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Catheter-related blood stream infection caused by Mycobacterium chelonae in a child with myeloid leukemia associated with Down syndrome

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Abstract
Rapidly growing nontuberculous mycobacteria should be considered if GPRs gram-positive rods are detected in blood cultures 2-3 days after the blood sample collection.

Keywords
Catheter-related blood stream infection, central venous catheter, mycobacterium chelonae, rapidly growing nontuberculous mycobacteria

1 | INTRODUCTION

Rapidly growing nontuberculous mycobacteria (RGM) are rare causative pathogens of catheter-related blood stream infection (CRBSIs) and can sometimes be misdiagnosed as gram-positive rods (GPRs). Therefore, RGM should be considered if GPRs are detected in blood cultures 2-3 days after sample collection.

A central venous catheter (CVC), which is necessary for the treatment of children with cancer,1 often leads to complications such as infections, occlusion, breakage, and thrombosis, not only at the time of insertion but also during use.1,2 The catheter-related blood stream infection (CRBSI) is a common complication in pediatric cancer patients. It has been estimated that 14%–51% of CVCs implanted in children with cancer may be complicated by bacteremia.1 The most common organisms that cause CRBSIs are coagulase-negative staphylococci, Staphylococcus aureus, Enterococcus spp., Escherichia coli, Klebsiella spp., and Candida spp.1,2

Rapidly growing nontuberculous mycobacteria (RGM) are defined as nontuberculous mycobacteria (NTM) that persist in a variety of environmental sources, such as water, soil, and aquatic animals, and that form mature colonies on solid agar within 7 days.3 More than 70 RGM species have been reported so far.3 NTM can cause lymphadenopathy, skin and soft tissue infections, pulmonary disease, and disseminated disease.3 In hospitals, RGM may also be responsible for outbreaks of infections that originate from contaminated medical equipment and water.3 However, RGM are considered a rare cause of CRBSIs.4-6 Herein, we report a patient of a myeloid leukemia associated with Down syndrome (ML-DS) who developed a CRBSI caused by Mycobacterium chelonae.
2 CLINICAL CASE PRESENTATION

A 43-month-old female patient with trisomy 21 was admitted to our hospital due to fever. She was diagnosed with ML-DS at 24 months old. She achieved complete remission (CR) after the first course of induction chemotherapy and remained in CR during treatment with additional chemotherapy. However, she relapsed 1 month after the completion of chemotherapy. She received reinduction chemotherapy and achieved a second CR after the first course of reinduction chemotherapy. She underwent bone marrow transplantation (BMT) in the second CR. However, the second relapse occurred after BMT at 37 months old. The following chemotherapy which consisted of azacitidine reduced leukemic cell counts in the bone marrow, and she achieved a third CR. She was closely being followed up at the outpatient department without further intervention.

At the time of admission, she was on sulfamethoxazole/trimethoprim and voriconazole for infection prophylaxis and was also prescribed prednisolone (0.25 mg/kg/day) for the treatment of chronic graft-versus-host disease (GVHD). Since her peripheral intravenous catheterization was very difficult to access, a Hickman-type CVC with a double lumen accessed from the right internal jugular vein through a subcutaneous tunnel was used. This CVC was inserted at the time of first relapse at 31 months old.

At admission, her general appearance was not good; she had a high temperature (39.7°C), her blood pressure was 98/60 mm Hg, pulse 162 /min, respiratory rate of 36 /min with an O2 saturation of 100% on room air. She vomited twice in the consultation room. No remarkable physical findings except slightly increased bowel sounds and rash caused by chronic skin GVHD that extended from the trunk to the legs were observed. No tenderness, redness, or swelling was observed in the region where the CVC was inserted or in the subcutaneous tunnel. Laboratory examinations revealed a white blood cell count of 3,800 /µL with 66.0% neutrophil and CD4-positive cell count of 317 /µL, and a hemoglobin level of 10.9 g/dL. Although the platelet count was 23,000 /µL at admission, her platelet counts changed from 20,000 to 50,000 /µL during the outpatient follow-up period. CRP was 5.69 mg/dL. Immunoglobulin G (IgG), IgA, and IgM were 729, 21, and 50 mg/dL, respectively.

