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Case Report
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First Case of VAD-Associated Mediastinitis by *Gordonia bronchialis*: A Case Report and a Review of an Emergent Pathogen

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Abstract

Background: Infections are frequent and particularly serious complications of the implantation of ventricular assist devices for the treatment of heart failure, *Gordonia* species have recently been found to cause human infections. Specifically, *Gordonia bronchialis* has been associated with sternal wound infection.

Methods: The present is the first case of VAD-associated mediastinitis by *Gordonia bronchialis*. A review of previously reported cases of *Gordonia* spp. infections was performed. Relevant clinical and epidemiological features were summarized.

Results: A 49-year-old patient had a history of end-stage ischemic cardiomyopathy and severe pulmonary hypertension that precluded heart transplantation. A VAD was implanted as a bridge to candidacy. Recourse was complicated due to the development of mediastinitis secondary to *Gordonia bronchialis*. A total of 69 cases of *Gordonia* spp. infections have been reported. The most frequently isolated species was *G. bronquialis* (40.58%). Main risk factors were immunosuppression and patients harboring devices. The most frequent presentation was skin infection (30.43%). Most of the cases required further diagnostic testing in addition to a culture to achieve the diagnosis (78.26%). Antibiotic regimens were heterogeneous. The prognosis was favorable.

Conclusions: *Gordonia* spp. are rare but emergent pathogens which have been associated with the implanted devices and immunosuppression. Low mortality and morbidity have been reported.

Keywords: *Gordonia*; Mediastinitis; Ventricular Assist Device (VAD)

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Introduction

Implantable Ventricular Assist Devices (VADs) have technologically evolved in the last decades, becoming a feasible option in the treatment of advanced heart failure. They are especially useful as a destination therapy for patients considered non-suitable for heart transplant, but also as a bridge to transplant or candidacy (in the setting of potentially reversible contraindications). Despite remarkable technical and clinical improvements, long-term support still carries a substantial risk of complications with a negative impact on quality of life and survival [1]. Infectious complications associated with VADs are frequent and heterogeneous, with mediastinitis being the most feared result [2]. In the presence of the foreign surfaces of the VAD, deep mediastinal infections are more common and more difficult to treat than those of other cardiac surgeries [3,4]. Therapeutic strategies combining surgical treatment and long-term antibiotics are usually needed. Alternative surgical strategies, such as omentoplasty, have also been described as a useful approach to help to achieve mediastinal sterility in some patients, but survival is still severely compromised [5].

