

Gordonia Bacteremia

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Gordonia species are ubiquitous aerobic actinomycetes that rarely cause infection in humans. We report the second known case of *Gordonia otitidis* catheter-related bacteremia in an immunocompromised patient and review four additional cases of *Gordonia* bacteremia seen at our institution over the past 14 years. In addition, the existing literature on *Gordonia* infections is reviewed.

CASE REPORTS

This case report presents five cases of *Gordonia* bacteremia caused by four different *Gordonia* species, together with the clinical and microbiologic characteristics of these uncommon pathogens. Three of the five cases were line-related bacteremias that occurred in patients with acute myelogenous or acute lymphocytic leukemia.

Case 1 (*Gordonia otitidis*). The patient was a 38-year-old male with a history of acute monoblastic leukemia in remission after he underwent a matched unrelated donor allogeneic peripheral blood stem cell transplant in the autumn of 2012. He received myeloablative conditioning with CY-TBI (cyclophosphamide–total-body irradiation) and graft-versus-host disease prophylaxis with tacrolimus and minidose methotrexate. His posttransplantation course was remarkable for grade 1 graft-versus-host disease of the skin, which resolved with topical steroid use. Six months later, the patient presented with fever without any focal symptoms. The Hickman catheter site was without erythema, exudate, or tenderness. Blood cultures drawn from all of the ports of the Hickman catheter grew Gram-positive bacilli resembling *Corynebacterium* sp., which were later identified as *Gordonia otitidis* by 16S rRNA gene sequencing with a 100% match with the type strain of *G. otitidis*. A total of five positive sets of blood cultures were drawn from the Hickman catheter over a span of 4 days with times to positivity ranging from 20 to 113 h. *G. otitidis* grew in all bottles (aerobic, anaerobic, and MycoF/Lytic Bactec bottles; Becton Dickinson, Sparks, MD). The peripheral blood cultures remained negative. The Hickman catheter was removed on day 3, and there was no growth from the catheter tip culture. He received intravenous vancomycin for a total of 7 days. He defervesced quickly after line removal, and repeat peripheral blood cultures continued to be negative.

Case 2 (*Gordonia polyisoprenivorans*). A 48-year-old man diagnosed with acute myelogenous leukemia (AML) in the spring of 2012 underwent allogeneic transplantation of peripheral blood stem cells from a matched, unrelated donor with CY-TBI conditioning in August 2012. A Hickman catheter was placed in August 2012. He was hospitalized in September 2012 for *Enterococcus faecalis* (penicillin-susceptible) bacteremia and was treated with a 2-week course of intravenous penicillin G and vancomycin lock therapy. The Hickman catheter was not removed at that time. He subsequently developed a fever associated with arm and upper body swelling and cyanosis with plethora in December 2012. There was no evidence of infection at the site of the Hickman catheter. He was found to have superior vena cava syndrome re-

lated to a clot surrounding his catheter, which was sitting in the superior vena cava. Blood cultures drawn through all of the ports of the Hickman catheter grew a Gram-positive bacillus in six of six aerobic Bactec bottles after 32 h of incubation. The organism was subsequently identified as *G. polyisoprenivorans* by 16S rRNA gene sequencing (100% match with the type strain). Peripheral blood cultures were negative. The catheter was removed, and he was treated with thrombolytic therapy. Culture of the catheter tip also grew *G. polyisoprenivorans*. He was started on antibiotics empirically with vancomycin and cefepime prior to organism identification and susceptibility testing. Antibiotics were later switched to intravenous ceftriaxone after identification of the organism, and he completed 4 weeks of therapy with resolution of the infection. Repeat blood cultures were negative.

Cases 3 (*Gordonia terrae*). The third case was an 81-year-old woman with a history of end-stage renal disease on hemodialysis via a tunneled catheter, hypertension, and diabetes mellitus who was hospitalized for hypotension after dialysis and altered mental status. She received fluid resuscitation and was empirically treated with vancomycin and cefepime for possible sepsis. Peripheral blood cultures drawn at admission grew a small, Gram-positive bacillus resembling *Corynebacterium* sp. after 4 days in one of two sets of blood culture bottles. The bacillus was subsequently identified as *G. terrae* by 16S rRNA gene sequencing (99.99% match with the type strain). Cultures drawn from the dialysis catheter were negative. She remained afebrile throughout her hospitalization. The isolate was considered to be a contaminant, and antibiotics were stopped on day 3. Her mental status changes and hypotension had resolved on discharge.

Case 4 (*Gordonia bronchialis*). A 67-year-old female with a history of diabetes mellitus and autoimmune thyroiditis presented with fever, chronic cough, and altered mental status. She was diagnosed with herpes simplex virus 1 encephalitis and treated with acyclovir. Cultures of peripheral blood drawn at admission grew *G. bronchialis*, which was identified by 16S rRNA gene sequencing (100% match with the type strain), in one out of two sets after 6 days. She received multiple antibiotics, including

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cefepime, vancomycin, piperacillin-tazobactam, and cefazolin, for a total of 10 days during her hospitalization. The significance of the transient bacteremia of this patient was unclear. She did not have any indwelling catheters.

