A case of respiratory infection possibly caused by *Mycobacterium triviale*: Current problems on diagnostic and therapeutic strategies

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**Abstract**

*Mycobacterium triviale* is a subspecies of the *Mycobacterium terrae* complex, which rarely causes disease in humans. We encountered a case of respiratory infection, possibly caused by *M. triviale*, which was successfully treated by levofloxacin and clarithromycin. Although DNA-DNA hybridization identified *M. triviale* in one of three samples, clinical validations convinced us that it was the pathogen. 16s ribosomal RNA sequencing would have been reliable and ideal to perform in this case, although it is not covered by the insurance system in Japan. Nevertheless, this experience remains to be instructive because the clinical course, guidelines on the diagnosis, and therapeutic strategies for respiratory infections caused by *M. triviale* are not well-known or have not been established. Awareness of the possibility of respiratory infections caused by *M. triviale* and further collection and analysis of its predisposing conditions are essential.

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1. Introduction

*Mycobacterium triviale* is a subspecies of the *Mycobacterium terrae* complex that rarely causes disease in humans. *M. triviale* is a rare subspecies that was reported to account for only 0.09% of isolated non-tuberculous mycobacteria (NTM) [1]. To the best of our knowledge, only 5 cases of respiratory infection caused by *M. triviale* have been reported, including the present case [2–5]. These NTM cases are extremely rare; even if they were accumulated on a global scale, strategies on diagnosis and treatment will still remain controversial. We encountered a case of respiratory infection that was possibly caused by *M. triviale* and which was successfully treated by levofloxacin (LVFX) and clarithromycin (CAM), consistent with previous reports on good prognosis with medication. Given the rarity of *M. triviale* infections in humans, this case report may be of contribution to future establishment of diagnostic and treatment methods.

2. Case presentation

A 75-year-old woman was admitted to our institution with a 2-week history of cough, sputum production, and fever. She had undergone right middle and right lower lobectomy for a double lung cancer 13 years earlier and recently underwent chemotherapy for tumor recurrence in the right thoracic cavity just before admission. On physical examination, the patient was thin with a body mass index of 16.9. She was febrile, with a body temperature of 37.8 °C, but all other vital signs were normal. Vesicular sounds were weak on right chest auscultation. Chest X-ray and computed tomography (CT) revealed that compared with a previous study, there was a new contractive consolidation with cavity in the remaining right upper lobe (Fig. 1). Laboratory tests showed elevation of inflammatory markers: white blood cell count (WBC) 9180/μL and C-reactive protein (CRP) 9.87 mg/dL. We clinically diagnosed bacterial pneumonia; intravenous imipenem (IPM)/cilastatin (CS) was administered, but symptoms did not improve. Since fungal infection was a differential diagnosis of the CT findings, we added micafungin (MCFG). Treatment with IPM/CS and MCFG was continued for 2 weeks, but there was no improvement.

On further test, 3 sputum acid-fast bacillus (AFB) smears yielded...
a positive result of 2+, but polymerase chain reaction for tuberculosis and Mycobacterium avium complex (MAC) were both negative. We assumed the causative organism to be NTM other than MAC, including the progressive and rapidly growing Mycobacterium abscessus. With this in mind, we continued IPM/CS at 1000 mg/day and started LVFX at 250 mg/day and CAM at 800 mg/day. Symptoms, laboratory tests, and chest X-ray and CT improved after initiation of LVFX and CAM. AFB culture of all 3 sputum specimens was positive for NTM. DNA-DNA hybridization (DDH mycobacteria; Kyokuto Pharmaceuticals, Tokyo, Japan) identified M. triviale in one sputum specimen, but could not detect the specific NTM from the other two specimens. We assumed negative conversion of sputum AFB smear, and culture was noted 2 weeks after initiating pharmacotherapy with LVFX and CAM. We considered that the pathogenic bacteria do not contradict M. triviale by the result of DNA-DNA hybridization and the clinical course.

We suggested additional intake of anti-tuberculosis drugs, but the patient declined and we reluctantly continued treatment with only LVFX and CAM for 12 months; IPM/CS were discontinued after symptom resolution. Twelve months after completing pharmacotherapy with LVFX and CAM, there have been no clinical manifestations of recurrence and sputum AFB smear and culture have remained negative.

3. Discussion

We encountered a case of respiratory infection caused by M. triviale, an extremely rare pathogenic organism in humans. M. avium and M. intracellulare are common species that account for about 80% of all detected NTM cases, whereas about 150 rare bacterial species comprise the remaining 20% [6,7]. For these uncommon NTM species, much information has been accumulated for the major organisms including M. kansasii, M. abscessus, and M. fortuitum, but little is known about the other rare NTMs.

M. triviale, a subspecies of M. terrae complex, rarely causes disease in humans. In fact, this species has been reported to account for only 0.09% of isolated NTMs at a single Japanese medical institution [1]. Although a small number of reports has demonstrated the efficacy of anti-tuberculosis and macrolide-based antibacterial drugs against M. triviale [3,4], diagnostic and treatment methods for this pathogen have yet to be fully elucidated.

