Disseminated *Mycobacterium abscessus* Complex Infection Manifesting as Multiple Areas of Lymphadenitis and Skin Abscess in the Preclinical Stage of Acute Lymphocytic Leukemia

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Abstract

A 37-year-old woman was admitted to a hospital due to a prolonged fever and a rash on her legs. She had systemic lymphadenitis and a skin abscess on her left leg. Pathological findings of a left leg skin biopsy revealed abscess formation with granulomatous dermatitis, *Mycobacterium abscessus* complex was cultured from the resected left supraclavicular lymph node, and disseminated *M. abscessus* complex infection was diagnosed. She was treated with combination treatment with antimicrobials and percutaneous drainage, and her clinical findings improved. Four months later, she developed acute lymphocytic leukemia. Leukemia is a risk factor for disseminated *M. abscessus* complex infection, even before developing leukemia.

Key words: *Mycobacterium abscessus* complex, lymphadenitis, skin abscess, acute lymphocytic leukemia

Introduction

*Mycobacterium abscessus* complex (formerly *M. chelonae* subspecies *abscessus*) is a member of a group of rapidly growing mycobacteria (RGM) of nontuberculous mycobacteria (NTM), including *M. chelonae* and *M. fortuitum*, according to the in vitro findings. *M. abscessus* complex had been recognized as a distinct species for more than 20 years, separate from *M. chelonae/abscessus* or *M. fortuitum/chelonae* complex.

*M. abscessus* complex is globally found in the soil and water. Localized skin and soft tissue infections, especially after traumatic wounds or surgical procedures, are the most common infections caused by *M. abscessus* complex. The hosts are generally immunocompetent and most of these infections remain localized and responsive to surgical debridement/drainage, antimicrobial therapy or a combination thereof (1). On the other hand, disseminated infections caused by *M. abscessus* complex are uncommon and typically occur in immunocompromised hosts, such as human immunodeficiency virus (HIV) carriers or posttransplant patients receiving immunosuppressive agents.

We herein present a patient with a disseminated *M. abscessus* complex infection manifesting as multiple areas of lymphadenitis and a skin abscess who showed favorable responses to combination treatment with multiple antimicrobials and percutaneous drainage of the abscess and discuss the potential association with acute lymphocytic leukemia, which developed 4 months after the disseminated *M. abscessus* complex infection.

Case Report

A 37-year-old Japanese woman developed a fever, fatigue and 5 kg weight loss per month in the first month of 2014.
She had no history of smoking, foreign travel, insect bites, trauma or medical histories and had no comorbid diseases. She had been working as a cleaning staff member in the operating room in a hospital but had no exposure history to *M. abscessus* complex. She was admitted to a local hospital due to a prolonged fever and a rash on the left leg which appeared in the second month. A skin biopsy of the left leg was performed; acid-fast bacilli were not found in the acid-fast stain culture, while pathologically abscess formation leading to granulomatous dermatitis was observed (Fig. 1A). Contrast-enhanced computed tomography showed multiple areas of enlarged lymph nodes. A left supraclavicular lymph node biopsy was performed, and similar to the findings of the skin biopsy, abscess formation and granulomatous inflammation were noted (Fig. 1B-E). Acid-fast staining of the pus was positive, rapid-growing acid-fast bacilli were cultured, and *M. abscessus* complex was identified by the DNA-DNA hybridization (DDH) method. Unfortunately, subtype identification of three groups (*M. abscessus, M. massiliense,* and *M. bolletii*) using molecular methods was not performed (2). The administration of intravenous imipenem/cilastatin (1,500 mg/day), intramuscular amikacin...
(500 mg/day) and oral clarithromycin (1,000 mg/day) was initiated, however, the patient still had a fever and developed pus discharge from the left supraclavicular region in which the lymph node biopsy was performed. Therefore, she was referred to our hospital for further examination and treatment at four months after the admission to the former hospital.

On this admission, a physical examination revealed that the right submandibular, bilateral supraclavicular, and bilateral axillary lymph nodes were palpable. She also had multiple sites of pus on her skin (Fig. 1F), and pus discharge from two inserted drainage catheters into the left supraclavicular and axillary areas was observed.

The laboratory findings on this admission (Table) demonstrated that the white blood cell count was within the normal range (4,200/μL) with a decreased lymphocyte subpopulation (12.8%, 540/μL), a slightly increased serum C-reactive protein (CRP) level (2.23 mg/dL), increased serum level of soluble interleukin-2 receptor (1,345 U/mL), hypoalbuminemia (3.4 g/dL) and anemia (9.0 g/dL). Bacterial and mycobacterial blood and pus cultures were negative.

