CASE REPORT

A Case Report of Bursitis, Bacteremia, and Disseminated Infection of *Mycobacteroides (Mycobacterium) abscessus* subsp. *massiliense*

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Abstract:

We herein report a 59-year-old woman with a 2-year history of chronic bursitis of the hand who took 50 mg/day prednisolone for several autoimmune diseases. *Mycobacteroides abscessus* subsp. *massiliense* was isolated from the abscess and blood culture. Combination therapy (imipenem/cilastatin, amikacin, and clarithromycin) was administered for a month. Two months later, *M. massiliense* was detected from a blood culture again, and disseminated lesions were found. Clarithromycin and sitafloxacin were administered following eight weeks of the same regimen. Six months after the diagnosis, *M. massiliense* was isolated from a blood culture, and she expired due to multiple organ failure.

Key words: *Mycobacterium abscessus*, bursitis, bacteremia, disseminated infection

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Introduction

In Japan, the frequency of detection of nontuberculous mycobacteria (NTM) was reported to be in the order of *Mycobacterium avium-intracellulare* complex (MAC), *Mycobacterium kansasii*, and *Mycobacteroides (Mycobacterium)* abscessus complex (MABC) (1). In a recent Japanese report of NTM pulmonary diseases, MABC was the second-most frequently reported entity (2). MABC is a group of rapidly growing mycobacteria (RGM) that are resistant to drugs. MABC is classified into three subspecies: *M. abscessus* subsp. *abscessus* (*M. abscessus*), *M. abscessus* subsp. *bolletii* (*M. bolletii*), and *M. abscessus* subsp. *massiliense* (*M. massiliense*).

The number of RGM infections has been increasing in Japan, but reported cases of extrapulmonary RGM infections, including bacteremia caused by MABC, are still rare (3).

We herein report a case of chronic bursitis, recurrent bacteremia, and disseminated infections caused by *M. massiliense* in a patient treated with long-term prednisolone therapy.

Case Report

A 59-year-old Japanese woman visited our hospital because she noticed a mass on the back of her right hand. She had no history of trauma or soil exposure in her right hand. She had multiple underlying diseases of autoimmune hemolytic anemia (AIHA), idiopathic thrombocytopenic purpura (ITP) with splenectomy, and antiphospholipid antibody syndrome. She had been treated by rituximab, prednisolone 50 mg/day, and eltrombopag.

In June 20X(Y-2), she noted that her right opisthenar was...
swollen, and she had difficulty stretching her ring finger. Her white blood cell (WBC) count and serum C-reactive protein (CRP) level were 12,600/μL and 0.41 mg/dL, respectively. Needle puncture was performed at the orthopedic outpatient department. Due to subtle pain and inflammatory response, the treating physician diagnosed her with swollen right opisthenar caused by a benign tumor including the ganglion. No microbiological or pathological tests were performed at this time because of her low platelet levels and high doses of corticosteroids.

Around July 20XY, the mass had gradually enlarged (Fig. 1). In August, incision and drainage of the bursa were performed at the outpatient ward. Acid-fast staining (fluorescence method) of the specimen was positive, but the COBAS TaqMan MAI Test (Roche Diagnostics, Basel, Switzerland) for tuberculosis and MAC yielded negative results. Additional curettage was performed for the mass, and significant rice body formation was removed (Fig. 2). Her general condition was good, and she did not wish to remain hospitalized. Thus, two sets of blood cultures were obtained, and she was discharged.

Mycobacteria isolated from drainage specimens had grown on the Mycobacteria growth indicator tube at day 4 post-curettage. Gram-positive rods grew in the two blood culture samples after 5 days. The DNA-DNA hybridization (DDH) method identified the Mycobacteria isolated from drainage specimens and blood cultures as MABC. The results of antimicrobial susceptibility testing of MABC performed at our hospital are shown in Table a, and the isolate was only susceptible to clarithromycin (CAM). After the diagnosis of bursitis and bacteremia caused by MABC was only susceptible to clarithromycin (CAM). After the diagnosis of bursitis and bacteremia caused by MABC, we consulted with the National Institute of Infectious Diseases Leprosy Center to identify the subspecies and perform additional antimicrobial susceptibility testing. M. massiliense was identified by multiplex polymerase chain reaction (PCR). The results of additional drug susceptibility testing are shown in Table b.

