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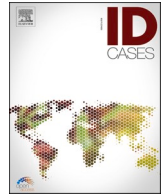
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Case report

Mycobacterium cosmeticum catheter-related bloodstream infection in an immunocompetent patient: A case report and review of the literature

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ABSTRACT

Background: *Mycobacterium cosmeticum* is an emerging rapidly growing mycobacteria (RGM) species that has been rarely reported to cause human disease. RGM catheter-related bloodstream infections (CRBSI) are often challenging to treat given the need for line removal, variable species-dependent antimicrobial susceptibility, combination antimicrobial treatment, and historically longer courses of antibiotics.

Case presentation: We present a case of an immunocompetent pediatric patient with severe hemophilia B and *M. cosmeticum* CRBSI. While the patient's hemophilia B precluded a standard line holiday, he successfully cleared his infection with two line exchanges followed by two weeks of antibiotics.

Conclusions: RGM, including emerging species *M. cosmeticum*, may be considered in patients with an indolent presentation of CRBSI. Our case suggests source control with shorter courses of antimicrobials can be successful.

Introduction

Rapidly growing mycobacteria (RGM) are a diverse group of nontuberculous mycobacteria defined by their ability to form mature colonies on agar plates within 7 days. RGM are ubiquitous in nature and have been increasingly identified as a cause of human infections worldwide. RGM cause a wide range of clinical disease in both immunocompromised and healthy individuals. They are not highly virulent and are associated with low mortality. However, their ability to form biofilms, which allows them to survive in varied hostile environments, also makes them well suited to colonize medical devices; therefore, catheter-related bloodstream infections (CRBSI) are a common form of RGM disease [1]. Here we present a rare case of an emerging RGM species, *Mycobacterium cosmeticum*, affecting an immunocompetent pediatric host with an underlying illness.

Case

We present a case of a 14-year-old male with severe hemophilia B on prophylactic home recombinant Factor VII infusions via a single lumen central venous catheter. Infusions were initiated following a prior

anaphylactic reaction to Factor IX and frequent severe episodes of spontaneous bleeding. The patient presented to the emergency department with fever. Two weeks prior to presentation, his parents noted cracking of his central line tubing. When his Factor VII infusion was next administered, a leakage of the medication was noted. Concurrently, the patient had chills and felt warm during this infusion. Soon thereafter, the patient developed fatigue, decreased appetite, and intermittent subjective fevers. No further doses of Factor VII were given due to the leakage from the central venous catheter. Family reports that the patient did not present to care during this two-week period due to distance from the healthcare facility. The present central line had been in place for two years. His medical history was notable for prior polymicrobial central line infections with *Aeromonas punctata*, *Pantoea species*, and *Rhizobium radiobacter* three years ago and with *Stenotrophomonas maltophilia*, *Staphylococcus epidermidis*, and *Achromobacter species* two years ago. The patient denied any recent travel, animal contacts, insect bites, procedures, or water exposure to the catheter.

On arrival to the emergency department, his temperature was 39.5 °C, heart rate 126 bpm, respiratory rate 14 bpm, blood pressure 126/84 mm Hg, and O₂ saturation 99 % on room air. On initial exam, he was in no acute distress and was well-appearing, with no erythema,

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Table 1

Antibiotic susceptibilities of *M. cosmeticum* isolated from blood cultures and catheter tip of a pediatric patient with a catheter-related bloodstream infection.

Antibiotic	MIC* (mcg/mL)	Interpretation
Amikacin	≤ 0.5	Susceptible
Cefoxitin	8	Susceptible
Ciprofloxacin	≤ 0.5	Susceptible
Clarithromycin	0.12	Susceptible
Doxycycline	≤ 0.25	Susceptible
Trimethoprim/Sulfamethoxazole	≤ 0.05	Susceptible

* Abbreviation: Minimum inhibitory concentration (MIC)

swelling, or tenderness at the central line site, but with tape wrapped around the distal end of the central line tubing. He was started on cefepime and vancomycin and given a normal saline bolus. Complete blood count showed anemia (hemoglobin 10.3 g/dL) with normal white blood cell (5930/mm³) and platelet (473,000/mm³) counts. Coagulation studies were notable for an elevated activated partial thromboplastin time (135.9 s), but normal prothrombin time and international normalized ratio. Central and peripheral blood cultures were also sent. Chest x-ray demonstrated appropriate placement of the central line catheter tip and a large right-sided pleural effusion.