Case 5 (*Gordonia* sp.). The patient was a 4-year-old female with a history of acute lymphoblastic leukemia who had had an indwelling Hickman catheter placed 2 months prior for chemotherapy. She presented with a nonneutropenic fever and sepsis. Blood cultures drawn from all of the ports of the Hickman catheter grew *Tsukamurella* species in nine sets and *Gordonia* species in three sets. Both organisms were identified by 16S rRNA gene sequencing. Peripheral blood cultures were not drawn on admission. The Hickman catheter was removed. Despite apparent *in vitro* resistance of the *Gordonia* isolate to trimethoprim-sulfamethoxazole, she was successfully managed with intravenous trimethoprim-sulfamethoxazole for 2 weeks, followed by oral clarithromycin for 4 weeks.

Gordonia species are aerobic actinomycetes that are ubiquitous in the environment. They are frequently isolated from soil and water. The genus *Gordonia* (previously known as *Gordona*) belongs to the family *Gordoniaceae* within the suborder *Corynebacterineae* and the order *Actinomycetales* (1). There are currently 29 species within the genus *Gordonia* (2). The majority of them were isolated from the environment for their unique and useful properties in biotechnology (1, 3). Some species of *Gordonia* have been reported to cause human infections. The cases of *Gordonia* bacteremia seen at the Mayo Clinic, Rochester, MN, from 1999 to 2013 are described in Table 1.

All members of the genus *Gordonia* are Gram-positive, catalase-positive, weakly acid-fast, thinly beaded coccobacilli. They are differentiated phenotypically from rapidly growing mycobacteria by the absence of arylsulfatase activity and from *Nocardia* by the inability to grow in the presence of lysozyme and the absence of aerial hyphae (4).

However, accurate identification of Gram-positive bacilli by conventional phenotypic methods is difficult. *Gordonia* species have been frequently misidentified as *Corynebacteria*, *Nocardia*, and *Rhodococcus* species by traditional methods (4–7). They are sometimes dismissed as contaminating diphtheroids. Because of the difficulty in identifying these organisms, it is believed that a number of *Gordonia* infections may go undetected. The incorporation of genotypic methods like 16S rRNA gene sequencing has improved the identification of clinically relevant aerobic actinomycetes (8).

The species of *Gordonia* that have been isolated from clinical specimens and/or infrequently reported as human pathogens are *Gordonia aichiensis*, *Gordonia araii*, *G. bronchialis*, *Gordonia effusa*, *G. otitidis*, *G. polyisoprenivorans*, *Gordonia rubripertincta*, *Gordonia sputi*, and *G. terrae* (9).

G. aichiensis has been isolated from human clinical specimens such as sputum (9, 10); however, there have been no reported cases of clinical infection and its role as a human pathogen remains unclear.

G. araii and *G. effusa* were first isolated from the sputum of a Japanese patient (11). *G. araii* has also been associated with orthopedic device infection (12).

G. bronchialis was associated with a cluster of sternal wound

TABLE 1 Cases of *Gordonia* bacteremia from 1999 to 2013 at the Mayo Clinic, Rochester, MN

No.	Age (yr)	Gender	Species	Underlying comorbidity(ies) ^a	Presence of indwelling CVC ^b	Type of infection	Treatment and duration	Clinical outcome	Yr of isolation
1	38	Male	<i>G. otitidis</i>	AML s/p-MUD allogeneic PBSCT	Hickman catheter	Line-associated bacteremia	Vancomycin for 7 days	Resolution of infection	2013
2	48	Male	<i>G. polyisoprenivorans</i>	AML s/p-MUD allogeneic PBSCT	Hickman catheter	Line-associated bacteremia	Vancomycin and cefepime prior to identification, followed by ceftriaxone for 4 weeks	Resolution of infection	2012
3	81	Female	<i>G. terrae</i>	ESRD, HD, DM, PAD	Tunneled dialysis catheter	Bacteremia; possible contaminant	Vancomycin and cefepime for 3 days ^c	Resolution of symptoms	2011
4	67	Female	<i>G. bronchialis</i>	DM; autoimmune thyroiditis, concurrent HSV encephalitis	None	Bacteremia	Multiple antibiotics ^d for a total of 10 days	Resolution of infection	2010
5	4	Female	<i>Gordonia</i> sp., not further identified	ALL with CNS relapse, concurrent <i>Tsukamurella</i> bacteremia	Hickman catheter	Line-associated bacteremia	TMP-SMX for 2 weeks, followed by clarithromycin for 4 weeks	Resolution of infection	1999

^a Abbreviations: ALL, acute lymphoblastic leukemia; CNS, central nervous system; ESRD, end-stage renal disease; HD, hemodialysis; PAD, peripheral arterial disease; MUD, matched unrelated donor; PBSCT, peripheral blood stem cell transplant; s/p, status post.