The same antimicrobials were administered to her for eight weeks after confirming negative blood culture. Treatment of recurrent M. massiliense bacteremia was switched to the following oral regimen: CAM, sitafloxacin (STFX), and faropenem (FRPM). Based on additional susceptibility to the following oral regimen: CAM, sitafloxacin (STFX), and faropenem (FRPM). Based on additional susceptibility testing are shown in Table b. The results of additional drug susceptibility testing are shown in Table b. The results of additional drug susceptibility testing are shown in Table b.
Table. Antimicrobial Susceptibility Testing of M. Massiliense Isolated from Blood Culture.

| Antimicrobial agent                  | *MIC (µg/mL) | NUH | NIID |
|--------------------------------------|--------------|-----|------|
|                                      | 20XY/8 | 20XY/11 | 20X(Y+1)/4 |
| Amikacin (AMK)                       | <8 S    | <8 S   | <8 S  |
| Ciprofloxacin (CPFX)                 | >2 R    | >2 R   | >2 R  |
| Clarithromycin (CAM)                 | <1 S    | <1 S   | <1 S  |
| Doxycycline (DOXY)                   | >1 I or R | >1 I or R | >1 I or R |
| Imipenem (IPM)                      | I       | 16 I   | 8 I   |
| Linezolid (LZD)                     | 8 S     | 8 S    | <2 S  |
| Moxifloxacin (MFLX)                 | >4 R    | >4 R   | 2 I   |
| Trimethoprim/Sulfamethoxazole (TMP/SMX) | >2/38 R | >2/38 R | >2/38 R |

* MICs were determined using broth microdilution methods (CLSI M24-A2).

NIH: National Institute of Infectious Diseases
S: susceptible, I: intermediate, R: resistant
(a) Antimicrobial susceptibility testing performed at NUH. (b) Antimicrobial susceptibility testing conducted at NIID. This result was available in February 20X(Y+1).

Discussion

To our knowledge, this is the first case of bursitis with rice bodies, repeated bacteremia, and disseminated infections caused by *M. massiliense*. At the time of the diagnosis, the patient’s chest CT findings were not specific. We therefore suspected that the bursitis had developed after unrecognized trauma of the right hand, which gradually worsened over the next two years. Additionally, long-term corticosteroids use for ITP and AIHA likely triggered bacteremia and disseminated lesions in this case.

MABC is considered the most pathogenic RGM to mainly cause respiratory infections. A retrospective cohort study of 108 MABC infections showed the following types: 59 (54.6%) respiratory infections, 21 (19.4%) bloodstream infections (BSIs), 10 (9.2%) skin and soft tissue infections, and 3 (2.8%) disseminated infections (4). Regarding disseminated MABC infections, the duration from the symptom onset to the diagnosis was over 3 months in 48% of cases (5). The mortality rate of patients with disseminated infections is relatively high, especially among immunosuppressed patients (5).

While the exact pathophysiology of rice body formation remains unclear, rice bodies are thought to form as the result of nonspecific responses to chronic synovial inflammation. Metaplasia of subsynovial connective tissue into cartilage nodules is observed. Rice bodies are associated with tuberculous arthritis, osteoarthritis and infective arthritis, and rheumatoid arthritis (6). Bursitis caused by NTM is thought...
to be a very rare presentation (7-9); thus, the optimal duration of antimicrobial therapy for bursitis caused by NTM is unclear. Long-term antimicrobial therapy is generally performed (8). Furthermore, the optimal duration of antimicrobial therapy for bursitis with rice bodies caused by MABC remains unknown.

Subspecies identification of MABC is recommended by the American Thoracic Society/the Infectious Diseases Society of America guideline (10). Subspecies identification helps infer antimicrobial susceptibility. For example, *M. abscessus* and *M. bolletii* have an activated *erm* gene and resistance to macrolide drugs, whereas *M. massiliense* is usually susceptible to CAM (11). DDH and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, which are usually performed in Japan, cannot distinguish MABC subspecies (12, 13). MABC is reportedly resistant to all standard anti-tuberculous drugs; thus, no reliable treatment regimen exists. It is important to select antimicrobials based on appropriate susceptibility testing. However, appropriate susceptibility testing for candidate agents, such as STFX and FRPM, is difficult to perform in Japanese general hospitals. We therefore suspect that most clinicians are not confident about how best to treat disseminated MABC infections who require long-term therapy. Early consultation with a specific center about species identification and antimicrobial susceptibility testing for MABC isolate might help improve the prognosis of patients with disseminated MABC infections who require long-term therapy. BrothMIC RGM® (Kyokuto Pharmaceutical Industrial, Tokyo, Japan) has been available in Japan since 2019 (14), so we have been able obtain susceptibility results of RGM based on the Clinical and Laboratory Standards Institute in community hospitals. While further evaluations are necessary for some antimicrobials on the panel, BrothMIC RGM® is expected to be useful for determining effective regimens for RGM infections.

In conclusion, the early diagnosis of disseminated MABC infection is essential, and the ideal treatment regimen and duration of treatment for severe MABC infections should be determined based on precise species identification and antimicrobial susceptibility testing. The accumulation of more
cases is necessary to determine the optimal management of disseminated MABC infection.

**Author’s disclosure of potential Conflicts of Interest (COI).**

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