

We encountered a peculiar case in which *M. massiliense* was isolated from peripheral blood and sputum during immunosuppressive treatment for ANCA-related vasculitis. To our knowledge, this is the second reported case of lethal pulmonary *M. massiliense* disease with septicemia (3).

Case Report

A 75-year-old man was admitted to our hospital because of fever and rapidly progressive dyspnea. He had been diagnosed as having interstitial pneumonia due to ANCA-related

vasculitis three months earlier and administration of immunosuppressive drugs was immediately initiated (methylprednisolone 1 g/day for three days and subsequently prednisolone 40 mg/day for two weeks) by the previous hospital. Thereafter, the dose of prednisolone was decreased by 5 mg/day every two weeks and maintained at 20 mg/day until admission to our hospital. His clinical findings and abnormal radiograph findings were improved. Prevention therapy for immunosuppressive treatment was performed with sulfamethoxazole/trimethoprim (ST), but not isoniazid (INH) during the administration of prednisolone. He had a smoking history of 20 cigarettes/day for forty years. On physical examination, coarse crackle was auscultated over the bilateral lung fields. Laboratory data on admission is shown in Table 1. Slight anemia, moderate inflammatory response, hypoalbuminemia, mild liver and renal dysfunction, and severe hypoxia were recognized. Purified protein derivatives (PPD) and QuantiFERON TB-Gold test showed negative responses. Chest radiograph showed diffuse interstitial shadows in the bilateral lung fields with infiltration shadows in the bilateral middle and lower lung fields (Fig. 1). Computed tomography (CT) of the chest showed diffuse linear and reticular shadows in the bilateral lungs with consolidation shadows in the bilat-

¹Division of Respiratory Diseases, Department of Medicine, Kawasaki Medical School, Japan and ²Leprosy Research Center, National Institute of Infectious Diseases, Japan

Received for publication October 25, 2010; Accepted for publication January 17, 2011

Correspondence to Dr. Yoshihiro Kobashi, yoshihiro@med.kawasaki-m.ac.jp

Table 1. Laboratory Data on Admission

Peripheral blood		Serology	
RBC	355 × 10 ⁴ /μL ↓	ANF	(—)
Hb	11.1 g/dL ↓	RF	<20u/mL
Ht	33.0% ↓	PR3—ANCA	<10EU
WBC	9030/μL	MPO—ANCA	≥640EU ↑
Seg	90%	CH ₅₀	>58.0u/mL ↑
Eo	1%	KL-6	392u/mL
Lym	5%	SP-D	118ng/mL
Mono	4%	β-D-glucan	10.8pg/mL
Plate	32.0 × 10 ⁴ /μL		
Chemical screening		Arterial blood gas	
TP	7.1g/dL	pH	7.424
Alb	2.8g/dL ↓	PaO ₂	67.0mmHg ↓
AST	86u/L ↑	PaCO ₂	33.0mmHg
ALT	55u/L ↑	HCO ₃ [−]	21.1mEq/L
Bil (T)	0.9mg/dL	BE	−2.4mEq/L
ALP	214u/L		
LDH	351u/L ↑	Urine	
ChE	98u/L ↓	Protein	(±)
r-GTP	52u/L	Blood	(++)
Crn	1.39mg/dL ↑	Glucose	(—)
BUN	80mg/dL ↑	RBC	30~49/H μF
UrA	9.0mg/dL ↑	WBC	1~4/H μF
CRP	10.06mg/dL ↑	PPD	0 × 0 / 0 × 0
Na	144mEq/L	QFT-2G	(—)
K	3.7mEq/L		
Cl	110mEq/L		

PPD: purified protein derivatives, QFT-2G, QuantiFERON-2G

Figure 1. Chest radiograph showed diffuse interstitial shadows in the bilateral lung fields with infiltration shadows in the bilateral middle and lower lung fields. **Figure 2.** Computed tomography (CT) of the chest showed diffuse linear and reticular shadows in the bilateral lungs with consolidation shadows in the bilateral lower lobes.

eral lower lobes (Fig. 2).

We present the clinical course of this patient in Fig. 3.

We initially diagnosed the patient as having bacterial pneumonia and exacerbation of interstitial pneumonia with ANCA-related vasculitis. Therefore, two antimicrobial drugs (MEPM and CPMX) and steroid pulse therapy (methylprednisolone 1 g/day for three days) were administered to this

Figure 3. Clinical course

patient after admission. Although there were no common causative microorganisms such as *Streptococcus pneumoniae*, smear examination of acid-fast bacilli from the peripheral blood and sputum was positive (3+). We initiated the antituberculous treatment because mycobacterial infection was suspected on day seven of admission. However, polymerase chain reaction (PCR) examination for *Mycobacterium tuberculosis* (*M. tuberculosis*), *M. avium* and *M. intracellulare* was all negative. Gram-positive bacilli were identified five days later from routine blood culture and acid-fast bacilli were cultured two weeks later on Ogawa egg medium slants. We changed the antituberculous treatment to combination chemotherapy consisting of clarithromycin (CAM), amikacin (AMK), imipenem/cilastatin (IPM/CS) and levofloxacin (LVFX) because of the rapidly spreading mycobacterial infection thought to be caused by *M. abscessus*. Finally, genotypic analysis of 16S rRNA, *hsp65*, *rpoB* genes and the 16S-23S rRNA internal transcribed spacer sequence of the isolates from peripheral blood and sputum identified *M. massiliense* (genotype analysis of *rpoB* genes: Fig. 4). Drug sensitivity test using the Brothmic NTM method (Japan) for *M. massiliense* was characterized by high MIC to most antimicrobial drugs tested. The isolate was sensitive only to clarithromycin (CAM) (Table 2). However, the clinical response was poor and the patient died of respiratory failure one week after the initiation of combination therapy. Because we could not perform an autopsy, it was difficult to determine the cause of respiratory failure in this patient.