^b CVC, central venous catheter.

^c The organism was considered to be a contaminant and not clinically significant.

^d Vancomycin, cefepime, piperacillin-tazobactam, and cefazolin.

infections after coronary artery bypass graft (CABG) that was later traced to a colonized nurse (13). It has also been isolated from the cerebrospinal fluid of a 45-day-old premature neonate with an intraventricular shunt who was treated with 6 weeks of amikacin and meropenem after shunt removal (5). Other reported cases include a recurrent breast abscess (14), bacteremia (15), an association with a sequestered lung (16), and pleural space infection (2).

G. otitidis was first isolated from two Japanese patients; the first isolate was from the ear discharge of a 28-year-old female with otitis externa; the second specimen was from the pleural fluid of a 60-year-old male with bronchitis (17). A case of catheter-related bacteremia with dissemination to the lungs (miliary nodules) in an 11-year-old boy has been described. Therapy with 6 weeks of imipenem plus clarithromycin and catheter removal was successful (5). Ours is the second reported case of bacteremia due to this species.

G. polyisoprenivorans was first isolated in 1999 from foul water inside a deteriorated automobile tire (18). It is one of the most effective rubber-degrading organisms known (19). Its ability to utilize degrading rubber as a sole carbon source, along with bio-surfactant production to form biofilms for attachment, may explain the association of bacteremia in immunocompromised patients with chronic indwelling catheters (1, 19, 20). In addition to our case, four other cases of *G. polyisoprenivorans* bacteremia have been reported and all of the cases thus far have been associated with an indwelling central catheter. The first case of bacteremia was reported by Kempt et al. in 2004 in a 26-year-old woman with chronic myelogenous leukemia who received an allogeneic bone marrow transplant. Before transplantation, a Hickman catheter was placed for myeloablative conditioning therapy. Three months after receiving the transplant, she developed a fever 1 day after flushing the Hickman catheter. A blood sample taken from the Hickman catheter grew *G. polyisoprenivorans*. The Hickman catheter was removed, and she was successfully treated with piperacillin-tazobactam for 3 days, followed by a 1-week oral course of amoxicillin and ciprofloxacin (21). The second case was reported by Verma et al. in 2006 in a 78-year-old male with myelodysplastic syndrome and aplastic anemia who had an indwelling Hickman catheter for frequent blood transfusions. Peripheral blood cultures drawn during a febrile episode grew a Gram-positive rod that was initially identified as *Corynebacterium pseudodiphtheriticum*. The fever resolved without antibiotics. Three weeks later, he developed infective endocarditis of the aortic and mitral valves and underwent aortic valve replacement with debridement of the mitral valve. The organism was submitted to the Actinomycete Reference Laboratory at the Centers for Disease Control and Prevention (CDC) and identified by genotypic methods as *G. polyisoprenivorans*. The patient died after 6 weeks despite using three different antibiotic regimens (4). The third case was reported by Gupta et al. in 2010 in a 17-year-old woman with undifferentiated myeloblastic leukemia 5 weeks after cytarabine and mitoxantrone therapy. She was neutropenic and had a chronic central venous catheter. She was initially treated with azithromycin and ciprofloxacin for presumed *Rhodococcus equi* bacteremia. Three weeks later, she developed right lower lobe pneumonia with associated bacteremia. A blood culture (2/2) grew a Gram-positive rod after 4 weeks that was identified by the CDC as *G. polyisoprenivorans* (22). Interestingly, there was no evidence of infection at the site of the central venous catheter insertion in all three of these cases. The

fourth case was reported by Langer et al. in 2010 in a 17-year-old female with acute myelogenous leukemia who had an indwelling central venous catheter. She developed bacteremia and right lower lobe pneumonia with bilateral pulmonary nodules. The Gram-positive bacilli were initially misidentified as *Rhodococcus equi*. Her infection resolved after treatment with multiple antibiotic regimens. During an epidemiological investigation for an apparent *R. equi* outbreak, the patient's isolates were submitted to the CDC, where the isolate was identified as *G. polyisoprenivorans* (7).

G. rubripertincta was previously known as *Rhodococcus rubropertinctus* until 1989 (23) and was reported to have caused a lung infection clinically resembling tuberculosis in an immunocompetent host who responded to oral antituberculosis therapy (24).

G. sputi has been reported to cause a variety of infections ranging from mediastinitis in a patient after CABG (25) to catheter-associated bacteremia (15, 26–28), bacteremia with cutaneous lesions in an immunocompromised host on interleukin-2 therapy (29), and keratitis (28). It has also been isolated from the sputum of patients with chronic pulmonary disease (17).

