

Native Valve Endocarditis Due to *Gordonia polyisoprenivorans*: Case Report and Review of Literature of Bloodstream Infections Caused by *Gordonia* Species

Punam Verma,^{1,2,3*} June M. Brown,⁴ Victor H. Nunez,³ Roger E. Morey,⁴ Arnold G. Steigerwalt,⁴
Gerald J. Pellegrini,⁴ and Harold A. Kessler³

*Division of Clinical Microbiology,¹ and Departments of Pathology² and Internal Medicine (Section of Infectious Diseases),³
Rush Medical College, Rush University Medical Center, Chicago, Illinois 60612, and Meningitis and
Special Pathogens Branch, Division of Bacterial and Mycotic Diseases, National Center for
Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333⁴*

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We report the first case of endocarditis caused by *Gordonia polyisoprenivorans* and concisely review the English literature regarding bloodstream infections caused by *Gordonia* species.

CASE REPORT

A 78-year-old male with a past medical history of multiple episodes of gastrointestinal bleeding secondary to Osler-Weber-Rendu and myelodysplastic syndrome with pancytopenia was admitted to our hospital on 12 September 2003 for repair of an incarcerated left inguinal hernia. In August 2002, the patient had a right internal jugular Hickman catheter placed for frequent blood transfusions. The patient was found to have a hemoglobin level of 6.6 g/dl on admission, and he reported melena. Endoscopic evaluation did not reveal an active bleeding site. The patient was noted to have a heart murmur suggestive of aortic stenosis, and a transthoracic echocardiogram confirmed aortic valve disease with a valve area of 1.2 to 1.3 cm². No vegetations were seen. The patient was given a blood transfusion, and the inguinal hernia was repaired. Two days prior to surgery, the patient had an isolated fever spike to 102°F during blood transfusion. Two sets of peripheral blood cultures were obtained. The fever resolved without antibiotic administration. Three of four blood culture bottles were positive for gram-positive rods, identified as *Corynebacterium pseudodiphtheriticum* the day following patient discharge on 19 September 2003. He was admitted to an outside hospital on 15 October 2003 for recurrent anemia and gastrointestinal bleeding. Upper endoscopy showed angiodysplastic lesions, which were cauterized. Shortly after the procedure, the patient complained of chest pain and was found to have developed third-degree heart block. A transthoracic echocardiogram showed the presence of vegetations on the aortic and mitral valves. Three sets of blood cultures were obtained, which all yielded a gram-positive bacillus identified as *Corynebacterium* species. The patient started treatment with vancomycin and levofloxacin, a temporary transvenous pacemaker was implanted, and

the patient was then transferred to our institution on 21 October 2003.

Upon physical examination at our institution, the patient was afebrile and tachycardic but in no distress. Cardiac examination revealed a systolic murmur that was loudest at the apex. He had no peripheral stigmata of endocarditis. The site of his Hickman catheter showed no evidence of infection at the insertion site or along the subcutaneous track. Results of clinical laboratory tests showed a white blood cell count of 2.9×10^9 white blood cells/liter. Antimicrobial treatment was changed to intravenous (i.v.) treatment with ampicillin (3 g i.v. every 6 h) and gentamicin (60 mg i.v. every 12 h). A repeat transthoracic echocardiogram revealed a 25-mm multilobulated, mobile vegetation on the aortic valve and a 10-mm pedunculated, mobile mitral valve vegetation. The Hickman catheter was removed, and a peripherally inserted central venous catheter (CVC) was implanted. On the following day, the patient underwent aortic valve replacement surgery and debridement of the mitral valve vegetation. Histopathological examination of the excised aortic valve showed acute endocarditis, with deformed fibrotic cups with marked calcifications. No microorganisms were seen on special stains. Aortic and mitral valve tissue specimens were submitted to the clinical microbiology laboratory for culture and Gram stain. The aortic valve showed many white blood cells, many red blood cells, and many beaded gram-positive bacilli. The mitral valve specimen showed red and white blood cells but no microorganisms. One of six blood cultures obtained on the day of admission was positive for a beaded gram-positive bacillus. Intravenous treatment with ampicillin and gentamicin was discontinued, and treatment was continued with imipenem-cilastin (500 mg i.v. every 8 h) and amikacin (500 mg i.v. every 8 h). Two blood cultures obtained 4 weeks postoperation were negative. The patient's hospital course was complicated by the development of encephalopathy, and approximately 6 weeks after surgery, the family decided to withdraw care, and the patient died.