To the best of our knowledge, only 5 cases of M. triviale have been reported, including this case [2–5]. Table 1 shows a summary of these cases. The age of the patients widely range from 6 months to 75 years. Women were affected more often than men, with a ratio of 4:1. Three of the five cases involved respiratory infections, indicating that the respiratory tract was a relatively common site of M. triviale infection. All patients responded well to a combination of conventional anti-tuberculosis drugs and antibiotics and had good prognoses. In this present case, our patient responded well without recurrence after taking only LVFX and CAM. This regimen may be a valid choice for the treatment of M. triviale for patients who may not tolerate high doses of anti-tuberculosis drugs. However, it is essential to accumulate further evidence, especially regarding the

**Abbreviations**

| Abbreviation | Description |
|--------------|-------------|
| AFB          | an acid-fast bacillus |
| CAM          | clarithromycin |
| CRP          | C-reactive protein |
| CT           | computed tomography |
| IPM/CS       | imipenem/cilastatin |
| LVFX         | levofloxacin hydrate |
| MAC          | mycobacterium avium complex |
| MCFG         | micafungin |
| NTM          | non tuberculosis |
| WBC          | white blood cell |

Fig. 1. Chest X-ray and CT before treatment. A) Chest X-ray before admission shows volume loss on the right lung due to right middle lobe and right lower lobe lobectomy. B) Chest X-ray on admission shows apparent consolidation in the right lung field. C) Chest computed tomography before admission shows volume loss on the right lung due to right middle lobe and right lower lobe lobectomy. D) Chest computed tomography on admission shows contractive consolidation with a cavity in the right upper lobe.
potential for drug resistance.

Diagnosis of rare NTM is difficult. Although we identified *M. triviale* from DNA-DNA hybridization in only one specimen, we strongly believe that *M. triviale* was the pathogen in this case because of the following reasons: 1) AFB smears and culture tests of sputum were positive in 3 of 3 specimens; 2) the quantity grade of AFB smear was 2+ for all 3 specimens; 3) the timing of improvements in clinical symptoms, laboratory and radiologic findings, and negative conversion of AFB smear tests matched the timing of initiation of LVFX and CAM; 4) no other evidence suggested other diseases and pathogens; and 5) unlike MAC, *M. triviale* is rarely a contaminant on culture. Although 16S ribosomal RNA sequencing analysis may yield a conclusive diagnosis [8,9], this was not performed in the present case. Performance of these additional tests should be considered when infection by rare NTM is suspected; however, these tests are not commercially available and not covered by insurance in Japan. At present, the clinical features, diagnostic methods, and treatment strategies for *M. triviale* respiratory infection are not yet fully elucidated. Awareness of the possibility of this condition is important and further collection and analysis of suspected cases are mandatory.

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**Fig. 2.** Chest X-ray and CT after treatment. A) Chest X-ray after medication shows resolution of the consolidation in the right lung field. B) Chest computed tomography after pharmacotherapy shows resolution of the contractile consolidation in the right upper lobe.

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**Table 1.** Summary of previously reported cases of *Mycobacterium triviale*.

| Report year | Age/Gender | Symptoms | Comorbidity | Site of infection | Treatment | Duration of treatments | Prognosis |
|-------------|------------|----------|-------------|------------------|-----------|-----------------------|-----------|
| 1974        | 6 months Male | Fever    | None | Left hip joint | RFP + INH + CAM | N/A            | recovered |
| 2002        | 47 years Female | None    | Progressive ossifying peritoneal peritonitis | Lung | RFP + INH + PZA + LVFX | N/A            | recovered |
| 2007        | 51 years Female | Chronic peritonitis | Peritoneal dialysis | Peritoneum | RFP + INH + PZA + LVFX | N/A            | recovered |
| 2011        | 2 years Female | Cough, sputum | Bronchial asthma | Lung | RFP + EB + CAM + CPFX | N/A            | recovered |
| 2015 (this case) | 75 years Female | Cough, fever | Lung cancer | Lung | CAM + LVFX | 12 months | recovered |

RFP: rifampicin, INH: isoniazid, CAM: clarithromycin, PZA: pyrazinamide, EB: ethambutol hydrochloride, CPFX: ciprofloxacin hydrochloride, LVFX: levofloxacin hydrate, N/A: not available.
In conclusion, we reported a rare case of respiratory infection caused by *M. triviale* that was successfully treated by LVFX and CAM. Consistent with previous reports, prognosis of this condition was good after medications. 16s ribosomal RNA sequencing should be considered for conclusive diagnosis when rare infections by NTM are suspected. Collection and analysis of suspected cases are mandatory for future establishment of diagnostic and therapeutic strategies.

**Conflict of interest**

None declared.

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