On hospital day 2, the patient underwent central venous catheter exchange by interventional radiology, and the original catheter tip was sent for culture. Line exchange, rather than line removal, was performed due to concerns for catastrophic bleeding without a new line in place to tamponade bleeding, as patient had gone over a week without his scheduled Factor VII infusions. He also underwent thoracentesis and chest tube placement, yielding 600 mL of frank blood.

On hospital day 3, his initial central blood culture was reported to be growing gram variable rods, and on hospital day 5 this was identified as acid-fast bacilli, consistent with a RGM species, at which point cefepime and vancomycin were discontinued. On hospital day 6, the organism was identified as *Mycobacterium cosmeticum*. The initial peripheral blood culture remained negative. He was assessed by interventional radiology and cardiothoracic surgery and determined not to be a good candidate for line removal due to bleeding risk. The patient was started on triple therapy with ciprofloxacin, clarithromycin, and trimethoprim-sulfamethoxazole. On hospital day 8, the catheter tip culture sent at the time of line exchange and a repeat blood culture drawn on hospital day 3 from the new central line also returned positive and the patient was transitioned to triple therapy with ciprofloxacin, azithromycin, and

amikacin for broader coverage while awaiting susceptibilities. Multiple repeat blood cultures drawn from the new central line after hospital day 3 were negative. No additional sites of infection were identified.

After careful surgical consideration, repeat line exchange was safely conducted on hospital day 17 for additional source control. Further cultures from this central line were not obtained. On hospital day 17, susceptibilities for *Mycobacterium cosmeticum* were found to be favorable for first-line agents (Table 1). After line exchange, he completed an additional 7-day course of amikacin and a 14-day course of both azithromycin and ciprofloxacin, for a total duration of 24 days of antibiotics. He completed the course without complications and was discharged with the new central line in place. No antimicrobial toxicities were experienced. Five months after discharge he continues to do well with no further infectious concerns.

The initial species identification of *Mycobacterium cosmeticum* was made by VITEK MS MALDI-TOF (BioMérieux, NC, USA) using a library that is not yet FDA-approved. Given the uncertainty of these results, the challenges associated with species identification of less common mycobacteria, and the lack of published data on *M. cosmeticum* identification by MALDI-TOF [2], we performed whole-genome sequencing (WGS) to further validate the species identification.

DNA was extracted from the isolate (UCLA_1632) using the Qiagen EZ1 Tissue Kit. Libraries were prepared using Tecan MagicPrep NGS System. Isolate UCLA_1632 was sequenced using the Illumina Miseq platform with 2 × 250 bp protocol. To classify the isolate phylogenetically we first identified a related bacterial species using KmerFinder on the Center for Genomic Epidemiology online platform [3,4]. The top hit was downloaded onto the CLC Genomics Workbench 23.0.4. The reference genes for 16 S rRNA, groL (hsp65), and rpoB were extracted from this candidate. The paired sequencing reads of our isolate were aligned to these genes. The consensus sequences that mapped to each of these genes were run on NCBI BLAST to identify species of bacteria with high query cover and percent identity. The whole genomes of the top candidates were downloaded onto the CLC Genomics Workbench (See Supplementary Table 1). A K-mer tree was then created with these candidates and isolate UCLA_1632 using the K-mer Tree function on CLC via the FFP method, with a K-mer length of 16 (Fig. 1). K-mer Tree analysis demonstrated that our isolate clustered most closely with *M. cosmeticum*, confirming the MALDI-TOF identification. By BLAST analysis isolate UCLA_1632 and *M. cosmeticum* shared > 99 % identity for the 16 S rRNA gene, the highest we found, further confirming our speciation.