The blood culture and the aortic valve isolates recovered at our institution yielded colonies that were morphologically similar to the gram-positive bacillus recovered from the patient's prior two hospitalizations. The organism was a beaded, gram-

* Corresponding author. Present address: Department of Pathology and Clinical Laboratories, Virginia Mason Medical Center, Mail Stop C6-LAB, 1100 Ninth Avenue, P.O. Box 900, Seattle, WA 98101. Phone: (206) 223-6868. Fax: (206) 223-7540. E-mail: punam.verma@vmmc.org.

positive bacillus that produced small dry colonies on sheep blood agar after 24 h of incubation in 5% CO₂ at 35°C. After 3 days of incubation, the colonies became mucoid, and after 7 days of incubation, the colonies turned yellow-orange. The organism was catalase positive, was negative for cytochrome oxidase activity, and failed to grow anaerobically. The biochemical profile determined by the RapID CB Plus system (Remel Inc., Lenexa, Kans.) identified the organism as *Corynebacterium pseudodiphtheriticum* (RapID CB Plus code 0006531; 97% probability). Since the Gram stain morphology did not correlate with the identification obtained by the commercial system, a Kinyoun acid-fast stain modified for aerobic actinomycetes was performed, which showed that the organism was weakly acid fast. The organism was submitted to the Actinomycete Reference Laboratory of the Centers for Disease Control and Prevention, which confirmed the identification of this organism as *Gordonia polyisoprenivorans* based primarily on genotypic methods.

The isolate was examined for aerial hyphae, acid-fast stain reaction, and biochemical characteristics as previously described (5, 14, 21). Differentiation with biochemical tests was unreliable, as there are no phenotypic markers that are able to conclusively separate *G. polyisoprenivorans* from other phylogenetically related *Gordonia* spp. MICs were determined according to CLSI (formerly NCCLS) guidelines (16). The interpretive criteria used for all drugs, except ampicillin and vancomycin, were those recommended by the CLSI for *Nocardia* species and other actinomycetes. The MIC results were as follows: amikacin, ≤ 0.025 $\mu\text{g/ml}$ (susceptible); ampicillin, ≤ 0.5 $\mu\text{g/ml}$ (no interpretive criteria for breakpoints are available); ceftriaxone, ≤ 1 $\mu\text{g/ml}$ (susceptible); clarithromycin, 16 $\mu\text{g/ml}$ (resistant); minocycline, 2 $\mu\text{g/ml}$ (intermediate); sulfamethoxazole, 16 $\mu\text{g/ml}$ (susceptible); trimethoprim-sulfamethoxazole, 0.5/9.5 $\mu\text{g/ml}$ (susceptible); imipenem, 0.5 $\mu\text{g/ml}$ (susceptible); amoxicillin-clavulanate, $\leq 0.5/0.25$ $\mu\text{g/ml}$ (susceptible); ciprofloxacin, ≤ 0.06 $\mu\text{g/ml}$ (susceptible); linezolid, 2 $\mu\text{g/ml}$ (susceptible); and vancomycin, 1 $\mu\text{g/ml}$ (no interpretive criteria for breakpoints are available).

All molecular techniques, including DNA extraction, PCR, 16S rRNA gene sequence determination, and DNA-DNA hybridization, were performed as previously described (3, 15). The 1,445 bp sequenced were compared to the 16S rRNA gene sequence of *G. polyisoprenivorans* ATCC BAA-14^T (GenBank accession number AB054838); 1,444 of 1,445 bp of the patient's isolate were similar to the type strain; however, positions 156, 160, 167, 170, 426, and 1405 contained mixed base pairs. DNA-DNA hybridization studies showed 80% relatedness with a 1.0% divergence between the patient isolate, W8130, and *G. polyisoprenivorans* ATCC BAA-14^T and confirmed the identity of the isolate as *G. polyisoprenivorans*.