Initially, bacterial colitis was suspected as the cause of fever, and cefmetazole at a dose of 100 mg/kg/d was initiated through the CVC, which resolved her high-grade fever. On day 3 of hospitalization, gram-positive rods (GPRs) were detected in the blood culture collected from the CVC at the time of admission. We had failed to collect two sets of blood culture samples at admission. Since she remained afebrile and the contamination was suspected, the antibiotics treatment regimen did not be changed, another two sets of blood culture samples were collected from the CVC and peripheral blood, and the CVC was left in place. However, on day 5 of hospitalization, GPRs were again detected from another two sets of blood culture samples, and *M. chelonae* was isolated from the blood culture sample collected at admission (Figure 1).

Blood was collected in BD BACTEC™ Peds Plus™/F Culture Vials (Plastic) (Becton Dickinson, Sparks, MD, USA). Blood cultures were incubated in the BD BACTEC FX system. *M. chelonae* was identified by matrix-assisted laser desorption ionization-time of flight mass spectrometry using a MALDI Biotyper (Bruker Daltonik, Germany).

An intravenous line was established, and the antibiotics regimen was switched from cefmetazole to imipenem/cilastatin (100 mg/kg/day), clarithromycin (15 mg/kg/day), and amikacin (8 mg/kg/day), and the CVC was removed on the following day. After the susceptibility test confirmed the presence of *M. chelonae*, amikacin was stopped and tobramycin was initiated at a dose of 5 mg/kg/day (Table 1). The combination of antibiotics including imipenem/cilastatin, clarithromycin, and tobramycin was continued until day 27 of hospitalization. After the completion of antibiotic treatment, no recurrence occurred. No evidence of abscess formation was observed on imaging during her admission including brain MRI, chest and abdominal CT, and cardiac ultrasonography. There was no evidence of *M. chelonae* in the blood culture samples collected on day 15 of hospitalization. The growth of GPRs was detected in the blood culture sample from the CVC more than 2 hours earlier than that

![Figure 1](image.png)
obtained from the peripheral blood on day 3 of hospitalization. Therefore, she was diagnosed as a CRBSI caused by M. chelonae.

3 | DISCUSSION

We herein reported a patient with ML-DS who developed a CRBSI due to M. chelonae, M. fortuitum, M. abscessus, and M. chelonae are well-known RGM, which appear similar to GPRs by Gram staining and can grow as small colonies on sheep blood and chocolate agar. However, these characteristics depend on the Gram staining technique, blood culture media, and culture conditions such as temperature. Therefore, the early diagnosis of CRBSIs caused by RGM is challenging. In a report of six patients, Hawkins C, et al indicated that CRBSIs caused by RGM in all cases were initially considered as the growth of gram-positive bacilli by Gram staining of the aerobic blood culture broths after 2-5 days of incubation. RGMs have also been reported to be misidentified as Corynebacterium spp, Rhodococcus spp, and Nocardia spp.

We summarized the current literature of CRBSIs caused by RGM in pediatric hematology and oncology patients. To do this, we used the PubMed database to search for English language articles related to CRBSIs caused by RGM in children. (Table 2). Most cases were caused by M. fortuitum, M. chelonae, or M. mucogenicum among RGM. Two reports described the outbreak of bloodstream infection by RGM among different pediatric hematology and oncology departments. Both of those were caused by M. mucogenicum, and one report was related to the contaminated water supply in the institute. Two patients with trisomy 21 were

| Antibiotics       | MIC      | Susceptibility |
|-------------------|----------|----------------|
| Amikacin          | <8       | S              |
| Tobramycin        | <1       | S              |
| Clarithromycin    | <1       | S              |
| Ciprofloxacin     | 1        | S              |
| Sulfamethoxazole-Trimethoprim | >4 | R          |
| Imipenem          | 8        | I              |
| Meropenem         | >16      | R              |
| Linezolid         | 16       | I              |
| Azithromycin      | 2        | S              |
| Doxycycline       | <1       | S              |
| Moxifloxacin      | 2        | I              |

Abbreviations: I: Intermediate; MIC, minimum inhibitory concentration; R, resistant; S, susceptible.

