CASE REPORT

Catheter-related *Mycobacterium abscessus* bacteremia manifested with skin nodules, pneumonia, and mediastinal lymphadenopathy

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Abstract Although previously rare, catheter-related bloodstream infection caused by rapidly growing mycobacteria is now increasingly encountered, especially among cancer patients who have catheters implanted for chemotherapy treatments. A 73-year-old female patient with acute myeloid leukemia (AML) had *Mycobacterium abscessus* bacteremia with manifestations of multiple skin nodules, pneumonia, and mediastinal lymphadenopathy 4 months after the implantation of a peripherally inserted central catheter (PICC) for the delivery of chemotherapy. The catheter-related *M. abscessus* bacteremia was confirmed by positive blood cultures of specimens drawn from a PICC line and a peripheral vein. She defervesced with the administration of meropenem, amikacin, levofloxacin, clarithromycin, and by the removal of PICC. Her fever subsided for 3 months with the disappearance of skin and lung lesions; however, she died of AML relapse. Bacteremia and skin infection caused by *M. abscessus* can be detected by culture and pathological examinations and should be considered in
leukemia patients with a PICC. With appropriate laboratory diagnosis, M. abscessus bacteremia with disseminated infections can improve with catheter removal and combination antimicrobial therapy.

Introduction

Disseminated infection caused by rapidly growing mycobacteria (RGM) mostly occurs in immunocompromised patients. Among the various RGM infections involving blood, bone marrow, liver, spleen, lung, lymph node, and skin, the most common clinical feature is erythematous subcutaneous nodules [1–4]. In the past two decades, catheter-related bloodstream infection (CRBSI) with RGM has been increasingly reported, especially in immunocompromised patients [5–7]. The implanted catheters can be infected by RGM with manifestations of exit-site infections, tunnel infections, or catheter-related bacteremia [4]. However, reports of CRBSI caused by RGM in combination with disseminated infection to visceral organs are rare in the literature [5,7,8]. Little is known about the treatment of choice because only limited numbers of cases have been reported so far. Herein, we report a successful diagnosis and treatment experience of peripherally inserted central catheter (PICC)-related Mycobacterium abscessus bacteremia with disseminated infections in a patient with acute myeloid leukemia (AML).

Case report

A 73-year-old female patient was diagnosed with AML subtype M1 in June 2008. The PICC was placed in the left cephalic vein for chemotherapy treatment. The patient was treated with low-dose cytarabine (Ara-C) for AML, but then developed febrile neutropenia. However, the fever subsided with the administration of multiple antibiotics (combination of meropenem, levofloxacin, teicoplanin, and caspofungin), and she was discharged in August 2008.

In October 2008, she was admitted for further chemotherapy treatment. At the time of admission, her white blood cell count was 1.7 × 10^9/L with a differential count of 16% blasts, 14% neutrophils, 1% band forms, 53% lymphocytes, 1% monocytes, 0% eosinophils, and 1% basophils. A physical examination revealed that her body temperature was 38.3°C with no palpable lymph nodes or evidence of erythema or drainage surrounding the PICC insertion site. A chest radiography was unremarkable. The initial two sets of blood cultures drawn at admission due to fever were negative for bacterial growth. Piperacillin/tazobactam and amikacin were administered for neutropenic fever, but fever persisted.

Fourteen days after admission, she developed multiple tender or nontender erythematous skin nodules (5–20 mm in diameter) on four extremities and the trunk (Fig. 1A). Then, two pairs of blood cultures were drawn because fever persisted: one was from the PICC line and the other was from a peripheral vein. Three days later, pathogens were recovered from both the aerobic blood culture bottles (BacT/ALERT system; bioMérieux, Marcy, l’Etoile, France). Gram staining revealed the presence of Gram-positive bacilli (GPBs), and the possibility of the presence of Mycobacterium species was further suspected on the basis of results obtained using the acid-fast stain (AFS) test. Nonpigmented and pinpoint-shaped colonies were observed on blood and chocolate agar plates after 3 days of incubation at 37°C and 5% CO_2. The isolates from blood were also inoculated on Löwenstein–Jensen (L–J) medium and on the BD BACTEC mycobacterial growth indicator tube system (Becton, Dickinson and Company, Sparks, MD, USA). RGM infection was highly suspected due to rapid growth on routine aerobic culture plates and the culture tested positive for acid-fast bacilli (AFBs). She was treated empirically with intravenous meropenem (1 g every 8 hours), amikacin (500 mg daily), levofloxacin (750 mg daily), and oral clarithromycin (500 mg twice a day). PICC was removed and no microorganism was isolated from the catheter tip culture. Results of