Gordonia species are aerobic actinomycetes that are ubiquitous in the environment and are often found in soil and water (21). Members of this genus have undergone several taxonomic revisions and were only recently classified in the genus *Gordonia*, the type genus of family *Gordoniaceae* in the order *Actinomycetales* (2). Most of the 21 species belonging to this genus are known for their ability to biodegrade hydrocarbons

and other xenobiotics in the environment, thus playing an important role in bioremediation and biodegradation processes (2). All isolates of *Gordonia* spp. are typically gram-positive, catalase-positive, weakly acid-fast, thin, beaded coccobacilli that do not produce any aerial hyphae. The absence of arylsulfatase differentiates this genus from rapidly growing mycobacteria, and the absence of aerial hyphae and an inability to grow in the presence of lysozyme distinguishes them from the genus *Nocardia* (14, 21). Although high-performance liquid chromatography (HPLC) is limited by its inability to determine species-level identification, it is useful for separating *Gordonia* from the related genera *Dietzia*, *Corynebacterium*, *Rhodococcus*, and *Tsukamurella*. Five *Gordonia* spp. have been implicated in causing rare human infections in both immunocompromised and immunocompetent hosts. To date, only 11 case reports of bloodstream infections caused by *Gordonia* spp. were found in the English literature. Table 1 shows a review of these cases.

In 1999, *G. polyisoprenivorans*, a rubber-degrading bacterium isolated from stagnant water inside a deteriorated automobile tire, was first described (13). These organisms have the ability to use isoprene rubber as the sole source of carbon and energy. In 2001, two other rubber-degrading isolates of *G. polyisoprenivorans* were characterized. Both strains were 99.4% similar by 16S rRNA gene sequencing to *G. polyisoprenivorans* ATCC BAA-14^T and were confirmed as *G. polyisoprenivorans* by DNA-DNA hybridization (1). According to a MEDLINE search, this is the first report of endocarditis and the second report of human infection due to *G. polyisoprenivorans*. Kempf et al. (11) previously described a case report of *G. polyisoprenivorans* isolated from a single blood culture from a 26-year-old bone marrow transplant recipient who became febrile the day after her Hickman catheter was manipulated. Cultures of the catheter tip were negative. We also suspect that the source of infection in our patient was the Hickman catheter. More than 50% of the blood cultures as well as the aortic valve vegetation grew the same organism, satisfying the clinical criteria for infective endocarditis. It is well established that bacterial colonization and biofilm formation occur rapidly on intravascular devices if the organism is able to produce an exopolysaccharide, adhere to polymer surfaces, and develop a biofilm (6, 7). Overt symptoms are produced slowly. The presence of mycolic acids and the production of biosurfactants enable *G. polyisoprenivorans* to form biofilms (2). The ability of these organisms to degrade rubber, a component of intravenous devices, also contributes to the pathogenesis of these infections (1, 2, 13). There have been several previously reported cases that described the recurrence of infection despite the use of an appropriate prolonged antibiotic treatment (8, 9, 18, 22). The cause of persistent infections may be attributed to the ability of *Gordonia* spp. to form biofilms. Several previously published studies have found that sessile bacterial communities in biofilms have decreased susceptibility to antimicrobial agents compared to planktonic organisms and that conventional susceptibility methods do not accurately predict the actual susceptibility of organisms that exist in a biofilm (6, 7).

To date, there has been only one other documented case of endocarditis caused by a *Gordonia* species (12). As in our case, the patient had multiple medical problems that required the placement of a subcutaneous CVC. That patient was treated

TABLE 1. Bloodstream infections of humans with gordoniae and underlying conditions

<i>Gordonia</i> sp.	Type(s) of infection	No. of cases	Patient age (yr, sex) ^a	Underlying condition(s) ^b	Yr of isolation	Reference
<i>G. bronchialis</i>	Bacteremia	1	58, F	Sequestered lung	2004	20
<i>G. polyisoprenivorans</i>	Bacteremia due to CVC	1	26, F	BMT	2004	11
<i>G. terrae</i>	Bacteremia due to CVC	5	28, M	CML, splenectomy	2003	18
			44, F	Brain tumor		
			54, F	AML		
			46, F	Unknown primary cancer metastatic to the liver		
			60, M	Thyroid cancer with metastasis		
<i>Gordonia</i> sp. most closely resembling <i>G. sputi</i>	Catheter-related bacteremia and endocarditis	1	31, F	Splenectomy, hemoglobinopathy	2000	12
<i>G. sputi</i>	Bacteremia due to cutaneous lesions	1	34, M	Metastatic melanoma, IL-2 treatment	1996	19
<i>G. terrae</i>	Bacteremia due to CVC	1	43, F	Chronic intestinal pseudo-obstruction syndrome	1992	4
<i>Gordonia</i> sp. not identified	Bacteremia due to CVC	1	65, F	Breast and ovarian cancer	1992	4