| Characteristics | Number | Median age (range) 4 (0-18) |
|-----------------|--------|----------------------------|
| Sex             | Male   | 56                         |
|                 | Female | 30                         |
| Underlying disease | Trisomy 21 | 2                     |
|                 | Klinefelter syndrome | 1                    |
| Type of CRBSI   | Disseminated | 19                   |
|                 | CLABSI  | 49                         |
|                 | Exit site | 17                   |
|                 | Tunnel tract infection | 6                    |
|                 | TID pocket | 2                    |
| Hematology/Oncology diagnosis | ||
|                 | Hematological malignancies | 56                |
|                 | Solid tumors | 31                |
|                 | Others  | 6                          |
| Type of Catheter | Hickman | 49                        |
|                 | Brobiac | 7                          |
|                 | Port    | 8                          |
|                 | N/A     | 29                         |
|                 | HSCT    | 14                         |
| Organism        | Mycobacterium chelonae | 26              |
|                 | Mycobacterium fortuitum | 25             |
|                 | Mycobacterium mucogenicum | 22          |
|                 | Mycobacterium abscessus | 5             |
|                 | Mycobacterium neoaurum | 4             |
|                 | Mycobacterium fortuitum/chelonae complex | 4 |
|                 | M. chelonae-abscessus | 2             |
|                 | M. immunogenum | 2              |
|                 | M. aurum | 1                        |
|                 | M. hackensackense | 1           |
|                 | M. flurathenivornas | 1            |
|                 | M. lactica | 1                    |
|                 | M. smegmatis | 1               |
|                 | M. aurum/neoaaurum | 1         |

Removal of CVC

Yes 81
No 5
N/A 8

(Continues)
diagnosed as CRBSI caused by RGM.16,31 Fourteen patients underwent allogeneic hematopoietic stem cell transplantation before the occurrence of CRBSIs caused by RGM. Eight patients experienced the recurrence of RGM infections. Two patients experienced second RGM infections caused by another Mycobacterium species. One patient with acute myeloid leukemia experienced the bacteremia caused by M. abscessus, and in this case, multiple lung nodules on chest CT were observed. The removal of CVC and 4 total weeks of antibiotic treatment led to resolution. However, 2 months after the completion of antibiotic therapy, the patient experienced another episode of bacteremia caused by M. aurum/neoaurum.26 Another patient with acute lymphoblastic leukemia experienced an infection at the CVC exit site caused by M. fortuitum, and 7 months later, a totally implanted device pocket infection caused by M. abscessus occurred.6 No patients died of CRBSIs caused by RGM, although some patients died due to the progression of their malignancies.

Apiwattankul N, et al reported that the incidence of RGM infections in children with cancer was 0.4 cases/100,000 patient days.6 A retrospective analysis at a single center in Taiwan revealed that there was one patient with an CRBSI caused by RGM among 259 cases of CRBSIs in pediatric cancer patients.4 Because of the low incidence of RGM infections in pediatric cancer patients, we did not consider the possibility of RGM as the etiology of CRBSIs. Consequently, in the present case, the change of the antibiotics and the removal of CVC were delayed even though the GPRs were detected in blood cultures 2-3 days after sample collection. Furthermore, the removal of CVC was likely necessary for the resolution of CRBSIs caused by RGM.

In summary, RGM are rare causative pathogens of CRBSIs and can sometimes be mistaken for GPRs. Therefore, RGM should be considered if GPRs are detected in blood cultures 2-3 days after sample collection. Furthermore, the removal of CVC is a crucial intervention for the treatment of CRBSIs caused by RGM.

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CONFLICT OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS
TF, SU, YA, YN, CN, NN, NY, and TM: participated in patient’s evaluation and treatment. TF, SU, NN, and KI: reviewed and revised the manuscript. All authors read and approved the final manuscript.