Discussion

We report the second case of pulmonary *M. massiliense* disease with septicemia during immunosuppressive therapy (3). *M. massiliense* is a rapidly growing mycobacterium species, similar to *M. abscessus*, *M. bolletii* and *M. chelonae*. Therefore, although it was previously difficult to distinguish these four strains, genetic sequencing using *rpoB* (Fig. 4), *hsp65* and 16S-23S rRNA ITS gene sequence analyses has facilitated discrimination of these four strains (4-7). In this patient, because the sequencing showed 100% homology with *M. massiliense*, we correctly identified the causative microorganism.

Regarding the radiological features of pulmonary disease caused by rapidly growing mycobacteria (the causative microorganism was *M. abscessus* in most of these cases), Griffith et al indicated that the most frequent patterns were interstitial, interstitial/alveolar, and/or reticulonodular, while cavitation was an unusual consequence of rapidly growing mycobacterial disease occurring in only 16% of cases. The extension of the lesion was typically multilobar with the greater proportion involving three or more lobes and demonstrating bilateral involvement (8). In recent reports, radiological findings of pulmonary *M. abscessus* disease showed bilateral reticulonodular shadow patterns without cavity on chest radiograph and bronchiectatic lesion and multiple small nodular shadows (<5 mm) on chest CT (9, 10). These findings resembled those of cases showing pulmonary *Mycobacterium avium* complex (MAC) disease. Although there are no reports describing the radiological findings of pulmo-

method (Kyokuto Pharmaceutical Company, Tokyo, Japan). However, the results were not sufficiently reliable except that CAM for NTM disease and only CAM showed a sensitive MIC for pulmonary *M. massiliense* disease with septicemia. In the present case, the clinical response to combined therapy (CAM, IPM/CS, AMK, LVFX) was poor despite administration of a treatment regimen similar to that for *M. abscessus* disease according to the ATS guidelines (11). Although we previously reported cases of pulmonary *M. abscessus* disease showing a good clinical response to combined therapy (12), the recommended therapy for *M. massiliense* disease has not yet been established in the ATS guidelines because there have been so few cases of pulmonary *M. massiliense* disease accumulated to date. Because cases of infection with *M. massiliense* are suspected to have been included among reported cases of *M. abscessus* infection, we think that the frequency of isolating *M. massiliense* will increase with advances in microbiological technology in the future.

In conclusion, we encountered a case of severe pulmonary *M. massiliense* disease with septicemia that required differentiation from pneumonia during immunosuppressive treatment for ANCA-related vasculitis. It is important that we pay attention to the appearance of rapidly growing mycobacterial infection such as not only *M. abscessus* but also *M. massiliense* during long-term immunosuppressive treatment and perform repeated fast-acid bacilli examinations even if the patient shows atypical clinical findings such as in this case.

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

References

1. Hanna BA, Ebrahimzadeh LB, Elliot MA, et al. Multicenter evaluation of the BACTEC MGIT 960 system for recovery of mycobacteria. *J Clin Microbiol* **37**: 748-752, 1999.
2. Adekambi T, Colson P, Drancourt M. *rpoB*-based identification of nonpigmented and late-pigmenting rapidly growing mycobacteria. *J Clin Microbiol* **41**: 5699-5708, 2003.
3. Tortoli E, Gabini R, Galanti I, Mariottini A. Lethal *Mycobacterium massiliense* sepsis, Italy. *Emerg Infect Dis* **14**: 984-985, 2008.
4. Adekambi T, Reynaud-Gaubert M, Greub G, et al. Amoebal coculture of "*Mycobacterium massiliense*" sp. Nov. from the sputum of a patient with hemoptoic pneumonia. *J Clin Microbiol* **42**: 5493-5501, 2004.
5. Simmon KE, Pounder JI, Greene JN, et al. Identification of an emerging pathogen, *Mycobacterium massiliense*, by *rpoB* sequencing of clinical isolates collected in the United States. *J Clin Microbiol* **45**: 1978-1980, 2007.
6. Kim HY, Yun YJ, Park CG, et al. Outbreak of *Mycobacterium massiliense* infection associated with intramuscular injections. *J Clin Microbiol* **45**: 3127-3130, 2007.
7. Viana-Niero C, Lima KV, Lopes ML, et al. Molecular characterization of *Mycobacterium massiliense* and *Mycobacterium bolleti* in outbreaks of infections after laparoscopic surgeries and cosmetic procedures. *J Clin Microbiol* **46**: 850-855, 2008.
8. Griffith DE, Girard WM, Wallace RJ. Clinical features of pulmonary disease caused by rapidly growing mycobacteria. An analysis of 154 patients. *Am Rev Respir Dis* **147**: 1271-1278, 1993.
9. Daley CL, Griffith DE. Pulmonary diseases caused by rapid growing mycobacteria. *Clin Chest Med* **23**: 623-632, 2002.
10. Daehee H, Won-Jung KH, Chin AY, et al. Radiographic and CT findings of nontuberculous mycobacterial pulmonary infection caused by *Mycobacterium abscessus*. *AJR* **181**: 513-517, 2003.
11. Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med* **175**: 367-416, 2007.
12. Kobashi Y, Oka M. Clinical analysis of *Mycobacterium abscessus* pulmonary infection in our hospital. *Kekkaku* **85**: 1-6, 2010 (in Japanese).