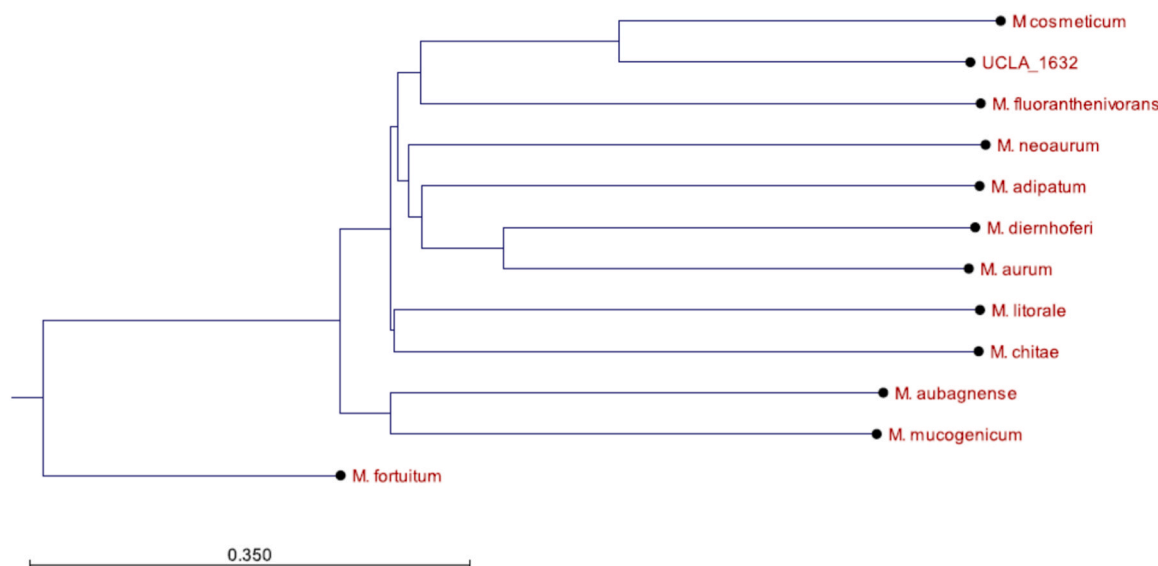


Fig. 1. K-mer based phylogenetic tree of the current reported isolate, UCLA_1632, and related Rapidly Growing Mycobacteria.

Table 2
Comprehensive review of *Mycobacterium cosmeticum* in the literature from first description in 2004 to 2023.