ETHICS STATEMENT
Written informed consent for publication of the case and images was obtained from the patient prior to the writing of this case report.
DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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REFERENCES
1. Cecinati V, Brescia L, Tagliaferri L, Giordano P, Esposito S. Catheter-related infections in pediatric patients with cancer. *Eur J Clin Microbiol Infect Dis*. 2012;31:2869-2877.
2. de Jonge RC, Polderman KH, Gemke RJ. Central venous catheter use in the pediatric patient: mechanical and infectious complications. *Pediatr Crit Care Med*. 2005;6:329-339.
3. 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*. 2007;175:367-416.
4. Chen SH, Yang CP, Jaing TH, Lai JY, Hung JJ. Catheter-related bloodstream infection with removal of catheter in pediatric oncology patients: a 10-year experience in Taiwan. *Int J Clin Oncol*. 2012;17:124-130.
5. Hawkins C, Qi C, Warren J, Stosor V. Catheter-related bloodstream infections caused by rapidly growing nontuberculous mycobacteria: a case series including rare species. *Diagn Microbiol Infect Dis*. 2008;61:187-191.
6. Apisitwattanak N, Flynn PM, Hayden RT, Adderson EE. Infections Caused by Rapidly Growing Mycobacteria spp in Children and Adolescents With Cancer. *J Pediatric Infect Dis Soc*. 2015;4:104-113.
7. Uemura S, Mori T, Nagano C, et al. Effective response to azacitidine in a child with a second relapse of myeloid leukemia associated with Down syndrome after bone marrow transplantation. *Pediatr Blood Cancer*. 2018;65:e27414.
8. Rodgers GL, Mortensen JE, Blecker-Shelly D, Fisher MC, Long SS. Two case reports and review of vascular catheter-associated bacteremia caused by nontuberculous Mycobacterium species. *Pediatr Infect Dis J*. 1996;15:260-264.
9. von Graevenitz A, Pünter-Streit V. Failure to recognize rapidly growing mycobacteria in a proficiency testing sample without specific request—a wider diagnostic problem? *Eur J Epidemiol*. 1998;14:519-520.
10. Fleming GA, Frangoul H, Dermody TS, Halasa N. A cord blood transplant recipient with Mycobacterium mucogenicum central venous catheter infection after infusion of tap water. *Pediatr Infect Dis J*. 2006;25:567-569.
11. Flynn PM, Van Hooser B, Gigliotti F. Atypical mycobacterial infections of Hickman catheter exit sites. *Pediatr Infect Dis J*. 1988;7:510-513.
12. Graham JC, Tweedle DA, Jenkins DR, Pollitt C, Pedler SJ. Nontuberculous mycobacterial infection in children with cancer. *Eur J Clin Microbiol Infect Dis*. 1998;17:394-397.
13. Hogg GG, Schinsky MF, McNeil MM, Lasker BA, Silcox VA, Brown JM. Central line sepsis in a child due to a previously unidentified mycobacterium. *J Clin Microbiol*. 1999;37:1193-1196.
14. Holland DJ, Chen SC, Chew WW, Gilbert GL. Mycobacterium neoaurum infection of a Hickman catheter in an immunosuppressed patient. *Clin Infect Dis*. 1994;18:1002-1003.
15. Kiska DL, Turenne CY, Dubansky AS, Domachowske JB. First case report of catheter-related bacteremia due to "Mycobacterium lacticola". *J Clin Microbiol*. 2004;42:2855-2857.
16. Levendoglu-Tugal O, Minoz J, Brudnicki A, Ozkaynak MF, Sandoval C, Jayaboseet S. Infections due to nontuberculous mycobacteria in children with leukemia. *Clin Infect Dis*. 1998;27:1227-1230.
17. Livni G, Yaniv I, Samra Z, et al. Outbreak of Mycobacterium mucogenicum bacteremia due to contaminated water supply in a paediatric haematology-oncology department. *J Hosp Infect*. 2008;70:253-258.
18. Marshall C, Samuel J, Galloway A, Pedler S. Mycobacterium mucogenicum from Hickman line of an immunocompromised patient. *J Clin Pathol*. 2008;61:140-141.
19. Navari RM, Sullivan KM, Springmeyer SC, et al. Mycobacterial infections in marrow transplant patients. *Transplantation*. 1983;36:509-513.
20. Reilly AF, McGowan KL. Atypical mycobacterial infections in children with cancer. *Pediatr Blood Cancer*. 2004;43:698-702.
21. Roy V, Weisdorf D. Mycobacterial infections following bone marrow transplantation: a 20 year retrospective review. *Bone Marrow Transplant*. 1997;19:467-470.
22. Shachor-Meyouhas Y, Sprecher H, Eluk O, Ben-Barak A, Kassiset I. An outbreak of Mycobacterium mucogenicum bacteremia in pediatric hematolgy-oncology patients. *Pediatr Infect Dis J*. 2011;30:30-32.
23. Suara R, Whitlock J, Spearman P. Mycobacteria fortuitum central venous catheter-related bacteremia in an infant with renal sarcoma. *Pediatr Hematol Oncol*. 2001;18:363-365.
24. Suryanarayan K, Campbell J, Eskinazi AE. Nontuberculous mycobacterial infections in pediatric acute leukemia. *J Pediatr Hematol Oncol*. 2002;24:558-560.
25. Washer LL, Riddell JT, Rider J, Chenoweth CE. Mycobacterium neoaurum bloodstream infection: report of 4 cases and review of the literature. *Clin Infect Dis*. 2007;45:e10-e13.
26. Wei MC, Banaei N, Yakrus MA, Stoll T, Gutierrez KM, Agarwal R. Nontuberculous mycobacteria infections in immunocompromised patients: single institution experience. *J Pediatr Hematol Oncol*. 2009;31:556-560.
27. Woo PC, Tsoi HW, Leung KW, et al. Identification of Mycobacterium neoaurum isolated from a neutropenic patient with catheter-related bacteremia by 16S rRNA sequencing. *J Clin Microbiol*. 2000;38:3515-3517.
28. Zainal Muttakin AR, Tan AM. Mycobacterium fortuitum catheter-related sepsis in acute leukemia. *Singapore Med J*. 2006;47:543-545.
29. Koranyi KI, Ranalli MA. Mycobacterium aurum bacteremia in an immunocompromised child. *Pediatr Infect Dis J*. 2003;22:1108-1109.
30. Nicholson O, Feja K, LaRussa P, et al. Nontuberculous mycobacterial in pediatric hematopoietic stem cell transplant recipients: case report and review of the literature. *Pediatr Infect Dis J*. 2006;25:263-267.
31. Engler HD, Hass A, Hodes DS, Bottone EJ. Mycobacterium chelonae infection of a Broviac catheter insertion site. *Eur J Clin Microbiol Infect Dis*. 1989;8:521-523.
32. Hong T, Butler WR, Hollis P, et al. Characterization of a novel rapidly growing Mycobacterium species associated with sepsis. *J Clin Microbiol*. 2003;41:5650-5653.
33. Hoy JF, Rolston KV, Hopfer RL, Bodey GP. Mycobacterium fortuitum bacteremia in patients with cancer and long-term venous catheters. *Am J Med*. 1987;83:213-217.