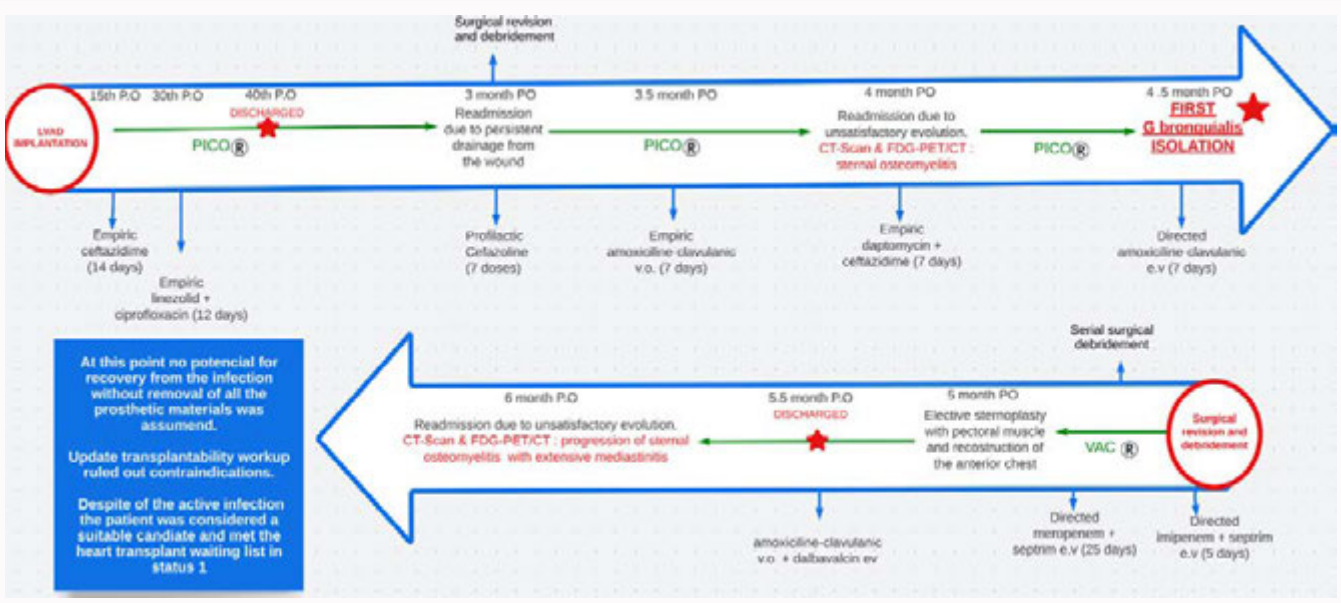


Figure 1: Diagram showing the patient's course from VAD implantation to re inclusion in the heart transplant waiting list in status 1. The figure includes the different antibiotic regimes and the local care and surgical approach.

Gram-positive bacteria that colonize skin and adhere to implanted material by creating biofilms, especially *Staphylococcus aureus* and *Staphylococcus epidermidis*, have been isolated more frequently [6]. It is important for clinicians to be familiar with local microbiology and antimicrobial resistance patterns, as these should be considered when choosing the initial treatment until directed therapy is initiated [7].

Gordonia spp. are rare but emerging human pathogens that cause a variety of infections in both immunocompromised and immunocompetent hosts. The genus *Gordonia* includes around 50 species, among which only a few have been reported to cause human infections [8]. The number of recognized infections caused by these pathogens is rising because of the increased use of long-term Central Venous Catheters (CVC) and other devices, the prolonged survival of immunocompromised patients, and the improvement in laboratory identification methods. In addition, it is believed that *Gordonia* has been frequently misidentified and that its incidence might be higher than reported. In fact, it has been proposed that other identification methods such as 16S rRNA gene sequencing or MALDI-TOF MS should be employed for the proper identification of aerobic actinomycetes to the species level, helping to detect and properly treat these infections [9,10].

Gordonia bronchialis has been associated with sternal wound infections [9,11,12], but no cases of VAD infection have been reported to date. This particular scenario could have specific morbidity and mortality implications; therefore, this report aims to present the first case of severe mediastinitis related to VAD due to *Gordonia bronchialis*.