Author (Year published)	Location	Age, Sex	Past Medical History	Presentation	Source	Clinical significance	Treatment	Outcome
Cooksey et al. (2004)[5]	Caracas, Venezuela	unk,F	Recent mesotherapy	-	Cutaneous	Definite	CIP* x 3 mo	-
Cooksey et al. (2007)[7]	Caracas, Venezuela	36yM	HIV	Fever, dyspnea, and cough	Respiratory (Sputum)	Unclear	TMP/SMX	Respiratory arrest and death 6 weeks after presentation
	Ohio, USA	77yM	Diabetes, CAD, hyperlipidemia, coal workers' pneumoconiosis, discitis	COPD exacerbation, urosepsis, and fever	Blood (CRBSI)	Definite	Removal of catheter	Condition improved without antimicrobials and discharged after 4 days
	Ohio, USA	43yF	Non-Hodgkin lymphoma	-	Blood (CRBSI)	Unclear	None	No infectious symptoms during or after admission
Addley et al. (2010)[14]	Derry, UK	63yF	Atrial septal defect, diabetes, ovarian cyst s/p distant laparotomy	Several months of abdominal distension, weight loss, and night sweats	Ascites	Likely infection	Drainage of ascites. Treated as presumptive tuberculosis due to delay in identification	No recurrence 1 year later
Boschetti et al. (2011)[12]	France	32yM	Previously healthy	1 month of abdominal pain, bloody diarrhea, and fever	Colon	Definite	3 mo of oral CLR and OFL	Resolution of infection with no recurrence in 4 years of follow up
Koay et al. (2015)[10]	TX, USA	0dF	Ex-27 week, isoimmune hemolytic disease	-	Blood	Definite	Umbilical line removed DOL 8. AMK and AZM started DOL 9 x 7 days.	Significant neurologic sequelae, thought to be unrelated to <i>M cosmeticum</i> bacteremia
Varghese et al. (2017)[6]	Saudi Arabia	39yM	Asthma, prior TB, HIV	Asymptomatic	Respiratory (Sputum)	Likely colonization	-	-
	Saudi Arabia	48yM	Lung transplant	-	Respiratory (Sputum)	Definite	-	-
	Saudi Arabia	59yM	Diabetes	-	Cutaneous	-	-	-
Vutescu & Koenig (2017)[13]	New Hampshire, USA	67yM	GERD, spinal stenosis, L knee osteoarthritis	Pain, swelling, and erythema of L knee 8 weeks after arthroplasty	Periprosthetic joint infection	Definite	6 mo of oral MFX, TMP/SMX, and CLR.	No recurrence 2 years later
Aljishi et al. (2021)[8]	Saudi Arabia	69yM	Renal transplant on immunosuppression, hx of R lung decortication	4 days dry cough, fever, chills, and fatigue	Respiratory (BAL)	Definite	IMI, AMK and CLR x 4 wk, then unspecified oral regimen	Clinical and radiologic improvement. Repeat BAL cultures negative after 6 weeks.
Grupel et al. (2023)[2]	Israel	42 mM	Neuroblastoma on chemotherapy	Febrile neutropenia	Blood (Infected CVC thrombus)	Definite	Catheter removal, IMI, CLR, and AMK x 4 weeks, then long term oral CLR and CIP	Resolution of clot within 2 months
Hu et al. (2023)[9]	China	31yF	Systemic sclerosis, interstitial pneumonia, CKD, acute left-sided heart failure	Fever, chills, hemoptysis, chest pain	Respiratory (Sputum)	Definite	RIF, EMB, CLR, and MFX x 21 days, then RIF, EMB and CLR x 14 days, then RIF and CLR x 4.5 mo	Clinical and radiologic improvement.

* Abbreviations: rifampin (RIF), ethambutol (EMB), clarithromycin (CLR), ciprofloxacin (CIP), moxifloxacin (MFX), ofloxacin (OFL), amikacin (AMK), azithromycin (AZM), trimethoprim/sulfamethoxazole (TMP/SMX), imipenem (IMI), Day of life (DOL), Central Venous Catheter (CVC).

Discussion

Mycobacterium cosmeticum is a RGM species first identified in the drains of a nail salon in Atlanta, Georgia and determined to be a cause of cutaneous infection in Venezuela in 2004 [5]. In addition to skin and soft tissue infections [6], it has subsequently been found to cause a variety of infections including pneumonia [6–9], catheter-related bloodstream infections [2,7,10,11], colitis [12], periprosthetic joint infections [13], and ascites [14] (Table 2).

Our patient was found to have CRBSI caused by *M. cosmeticum*. We suspect that his infection was caused by water exposure to his catheter,

as *M. cosmeticum* has been isolated from aqueous environments [5], and our patient had a cracked line. He had also previously presented with CRBSIs with water-associated organisms including *Aeromonas punctata*, *Stenotrophomonas maltophilia*, and *Achromobacter species*. Although it was initially identified on regular blood culture alone, AFB cultures can be considered in patients presenting with prolonged symptoms.