Figure 1. (A) Multiple erythematous skin nodules on the right lower extremity. (B) Enlarged erythematous skin nodules with central ulceration on the right lower extremity after 5 weeks of antimicrobial therapy.
skin biopsy revealed multiple granulomas surrounded by epithelioid cells, histiocytes, lymphocytic infiltrate, and hemorrhage in the dermis (Fig. 2A). AFBs were also detected on the pathological specimen by AFS method (Fig. 2B). Colonies of blood isolates that grew on the L–J medium were further identified as M. abscessus by the polymerase chain reaction–restriction fragment length polymorphism method based on the evaluation of the gene encoding for the 65-kDa heat-shock protein (hsp65) [9]. The in vitro antibiotic susceptibility of the microorganism was tested using a broth microdilution minimum inhibitory concentrations (MICs) method and was interpreted according to the guidelines of the Clinical and Laboratory Standards Institutes [10]. The strain was found to be susceptible to amikacin (MIC: 4 µg/mL), clarithromycin (MIC: 0.125 µg/mL), and imipenem (MIC: 4 µg/mL), but it had intermediate susceptibility to ciprofloxacin (MIC: 2 µg/mL), tobramycin (MIC: 8 µg/mL), and doxycycline (MIC: 2 µg/mL).

Her fever did not subside quickly despite catheter removal and administration of multiple antimicrobial agents. She had cough with purulent sputum, dyspnea, swallowing pain, dysphagia, and chest pain. A chest radiography was performed which revealed mediastinal widening and right upper lung consolidation (Fig. 3A). The sputum microbiologic studies did not show the presence of any microorganisms. Chest computed tomography showed lymphadenopathy in the right hilar, paratracheal, subcarinal, paraaortic, highest mediastinal, and bilateral supraclavicular areas and right upper lung consolidation. A gallium-67 scan revealed intensely increased radioactive foci in the mediastinum, adjacent bilateral lung hilar regions, and supraclavicular regions and multiple hot and warm spots scattered in the trunk (Fig. 4). Transthoracic echocardiography revealed no vegetation.

She was afebrile after 3 weeks of a combination antimicrobial regimen (meropenem, amikacin, levofloxacin, amoxicillin–clavulanate, linezolid, and daptomycin). Her fever did not subside quickly despite catheter removal and administration of multiple antimicrobial agents. She had cough with purulent sputum, dyspnea, swallowing pain, dysphagia, and chest pain. A chest radiography was performed which revealed mediastinal widening and right upper lung consolidation (Fig. 3A). The sputum microbiologic studies did not show the presence of any microorganisms. Chest computed tomography showed lymphadenopathy in the right hilar, paratracheal, subcarinal, paraaortic, highest mediastinal, and bilateral supraclavicular areas and right upper lung consolidation. A gallium-67 scan revealed intensely increased radioactive foci in the mediastinum, adjacent bilateral lung hilar regions, and supraclavicular regions and multiple hot and warm spots scattered in the trunk (Fig. 4). Transthoracic echocardiography revealed no vegetation.
and clarithromycin), and the result of follow-up blood culture was negative. Antimicrobial agents were changed to an oral therapy consisting of clarithromycin (500 mg twice a day) and levofloxacin (750 mg daily). Her skin nodules developed central ulceration, and no new skin nodules were noted when she was referred to our hematology outpatient department 2 weeks after discharge (Fig. 1B). The patient remained afebrile for 3 months with two oral antimicrobial agents after diagnosis of \( M. \text{abscessus} \) infection. The follow-up chest radiography revealed partial resolution of right upper lung consolidation and decreased mediastinal widening (Fig. 3B). The antimicrobial agents were administered continuously, and she did not develop fever or new skin or pulmonary symptoms. However, in February 2009, she died due to AML relapse.

**Discussion**

Catheter-related bacteremia caused by RGMs has been increasingly reported, most of which involve species such as \( M. \text{fortuitum} \), \( M. \text{chelonae} \), and \( M. \text{abscessus} \) [4]. Other rare mycobacterial species such as \( M. \text{mucogenicum} \), \( M. \text{flavescens} \), \( M. \text{smegmatis} \), \( M. \text{septicum} \), \( M. \text{aurum} \), \( M. \text{immunogenenum} \), \( M. \text{peregrinus} \), and \( M. \text{mageritense} \) have also been reported [4,6,7,11].

