Gordonia araii Infection Associated with an Orthopedic Device and Review of the Literature on Medical Device-Associated *Gordonia* Infections[▽]

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Gordonia **infections in humans are rare and usually affect immunocompromised patients. We present the first case of** *Gordonia araii* **infection associated with a medical device in an immunocompetent patient. Sequencing was required for conclusive identification. We compared our case to the 16** *Gordonia* **species-associated medical device infections reported to date.**

CASE REPORT

A healthy 27-year-old male presented to the Surgical Unit at the Wright-Patterson Medical Center following a sports-related injury of the right anterior cruciate ligament (ACL) and a right medial meniscus tear. Orthopedic surgery attached a hamstring tendon autograft by using an ACL femoral fixation implant (Scandius), a bioabsorbable tapered screw, and a tibial sheath (Mitek Surgical). A vacuum-assisted closure device was placed in the wound for 4 weeks.

Six weeks following the surgery, the patient complained of fever, knee pain, and knee swelling and received incision and drainage at the surgical site. Routine bacterial cultures on brain heart infusion agar with 5% sheep blood were negative. A vacuum-assisted closure device was again placed for 4 weeks following this procedure.

He presented again, 10 weeks after the initial surgery, complaining of redness and swelling of the right knee, and was noted to have wound dehiscence at the surgical site. He received another incision and drainage. Routine bacterial cultures on brain heart infusion agar with 5% sheep blood were again negative.

He presented a fourth time, 21 weeks after the initial repair, with discharge from two sinus tracts which exited near the surgical site. A magnetic resonance imaging study revealed an effusion, an intact ACL graft, and edema in both the tibia and the femur at the graft attachment site. He denied symptoms at any other site, and his peripheral white blood cell count was normal. He was taken to surgery, where the right knee was incised and drained. All foreign materials, including the bioabsorbable implant, were removed and sent for culture. Following surgery, the patient was placed on intravenous levo-

floxacin (500 mg daily) and intravenous vancomycin (1 g twice daily).

On the basis of antimicrobial testing results obtained from the National Jewish Medical and Research Center (NJMRC), on day 16 of the fourth presentation, the patient was switched to intravenous trimethoprim-sulfamethoxazole (TMP-SMX; 175 mg to 875 mg) twice daily to complete a 31-day course of antibiotic treatment. The patient had a full recovery from both the infection and the knee surgery. Follow-up a year later and an inquiry 3 years later indicated no further problems.

Laboratory analysis of joint fluid revealed a total white blood cell count of 4,750/mm^3, with a differential of 36% segmented neutrophils, 53% lymphocytes, and 11% monocytes.

Three days after the samples were cultured, light growth of gram-positive bacilli was noted to occur on a brain heart infusion agar plate with 5% sheep blood, from the bio-absorbable screw. After 11 days of incubation, heavy growth of gram-positive bacilli was noted to occur on Sabouraud dextrose agar (Emmons modified) and on Lowenstein-Jensen medium. All growth from the different media was partially acid fast.

For further evaluation, the isolate was sent to the NJMRC, located in Denver, CO. Results of high-performance liquid chromatography analyses for mycolic acids and partial 16S rRNA gene sequencing presumptively identified the isolate as a *Gordonia* species (results not shown).

Antimicrobial susceptibilities were determined at the NJMRC by broth microdilution using Sensititre frozen custom CML9FNJD panels, following the guidelines of the manufacturer, Trek Diagnostics Systems (Westlake, OH), and the interpretive criteria for breakpoints of all antimicrobial agents, except vancomycin, that were recommended by the Clinical and Laboratory Standards Institute (CLSI) for mycobacteria, nocardiae, and other aerobic actinomycetes (10). The MIC results obtained were as follows: for amikacin, ≤8.0 µg/ml (susceptible); for amoxicillin-clavulanate, ≤4.0 to 2.0 µg/ml (susceptible); for azithromycin, >256.0 µg/ml (resistant); for ceftriaxone, ≤8.0 µg/ml (susceptible); for ciprofloxacin, ≤1.0 µg/ml (susceptible); for clarithromycin, 4.0 µg/ml (intermediate); for imi-

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penem, ≤2.0 µg/ml (susceptible); for linezolid, ≤1.0 µg/ml (susceptible); for minocycline, ≤1.0 µg/ml (susceptible); for TMP-SMX, ≤0.5 to 9.5 µg/ml (susceptible); and for vancomycin, 2.0 µg/ml (no interpretive corresponding breakpoints available).

The same microorganism was forwarded to the Special Bacteriology Reference Laboratory (SBRL) at the Centers for Disease Control and Prevention in Atlanta, GA, for species identification and antimicrobial susceptibility testing. Reference testing included conventional biochemical characterization (1), full-length 16S rRNA gene sequencing (4), partial gyrase B (gyrB) sequencing (12, 15), DNA-DNA hybridization (3), and antimicrobial susceptibility assessment, using panels from PML Microbiologicals, Inc. (Wilsonville, OR), according to CLSI methods as described previously (10) and using breakpoints recommended by the CLSI for mycobacteria, nocardiae, and other aerobic actinomycetes for all drugs, except vancomycin. All comparative analyses were performed using the SBRL type strain reference database.