Notably, *M. cosmeticum* has two highly genetically related species, *M. fluoranthenivorans* and *M. neoaurum*, which can pose challenges for species identification in clinical laboratories. We found these two species had 98.8% identity in the 16 S rRNA gene of our patient's isolate. This high percent identity within the 16 S rRNA gene supports other

published reports on the difficulty of speciating these mycobacteria based on the 16 S rRNA gene alone [2]. By K-mer Tree analysis, isolate UCLA_1632 and *M. cosmeticum* were next most closely related to *M. fluoranthenorans*, then followed by *M. neoaurum*. Interestingly *M. fluoranthenorans* has only been isolated from soil and has not been associated with human infection [15], whereas *M. neoaurum* has been isolated and shown to be a causative agent in over a dozen human infections, mostly associated with the use of medical devices in severely ill patients [16].

However, differentiation of these species may not be clinically warranted as they are generally susceptible to most antibiotics commonly used to treat RGM [16].

As *M. cosmeticum* is a rare pathogen, there are no randomized trials or evidence-based guidelines on which to base treatment decisions. Additionally, identification of the RGM species can take up to 1 week, so antibiotics are often empirically started prior to availability of species identification and susceptibilities. RGM species have variable susceptibility patterns and no single agent is active against all RGM species [17]. Therefore, in cases of RGM CRBSI, it is recommended to start combination antibiotic therapy for empiric treatment. In our case, the patient was started on empiric combination therapy with ciprofloxacin, clarithromycin, and trimethoprim-sulfamethoxazole given initial concerns for toxicity with amikacin in a pediatric patient and as his infected line was removed rapidly on presentation. However, with a second positive blood culture, we switched to amikacin, as the literature demonstrates that nearly all RGM species are susceptible to amikacin [1,17]. We agree with El Helou et al. [1] that adding amikacin to an empiric regimen may be prudent to ensure an active agent is present, with close monitoring for toxicities. Once susceptibilities are available, treatment can be narrowed and converted to an oral regimen, although the optimal duration of treatment is unknown. Studies have demonstrated good outcomes with 2–4 weeks of antibiotic therapy for RGM CRBSIs [1,17]. One small case series of RGM CRBSIs even reported successful outcomes in immunocompromised patients receiving a median of 7 days of antibiotics following infected catheter removal [18]. Our patient achieved apparent cure with 14 days of antibiotics after line exchange and 24 days of antibiotics total, supporting that shorter treatment regimens may be adequate, especially with removal of the infected catheter.

In addition to antimicrobial therapy, removal of infected intravascular devices is another important component of treatment for RGM CRBSI. Line removal has been associated with a significant decrease in the rate of bloodstream relapse [1]. RGM CRBSI has been successfully treated with line removal alone [17,19], including patients with *M. cosmeticum* [7]. This approach of line removal alone with careful monitoring could be considered in select immunocompetent patients who may be at high risk for antimicrobial side effects, lack antimicrobial options due to resistance, or have a history of poor adherence.

As immunocompetent pediatric patients increasingly have long-term central lines, RGM should be considered in those presenting with subacute symptoms, exposed central lines, and those with ongoing signs of infection not responding to empiric antibiotics. Here we present a thorough review of the existing literature on *M. cosmeticum*, a still emerging pathogen that currently demonstrates susceptibility to most anti-mycobacterial regimens. Optimal management should be selected and adjusted based on existing RGM guidelines [1,20] and individual patient factors.

Ethical approval

Not Applicable.

Author Agreement Statement

We the undersigned declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We understand that the Corresponding Author is the sole contact for the Editorial process. He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

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CRediT authorship contribution statement

Colette J Matysiak Match: Writing – review & editing, Writing – original draft. **Kristina Adachi:** Writing – review & editing. **Karin Nielsen-Saines:** Writing – review & editing. **Shangxin Yang:** Writing – review & editing. **Sanchi Malhotra:** Writing – review & editing, Supervision. **Julia S Turock:** Writing – review & editing, Writing – original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in Chief of this journal on request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.idcr.2024.e02051](https://doi.org/10.1016/j.idcr.2024.e02051).

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