In our case, \( M. \text{abscessus} \) bacteremia was associated with an indwelling catheter because all of the following criteria mentioned by the Centers for Disease Control and Prevention (USA) were fulfilled: clinical features of bloodstream infection were present; growth of the same microorganism occurred in the peripheral blood and either a catheter segment or a blood culture drawn from the catheter; and other apparent sources of the infection were absent [12]. The interval from catheter implantation to the first positive blood culture for RGM was reported to be 1—24 months [6,7]. In the present case, it was 4 months. However, it is not common for the catheter tip culture to be positive for RGM [5—7]. Catheter infection with a positive tip culture is documented in only 15—25% of cases [6,7,11]. The negative tip culture in our case may be related to both appropriate antimicrobial agents before tip removal and the roll-plate technique used in our hospital for tip culture, which has been shown to be less sensitive than the sonication method [6].

Disseminated RGM infection is defined by at least one of the following characteristics: multiple cutaneous abscesses, visceral infection with or without cutaneous presentation, or blood or bone marrow infection with evidence of deep infection [2]. Both an underlying immunosuppressed condition and the presence of a long-term central venous catheter are the most frequently reported risk factors for the development of RGM bacteremia [6,7], as was observed in our patient. Neutropenia is also a risk factor for dissemination [7,13]. In immunocompromised patients, two forms of bacteremia due to \( M. \text{fortuitum} \) complex have been described: a disseminated cutaneous form (cellulitis, skin abscesses, and painful nodules) without known portal of entry and a vascular catheter-related form without
cutaneous or deep-seated involvement, except at the catheter insertion site [3,14]. Although \textit{M. abscessus} is a part of the \textit{M. fortuitum} complex, both cutaneous and deep-seated involvement of visceral organs occurred in our case that was different from the previously reported two forms of \textit{M. fortuitum} complex bacteremia. The pulmonary and lymph node lesions in our case were not proven to be caused by \textit{M. abscessus}, but because these lesions improved with therapy, \textit{M. abscessus} was suspected as the pathogen.

The appearance of \textit{M. abscessus} skin infections may manifest as discrete nodules, ulceration, or diffuse maculopapular eruption [2]. Biopsy of skin lesions may demonstrate the presence of microorganisms (with AFS), and culture of the tissue is often positive [2]. In contrast to the typical skin nodules, disseminated \textit{M. abscessus} infection can manifest with reactive skin presentations (negative culture and pathological findings for RGM), including generalized pustulosis, Sweet’s syndrome, erythema nodosum, and pustular psoriasis [1]. Our case revealed that skin biopsy can help to identify pathogens and differentiate infections from reactive skin presentations and other causes.

Different RGM species need local susceptibility surveillance reports to guide effective therapy [6]. Of the parenteral antibiotics, amikacin is an important effective agent against \textit{M. abscessus} [4]. Of the oral antibiotics, clarithromycin is the cornerstone of therapy for \textit{M. abscessus} [15]. The high variation in susceptibility of different RGM species to the currently available antimicrobial agents highlights the need of species identification and susceptibility testing for clinically significant and difficult-to-treat infections [7].

We suspected that delayed defervescence under treatment (3 weeks) with effective antimicrobial agents occurred due to the large bacterial burden as demonstrated by skin nodules, pneumonia, and mediastinal lymphadenopathy. The duration of antimicrobial therapy and the antimicrobial regimens for catheter-related RGM infections are not defined clearly because of the lack of controlled trials defining the optimal antibiotic therapy [5,6]. Combination therapy with at least two effective parenteral agents followed by oral therapy for weeks to months has been suggested [4,13]. In most cases with CRBSI caused by RGMs, the catheter should be removed for successful control of the infection [5,6]. A few cases responded to catheter removal alone, but the rate of relapsing bacteremia was significantly higher with delayed or no catheter removal than with timely catheter removal [6]. In our patient with catheter-related RGM bacteremia complicated by the dissemination involving visceral organs, prolonged therapy with combination antimicrobial agents for 3 months and catheter removal resulted in no detectable bacteremia and clinical improvement.

In conclusion, RGM bacteremia is relatively rare in CRBSI, but physicians should be aware of its presence in a febrile immunocompromised patient with an indwelling central venous catheter. When beaded GPBs are detected in positive blood culture bottles, AFS should be performed to confirm the mycobacterial infection. Dissemination to cutaneous and visceral organs may occur in catheter-related \textit{M. abscessus} bacteremia. Both timely catheter removal and proper combination antimicrobial therapy are required for the management of catheter-related RGM bacteremia.

References