Enhanced computed tomography of the neck, chest, abdomen, and pelvis showed multiple enlarged and necrotic-appearing lymph node swelling in the right submandibular, bilateral supraclavicular, and bilateral axillary areas (Fig. 2). The dose of imipenem/cilastatin was increased from 1,500 mg/day to 2,000 mg/day with amikacin and clarithromycin, in addition to drainage in the left supraclavicular and axillary areas, and followed by treatment with several combinations of multiple antimicrobials, as shown in Fig. 3. After 4 months of starting treatment, peripheral atypical lymphocytosis was observed. A bone marrow biopsy was performed.

**Table. Laboratory Findings on Admission.**

<table>
<thead>
<tr>
<th>&lt;Blood counts&gt;</th>
<th>&lt;Blood chemistry&gt;</th>
<th>&lt;Immunoserological test&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC 4,200/μL</td>
<td>TP 8.8 g/dL</td>
<td>HBV antigen Negative</td>
</tr>
<tr>
<td>Neut 85.5%</td>
<td>Alb 3.4 g/dL</td>
<td>HCV antibody Negative</td>
</tr>
<tr>
<td>Lymph 12.8%</td>
<td>AST 22 IU/L</td>
<td>HTLV-1 antibody Negative</td>
</tr>
<tr>
<td>Mono 0.4%</td>
<td>ALT 19 IU/L</td>
<td>HIV antibody Negative</td>
</tr>
<tr>
<td>Eosin 1.1%</td>
<td>T-bil 0.3 mg/dL</td>
<td>QFT Ts6-Gold Negative</td>
</tr>
<tr>
<td>Baso 0.2%</td>
<td>LDH 187 IU/L</td>
<td>IgG 2,782 mg/dL</td>
</tr>
<tr>
<td>RBC 356×10⁶/μL</td>
<td>Glu 94 mg/dL</td>
<td>IgA 208 mg/dL</td>
</tr>
<tr>
<td>Hb 9.0 g/dL</td>
<td>BUN 20 mg/dL</td>
<td>C3 210 mg/dL</td>
</tr>
<tr>
<td>Hct 48×10⁶/μL</td>
<td>Cre 0.5 mg/dL</td>
<td>C4 28 mg/dL</td>
</tr>
<tr>
<td>RBC 356×10⁶/μL</td>
<td>Na 137 mEq/L</td>
<td>RF 8.8 U/mL</td>
</tr>
<tr>
<td>Hb 9.0 g/dL</td>
<td>K 4.4 mEq/L</td>
<td>ANA &lt; 40</td>
</tr>
<tr>
<td>Hct 48×10⁶/μL</td>
<td>Cl 97 mEq/L</td>
<td>MPO-ANCA &lt; 1.0 U/mL</td>
</tr>
<tr>
<td>Fibrinogen 585 mg/dL</td>
<td>CRP 2.23 mg/dL</td>
<td>PR3-ANCA &lt; 1.0 U/mL</td>
</tr>
<tr>
<td>FDP 7.8 μg/mL</td>
<td>&lt;Serology&gt;</td>
<td>sIL-2R 1,345 U/mL</td>
</tr>
<tr>
<td>D-dimer 3.1 μg/mL</td>
<td>&lt;Pus culture&gt;</td>
<td>Bacterium Normal flora</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acid-fast bacillus No organisms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No organism</td>
</tr>
</tbody>
</table>

**Figure 2.** Contrast-enhanced neck and chest computed tomography of the patient. Enlarged right cervical (A) and bilateral supraclavicular (B) lymph nodes with central low-density areas and abscess formation in the left axillary soft tissue were observed (C, D).
and B-cell acute lymphocytic leukemia (B-cell ALL) was diagnosed. Systemic chemotherapy for ALL was started in addition to the antimycobacterial treatment. Nine months after the initiation of antimycobacterial therapies, the patient’s symptoms, such as the fever and pus drainage resolved, and only a small amount of lymph node swelling remained one year after initiating antimycobacterial treatment (Fig. 3).

**Discussion**

*M. abscessus* complex is an acid-fast bacillus that shows rapid growth on most types of solid medium for mycobacteria within 7 days. This organism is ubiquitous in the environment and has been found in soil, dust, and water. *M. abscessus* complex is distinguished from other rapidly growing mycobacteria according to its growth characteristics, biochemical tests, gas-liquid chromatography of metabolic products, and polymerase chain reaction (PCR) analysis (3).