Differentiation with biochemical tests was unreliable, as there were no distinguishing phenotypic markers that were able to conclusively separate our patient's isolate, strain W8543, from other related species of the genus Gordonia and other related aerobic actinomycetes. Strain W8543 was identical to the type strain of Gordonia araii (7). The isolate was aerobic and had pale yellow, crystalline colonies that did not produce aerial hyphae at 25 and 35°C on heart infusion agar plates in 7 days. The strain oxidized fructose, D-glucose, glycerol, mannose, salicin, and trehalose but not L-arabinose, cellobiose, dulcitol, i-erythritol, D-galactose, i-myo-inositol, lactose, maltose, D-mannitol, melibiose, raffinose, L-rhamnose, D-sorbitol, sucrose, or D-xylose. It hydrolyzed esculin but did not hydrolyze adenine, casein, hypoxanthine, tyrosine, urea, or xanthine. The results for utilization of acetamide as the sole carbon and nitrogen source and citrate as the sole carbon source were both negative. The result for the test for nitrate reduction was negative. The isolate did not grow in the presence of lysozyme.

The degree of sequence similarity for the 1,445-bp 16S rRNA gene fragment for isolate W8543 (GenBank accession number EF164924) was highest for G. araii strain IFM 10211[T] (GenBank accession number AB162800) (7), with 99.6%, followed by Gordonia effusa IFM 10200[T] (GenBank accession number AB162799) (7), with 97.9%, and Gordonia amarae DSM 43392[T] (GenBank accession number X80635), with 97.4%. Consistent with the analysis of the 16S rRNA gene, the 1,258-bp fragment of the gyrB gene of isolate W8543 (GenBank accession number EU483252) showed G. araii IFM 10211[T] (GenBank accession number EU483253) to be the most closely related Gordonia species, with 98.9% sequence similarity. The sequence similarities for the next-closest strains, Gordonia hirsuta JCM 10105[T] (ICB accession number gy10796), Gordonia hydrophobica JCM 10086[T] (ICB accession number gy10560), and G. effusa IFM 10200[T] (GenBank accession number EU483254) were 84.6%, 82.3%, and 81.7%, respectively. Phylogenetic analyses using either gene target (16S rRNA or gyrB) clustered isolate W8453 together with G. araii and separately from other Gordonia species.

DNA-DNA reassociation analysis further supported the identification of isolate W8543 as G. araii, with 78% related-

ness to G. araii IFM 10211[T], denoting same-species identity (16). Strain W8543 showed only 4% DNA relatedness to the nearest 16S rRNA gene phylogenetic neighbor, G. effusea IFM 10200[T].

Repeated testing of strain W8543 at the SBRL by using PML Microbiologicals, Inc., panels found susceptibility categories identical to those reported for the NJMRC experiment using Trek panels, with the following exceptions: the TMP-SMX and clarithromycin susceptibility results for the SBRL were different from those for the NJMRC experiment using Trek panels in that the NJMRC results showed a greater-than-twofold dilution difference from the SBRL results. Although the interpretive categories were the same for TMP-SMX (susceptible), they were not the same for clarithromycin (intermediate [NJMRC] and susceptible [SBRL]). This discrepancy may be due to differences in the panels used as well as differences in visual assessment.

This case prompted us to perform a literature review of implanted medical devices associated with Gordona and Gordonia species infections as well as infections associated with "Rhodococcus bronchialis," "Rhodococcus rubropertinctus," "Rhodococcus sputi," and "Rhodococcus terrae," which were reclassified in 1988 as Gordona species. We found no medical device-associated references associated with the Rhodococcus species by using PubMed search tools. To the best of our knowledge, there are only 16 corresponding cases reported in the literature as of 8 May 2008 (Table 1). Most cases were in patients that were either immunocompromised or receiving total parenteral nutrition (2, 5, 6, 8, 9, 11, 14). Nine of the 16 cases resolved after removal of the infected device and antibiotic treatment, resulting in the successful recovery of all these patients. However, following this treatment regimen, one patient died for reasons not explained in the literature. For the six remaining cases, the medical device was left in situ and antimicrobial treatment was given, resulting in the successful recovery of five patients, and one patient died. Our review indicated the apparent lack of a standard antimicrobial regimen for the treatment of Gordonia-associated infections. Overall, a wide variety of commonly prescribed antimicrobial agents and combinations were used, including aminoglycosides, beta-lactams (aztreonam, cephalosporins, and penicillins) with or without beta-lactamase inhibitors, carbapenems, fosfomycins, fluoroquinolones, glycopeptides, lincosamides, macrolides, and rifampin, irrespective of the Gordonia species identified. Considering the present data and the various medical conditions, it is not clear whether the removal of the medical device, a specific antimicrobial treatment, or a combination thereof was associated with successful treatment of the infection. However, Blaschke et al. recommend the removal of infected catheters as part of the treatment regimen for associated Gordonia infections in adolescents (2).