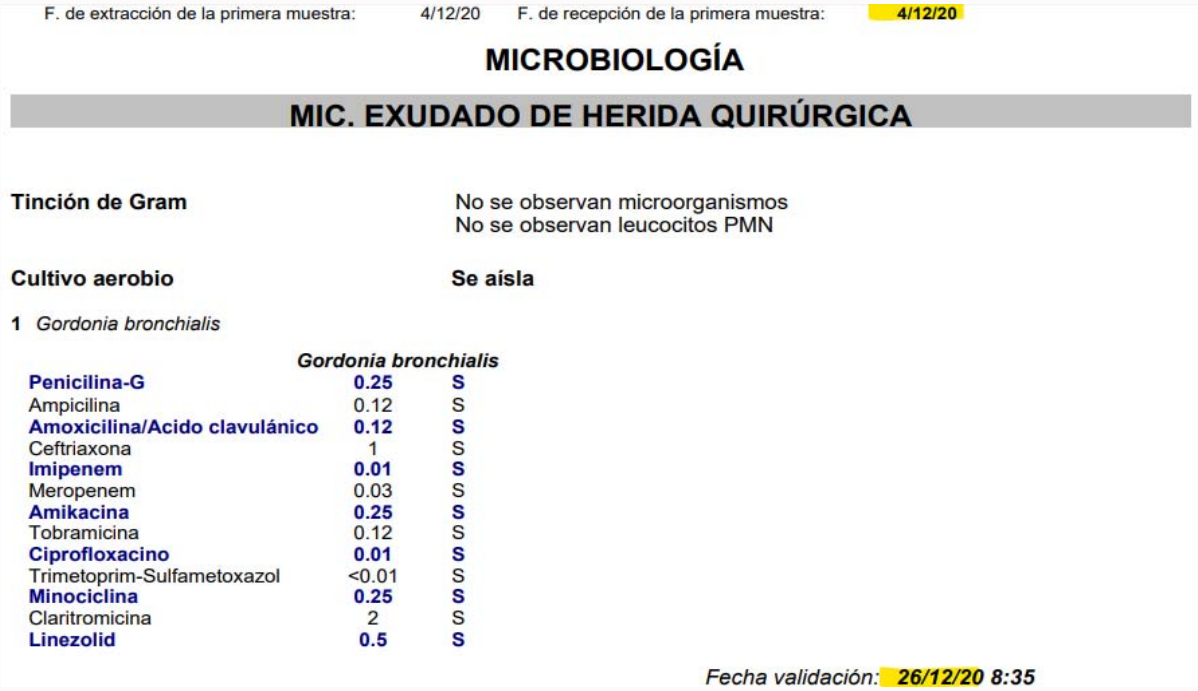
Case Presentation

A 49-year-old patient had a prior history of ischemic cardiomyopathy with severe left ventricular dysfunction that led to frequent hospital admissions for congestive heart failure despite optimal medical therapy. The ability of transplant was assessed, and right heart catheterization revealed severe secondary pulmonary hypertension that precluded heart transplantation. Despite pulmonary-specific vasodilator treatment and diuretics the situation did not improve. For this reason, a centrifugal left VAD HeartMate 3® was implanted following the standard protocol, as a bridge to candidacy.

This course was initially favorable, but on the 15th postoperative day, the patient began to experience sternal pain and intermittent fever. The chest wound was stable, but it showed inflammatory signs. CT-scan discarded mediastinitis, so a superficial sternal wound infection was diagnosed. No etiological agent was isolated, so the patient was treated with broad spectrum antibiotics, local wound care and negative pressure wound therapy (PICO®). Medical treatment, wound care strategy and surgical management during the clinical course are summarized in Figure 1. The evolution seemed favorable, and the patient was discharged 40 days after admission under treatment with oral antibiotics and PICO® therapy.

Three months after VAD implantation, pump parameters were stable, the patient remained afebrile and Acute Phase Reactants (APR) were normal. However, due to persistent drainage from the wound, elective surgical debridement was performed. There were no signs of bone compromise, so it was not debrided. Cultures were negative and a 7-day cycle of cefazolin was completed before the patient was discharged. One month later, drainage from the wound persisted. Ambulatory antibiotic treatment was initiated but because of unsatisfactory progression he was readmitted to the hospital for further investigation. On admission, physical examination was remarkable for erythema, heat, pain and purulent drainage over the sternal wound. Full laboratory analysis showed creatinine levels of 1.25 mg/dl and GFR of 67 mL/min/1.73 m^2; a BNP value of 2,631; and normal APR with a C-reactive protein of 2.90 ml/dl and no leukocytosis. A transthoracic echocardiogram ruled out infective endocarditis.

Empiric antibiotic treatment with daptomycin and ceftazidime was initiated and a mediastinum-focused CT-scan was performed. It revealed signs of sternal osteomyelitis involving the manubrium and upper part of the sternum body with inflammatory changes in the surrounding soft tissues, but no collections. Surgical revision of the



F. de extracción de la primera muestra: 4/12/20 F. de recepción de la primera muestra: 4/12/20

MICROBIOLOGÍA

MIC. EXUDADO DE HERIDA QUIRÚRGICA

Tinción de Gram No se observan microorganismos
No se observan leucocitos PMN

Cultivo aerobio **Se aísla**

1 *Gordonia bronchialis*

	Gordonia bronchialis	
Penicilina-G	**0.25**	**S**
Ampicilina	0.12	S
Amoxicilina/Acido clavulánico	**0.12**	**S**
Ceftriaxona	1	S
Imipenem	**0.01**	**S**
Meropenem	0.03	S
Amikacina	**0.25**	**S**
Tobramicina	0.12	S
Ciprofloxacino	**0.01**	**S**
Trimetoprim-Sulfametoxazol	<0.01	S
Minociclina	**0.25**	**S**
Claritromicina	2	S
Linezolid	**0.5**	**S**

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Figure 2: Antibiotic susceptibility of the *Gordonia bronquialis* isolated from sternal wound culture. Note that results were obtained 22 days after the sample was sent to the microbiology laboratory (yellow).

wound was performed. VAC (Vacuum Assisted Closure) therapy was initiated. After 6 days on empiric treatment, a culture of the sternal wound, which was taken 22 days prior, grew positive for *Gordonia bronchialis*. Amoxicillin-clavulanic was substituted for the previous antibiotic regimen.

Ten days after admission, no improvement was observed and a more aggressive surgical debridement including bone, joint and soft tissue was performed, while keeping VAC and performing serial debridement. The antibiotic regimen was modified again after antibiogram sensitivity test results were obtained. Meropenem and trimethoprim-sulfamethoxazole were finally chosen due to their high susceptibility (Figure 2).

After two weeks on this antibiotic regimen combined with serial surgical debridement and VAC therapy, infection was considered under control. Elective sternoplasty with pectoral muscle and dermal flaps for reconstruction of the anterior chest was completed successfully. The patient was discharged on intravenous dalbavancin and oral amoxicillin-clavulanate on an ambulatory basis.