*M. abscessus* complex is increasingly recognized as a pathogen in both healthy and immunocompromised hosts with a wide spectrum of clinical symptoms. Environmentally acquired infections include post-traumatic skin infections, soft tissue, bone (1), pulmonary (4), ophthalmologic (1) and ear infections (5), cervical lymphadenitis (6) and disseminated disease (1, 7).

Multiple lymphadenitis due to *M. abscessus* complex infection, as observed in our patient, is extremely rare, and only 7 cases have been reported thus far (8-10); these patients showed cervical, supraclavicular or intra-abdominal lymph node involvement. The pathological findings of various tissues are usually nonspecific and not diagnostic, and mycobacterial culture is more specific and helpful for diagnosing *M. abscessus* complex infection. In our patient, a cervical lymph node biopsy and culture were necessary to establish the diagnosis. Localized skin and soft tissue infections, especially after traumatic wounds or surgical procedures, are the most common infections caused by *M. abscessus* complex. However, the route of entry of *M. abscessus* complex in disseminated disease is generally unknown (8). The present case did not have trauma, surgical procedures or exposure to contaminated soil and water, thus the route of entry of *M. abscessus* complex was not identified. Our case required not only medical treatment, but also abscess drainage. To the best of our knowledge, our patient is the first reported case of multiple lymphadenitis due to *M. abscessus* complex infection in Japan.

Disseminated RGM infection is defined by at least one of the following characteristics: multiple cutaneous abscesses, visceral organ infections with or without cutaneous presentation, or the evidence of a deep infection such as blood or bone marrow infection. Our patient showed cutaneous abscesses and multiple lymphadenitis with visceral infection that were consistent with disseminated RGM disease.

Disseminated *M. abscessus* complex infection in an immunocompetent host is rare, and disseminated disease due to RGM has been reported in immunocompromised adults.
Wallace showed that nine patients had disseminated disease caused by RGM and among these patients, four had received renal transplants, one had Felty’s syndrome, one had acute myelogenous leukemia, one had lymphoma and one had chronic hemodialysis (1). Our patient showed no obvious immune defects without mild lymphocytopenia at the first presentation, however, 4 months after the initiation of antimycobacterial treatment, she was found to have ALL. We speculated that our patient had an immunocompromised status when she developed the M. abscessus complex infection. Leukemia is a known risk factor for disseminated mycobacteriosis, however, only one case of disseminated mycobacteriosis with ALL has been reported thus far (11).

The standard treatment for disseminated M. abscessus complex infection remains unclear. Resection, debridement or drainage of the infected lesions must be considered (12). M. abscessus complex isolates are typically resistant to standard antituberculous agents (13); thus, the drug susceptibilities of the isolates should be tested, although the antibiotic susceptibility of the isolate was not available in the present patient. An official statement of the American Thoracic Society/Infectious Disease Society of America recommends that patients should receive multidrug therapy, including macrolides and one or more parenteral agent (e.g., amikacin, cefoxitin or imipenem) or a combination of parenteral agents to prevent acquired resistance (13). The approaches for treating disseminated M. abscessus complex infection are typically empiric, and no prospective clinical trials have been conducted. In addition, immunocompromised hosts often receive more intense therapy (more frequent and higher doses of antibiotics, prolonged therapy or both) compared with immunocompetent hosts. Combined antibiotic therapy with imipenem/cilastatin, amikacin and clarithromycin was initially administered to our patient, then amikacin was changed to rifampin and ethambutol to prevent auditory disorder of amikacin at 2 months after starting antimicrobial treatment. After 5 months of combined antibiotic treatment, rifampicin was changed to levofloxacin due to nausea and vomiting, and intravenous imipenem/cilastatin was changed to faropenem.

In conclusion, disseminated M. abscessus complex infection manifesting as multiple lymphadenitis is relatively rare. Localized skin and soft tissue infections are common in patients with M. abscessus complex infections, however, in patients with disseminated M. abscessus complex infections, the possibility of an immunocompromised status should be considered. Therefore, physicians should be aware of an occult immunocompromised status, such as hematological malignancies including leukemia, in disseminated M. abscessus complex infection. The diagnosis of M. abscessus complex infection typically requires a biopsy and culture of the tissues, such as the lymph node. However, as the pathological findings of the tissues can be nonspecific and not diagnostic, mycobacterial cultures may be more specific and helpful.

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

Acknowledgement
The authors thank Drs. Mitsuru Kinjo, Taturo Shimokama (Department of Pathology, Steel Memorial Yawata Hospital), Kenichiro Murata (Department of Pathology, Kokura Memorial Hospital), and Yu Suzuki (Department of Respiratory Medicine Kokura Memorial Hospital) for their assistance.

References