Two case reports did not include species level identification (5, 9), possibly due to diagnostic difficulties with this group of bacteria. In the present study, biochemical testing did not provide conclusive species identification, and further characterization, using molecular approaches, was needed

TABLE 1. Medical device-associated infections due to *Gordonia* species[a]

Yr of publication (reference)	Patient gender	Patient age[b]	*Gordonia* species	Device	Bacteremia status	Underlying condition(s)	Antibiotic(s)	Use of device
1992 (5)	F	43	*G. terrae*	CVC	Present	Long-term total parenteral nutrition	Vancomycin	Left in situ
1992 (5)	F	65	*Gordonia* sp.[c]	CVC	Present	Long-term total parenteral nutrition	Gentamicin, vancomycin	Removed
2000 (9)	F	31	*Gordonia* sp.[c]	CVC	Present	Hemoglobinopathy	Fosfomycin, cefotaxime, netilmicin, oxacillin	Port removed
2003 (11)	M	28	*G. terrae*	CVC	Present	Malignancy	Vancomycin, ceftazidime	Left in situ
2003 (11)	F	44	*G. terrae*	CVC	Present	Malignancy	Vancomycin, ceftazidime	Left in situ
2003 (11)	F	54	*G. terrae*	CVC	Present	Malignancy	Imipenem, levofloxacin	Left in situ
2003 (11)	F	46	*G. terrae*	CVC	Present	Malignancy	Erythromycin, vancomycin, imipenem	Removed
2003 (11)	M	60	*G. terrae*	CVC	Present	Malignancy	Aztreonam, clindamycin, azithromycin	Removed
2004 (8)	F	26	*G. polyisoprenivorans*	Hickman catheter	Present	Bone marrow transplant	Piperacillin-tazobactam, amoxicillin, ciprofloxacin	Removed
2006 (14)	M	78	*G. polyisoprenivorans*	Hickman catheter	Present	Osler-Weber-Rendu and myelodysplastic syndromes	Imipenem-cilastin, amikacin	Removed
2007 (2)	NA	3	*G. terrae*	CVC	Present	Wilms' tumor	Ceftriaxone, rifampin	Removed
2007 (2)	NA	3	*G. terrae*	CVC	Present	T-cell acute lymphoblastic leukemia	Vancomycin, rifampin	Left in situ
2007 (2)	NA	11	*G. otitidis*	CVC	Present	Periodic fever syndrome, bowel necrosis	Imipenem, clarithromycin	Removed
2007 (2)	NA	5	*G. terrae*	CVC	Present	LACH syndrome	Ciprofloxacin	Removed
2007 (2)	NA	45 days	*G. bronchialis*	Intraventricular shunt	NA	Premature neonate	Meropenem, amikacin	Removed
2007 (6)	M	24	*G. terrae*	CVC	Present	Dyspnea, abuse of methandienone, sepsis	Levofloxacin, piperacillin-tazobactam	Left in situ
2009 (present study)	M	27	*G. araii*	Bioabsorbable tapered screw	NA	None	TMP-SMX	Removed

[a] Abbreviations: F, female; M, male; CVC, central venous catheter; LACH, leukoencephalopathy, arthritis, colitis, and hypogammaglobulinemia; NA, not available.
[b] Ages are in years unless otherwise noted.
[c] No identification was reported to the species level.

to identify the causative agent. The high degree of sequence identity (99.6%) observed between the 16S rRNA gene sequences for isolates W8543 and *G. araii* IFM 10211^T allowed for the presumptive identification at the genus and species as *G. araii*; the sequence identity for the next-closest strain, *G. effusa* IFM 10200^T, was lower, at 97.9%. Identification was then confirmed by sequencing the *gyrB* fragment, as an adjunct method, due to the greater species resolution than that for the 16S rRNA gene, at least for *Gordonia* species (12). DNA-DNA hybridization analysis strongly supported the final identification of the case isolate as *G. araii*.

In conclusion, the present report describes the first case of a confirmed *Gordonia araii* infection associated with a medical device in an immunocompetent individual. It is also the first report of an infection associated with this species in the United States. A literature review revealed that device-related *Gordonia* infections were rarely reported and apparently lack a standard approach for their treatment. The present investigation illustrates the need to consider sequencing approaches for identification of this pathogen and related microorganisms in the group of aerobic actinomycetes. In the context of medically critical conditions, physicians may refer to reference laboratories for conclusive identification of any rare infectious agent that has defied accurate and reliable identification with the use of conventional testing in order to further promote advancement in the diagnosis, treatment, and clinical management of such infections.

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