^a M, male; F, female.

^b BMT, bone marrow transplant; CML, chronic myelogenous leukemia; AML, acute myelogenous leukemia; IL-2, interleukin-2.

successfully with antibiotics (amoxicillin plus netilmicin followed by ceftriaxone alone) and did not require valvular surgery or removal of her CVC. Although this organism was phylogenetically closest to *Gordonia sputi*, it was not definitively identified or speciated, as it showed a DNA relatedness of 55% with *G. sputi* according to the stringent nuclease S1 method.

There have been several other cases of *Gordonia* bacteremia reported in the literature. Pham et al. (18) previously reported five cases of *G. terrae* bacteremia in patients from the M. D. Anderson Cancer Center with CVCs from 1992 to 2001; two of the five patients required the removal of the CVC for clearance of the bacteremia. Buchman et al. (4) previously reported two cases of *Gordonia terrae* bacteremia in patients receiving home total parenteral nutrition. One patient was successfully treated with antibiotics without the removal of her Hickman catheter. One case of *G. sputi* bacteremia in a young man with metastatic melanoma who was receiving intravenous interleukin-2 was previously reported (19). Lastly, a case of bacteremia due to *Gordonia bronchialis* in a diabetic patient with a sequestered lung was previously reported (20).

The inability of the available identification systems to accurately identify *Gordonia* spp. makes the identification of these organisms particularly challenging for clinical microbiology laboratories. In our case, the isolate was initially misidentified as a *Corynebacterium pseudodiphtheriticum* by a rapid commercial identification system (RapID CB Plus). Other case reports have also described difficulties in identifying members of this genus (4, 20, 22). Two case reports that described infections caused by *G. bronchialis* also reported the misidentification of *G. bronchialis* as *Rhodococcus* spp. when another commercial identification system was used, API Coryne (bioMérieux, Hazelwood, MO), with an API code of 1111104 (20, 22). Identification to the genus level required the use of HPLC analysis, and identification to the species level required genetic methods such as 16S rRNA gene sequencing. There is no standardized 16S rRNA gene sequence cutoff values that exist for defining potentially new *Gordonia* species or rarely encountered *Gordonia* species such as *G. polyisoprenivorans*. How similar a strain must be to a reference strain before a species should be

assigned is arbitrary and requires confirmation by further molecular analysis; a strain can reliably be assigned to a species if DNA-DNA relatedness is 70% or greater with 5% or less ΔT_m (difference in melting temperatures between the homologous and heterologous T_m) between the strain and the type strain of the species. Conversely, 100% 16S rRNA gene similarity to another strain usually means that they are the same species; however, this is not always true (10). Thus, reliable identification still requires confirmation by further molecular analysis such as DNA-DNA hybridization or sequencing of other genes.

The data reviewed here indicate that the use of indwelling catheters for long-term intravenous access appears to be a major risk factor for bloodstream infections due to *Gordonia* species. This case illustrates that rapid commercial identification systems may provide inaccurate results, and identification to the genus level may be achieved by HPLC methods (which were not performed with this isolate); however, identification to the species level may be achieved only by molecular methods such as 16S rRNA gene sequencing (17) and, in our case, DNA reassociation. DNA reassociation studies were performed because of the uniqueness of this isolate in the Actinomyces Reference Laboratory.

Our description of this endocarditis infection emphasizes the role of *G. polyisoprenivorans* as a human pathogen in a particular high-risk category such as catheter-related infections.

Nucleotide sequence accession number. The sequence of the strain of *G. polyisoprenivorans* (W8130) determined in this study has been deposited in the GenBank database under accession number DQ385609.

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