34. Wallace RJ Jr, Tanner D, Brennan PJ, Brown BA. Clinical trial of clarithromycin for cutaneous (disseminated) infection due to Mycobacterium chelonae. *Ann Intern Med*. 1993;119:482-486.

35. Takemori-Sakai Y, Iwata Y, Oe H, Sakai Y, Wada T. Bloodstream infection caused by Mycobacterium chelonae. *Pediatr Int*. 2018;60:599-600.

36. Al Yazidi LS, Marais BJ, Hazleton B, Outhred A, Kesson A. Nontuberculous Mycobacteria in Children: A Focus on Bloodstream Infections. *Pediatr Infect Dis J*. 2017;36:374-378.

37. Redelman-Sidi G, Sepkowitz KA. Rapidly growing mycobacteria infection in patients with cancer. *Clin Infect Dis*. 2010;51:422-434.

38. Wallace RJ Jr, Meier A, Brown BA, et al. Genetic basis for clarithromycin resistance among isolates of Mycobacterium chelonae and Mycobacterium abscessus. *Antimicrob Agents Chemother*. 1996;40:1676-1681.

39. Leao SC, Tortoli E, Viana-Niero C, et al. Characterization of mycobacteria from a major Brazilian outbreak suggests that revision of the taxonomic status of members of the Mycobacterium chelonae-M. abscessus group is needed. *J Clin Microbiol*. 2009;47:2691-2698.

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