G. terrae has been associated with skin infections (30, 31), brain abscesses and meningitis (32, 33), catheter-related bacteremia especially in immunocompromised patients (5, 34–36), primary bacteremia (28), wound infection (28), palpable abscess (3), suppurative granulomatous mastitis following nipple piercing (37), and bacteremia in the course of acute cholecystitis (6).

There are no guidelines for the management of *Gordonia* infections. Treatment should be individualized and based on the isolate's *in vitro* antimicrobial susceptibility test results. The previously reported cases have been treated with a variety of antimicrobials for various periods of time. Recently, the *in vitro* antimicrobial susceptibilities of 13 human isolates of *G. polyisoprenivorans* were reported by Moser et al. (20). Nearly half of the strains were resistant to trimethoprim-sulfamethoxazole. Some strains were resistant to tigecycline, minocycline, and clarithromycin. All isolates were susceptible to amikacin, ampicillin, ceftriaxone, imipenem, amoxicillin-clavulanate, ciprofloxacin, vancomycin, and linezolid (20). Our isolates were tested in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines available at the time of isolate identification (38). As a result, not all of the drugs listed in Table 2 were tested against all of the isolates, particularly the isolates identified prior to the March 2011 release of the latest CLSI guidelines for susceptibility testing of aerobic actinomycetes, including *Gordonia* species (38). All isolates were susceptible to imipenem, ciprofloxacin, and amikacin. The *G. polyisoprenivorans* isolate was resistant to clarithromycin. In addition, the *Gordonia* species (case 5) and *G. polyisoprenivorans* (case 2) had intermediate susceptibility to minocycline and the *Gordonia* species (case 5) was resistant to trimethoprim-sulfamethoxazole (Table 2).

Gordonia species are rare but emerging human pathogens that cause a variety of infections in both immunocompromised and immunocompetent hosts. Gram-positive bacilli found in blood cultures, especially those of patients with long-term indwelling catheters, should not be routinely dismissed as contaminating diphtheroids, especially in immunocompromised patients. Genotypic methods such as 16S rRNA gene sequencing should be employed for the proper identification of aerobic actinomycetes to the species level. The number of recognized infections due to *Gordonia* species may rise in the future because of the increased use of

TABLE 2 Growth rates and antibiotic susceptibility patterns of *Gordonia* spp. isolated from blood, 1999 to 2013

Isolate no.	Yr of isolation	Source	Species	Time to positivity	MIC, µg/ml (susceptibility) ^a											
					Amoxicillin-clavulanate	Cefepime	Ceftriaxone	Imipenem	Ciprofloxacin	Moxifloxacin	Clarithromycin	Amikacin	Tobramycin	Doxycycline	Minocycline	TMP-SMX ^b
1	2013	Line	<i>G. otitidis</i>	20 h	≤2/1 (S)	4 (S)	4 (S)	≤2 (S)	≤0.12 (S)	<0.25 (S)	0.5 (S)	≤1 (S)	0.5 (S)	≤1 (S)	≤0.25/4.75 (S)	4 (S)
2	2012	Line	<i>G. polyisoprenivorans</i>	32 h	8/4 (S)	4 (S)	8 (S)	≤2 (S)	0.5 (S)	≤0.25 (S)	16 (R)	2 (S)	1 (S)	4 (I)	≤0.25/4.75 (S)	4 (S)
3	2011	Peripheral blood	<i>G. terrae</i>	4 days	≤1/0.5 (S)	ND ^c	2 (S)	≤0.25 (S)	≤0.12 (S)	≤0.12 (S)	≤0.25 (S)	≤0.5 (S)	ND	≤1 (S)	16 (S) (sulfamethoxazole)	1 (S)
4	2010	Peripheral blood	<i>G. bronchialis</i>	6 days	≤1/0.5 (S)	ND	4 (S)	≤0.25 (S)	0.25 (S)	≤0.12 (S)	2 (S)	≤0.5 (S)	ND	≤1 (S)	ND	1 (S)
5	1999	Line	ND	24–48 h	ND	ND	4 (S)	1 (S)	1 (S)	ND	ND	8 (S)	ND	ND	>2/38 (R)	ND

^a S, susceptible; I, intermediate; R, resistant.

^b TMP-SMX, trimethoprim-sulfamethoxazole.

^c ND, not determined.

long-term indwelling central venous catheters, the extended survival of immunocompromised patients, and improved laboratory identification methods. There is no standardized treatment available for treating *Gordonia* infections because of the rarity of cases, so the choice of antimicrobial regimen should be guided by *in vitro* susceptibility test results. The duration of therapy is unclear and should be based on the host's underlying immune function and clinical response to therapy.

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