Six months after the HeartMate 3® implantation and while on treatment with dalbavancin and amoxicillin-clavulanic, the surgical wound showed signs of infection again. The patient was admitted to the hospital to receive intravenous antibiotic and to undergo elective surgical site revision. A CT-Scan and an FDG-PET/CT showed extensive osteomyelitis and mediastinitis (Figure 3). The pump was not affected, but proximal Dacron was in contact with a fluid mediastinal collection. Infection of the driveline was diagnosed, and it was decided to complete 15 days of antibiotic treatment before a new CT-Scan was performed, which showed further progression of the inflammatory signs (Figure 3).

As no potential for healing of the infection was expected, the transplant workup was updated. Right heart catheterization demonstrated the normalization of pulmonary pressures. Although the patient was under an active infection, it was considered that the transplant would necessarily involve the removal of all prosthetic materials that were probably responsible for the relapsing course of the infection. After a Multidisciplinary Shock team (MCS team) discussion, the patient was added to the heart transplant waiting list in status 1. The patient received intravenous antibiotic treatment with tigecycline, meropenem and rifampicin until the heart transplant surgery. On the 54th day on the waiting list and a total of 66 days of admission, the patient underwent cardiac transplantation. The patient was discharged to the ward on postoperative day 12 and home on postoperative day 22. He remains stable in last contact.

Search strategy and selection criteria and data extraction

A literature review was performed. Case reports including patients with established *Gordonia* spp. infection were evaluated for inclusion in this review. The search was made using PubMed. In addition, backward snowballing (i.e., review of references from identified articles and pertinent reviews) was performed. Data about authors, year of publication, baseline patients' features, clinical presentation, diagnostic approach, antibiotic treatment, and death were collected.

Statistical analysis

Data are presented as mean (minimum-maximum) and median (interquartile range) for continuous variables, and absolute and relative frequencies for categorical data. Qualitative variables using X^2 test or Fisher exact test when necessary. The results were statistically significant when two-tailed $p<0.05$. Statistical analyses were performed with the Stata software version 16.1 (College Station, TX).

Results

A total of 69 patients were included. Table 1 shows recorded data by species. The most frequently isolated *Gordonia* spp. species was *G. bronquialis* with a total of 28 cases (40.58%), followed by *G. terrae*

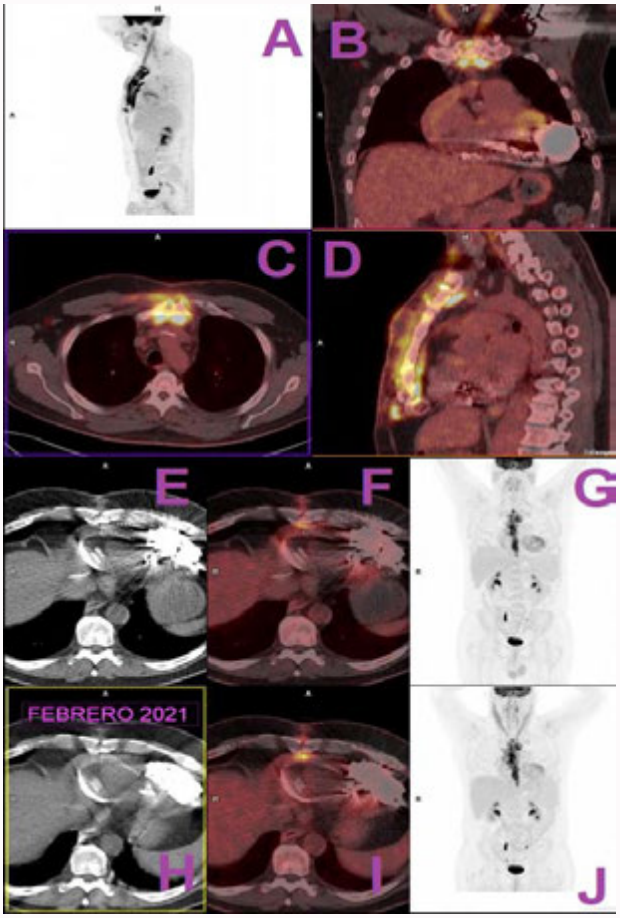

Figure 3: CT-Scan and an FDG-PET/CT showing extensive osteomyelitis and mediastinitis (A-D). Next CT-Scan and an FDG-PET/CT after 15 days of antibiotic shows further progression of the inflammatory signs (E-G *vs.* H-J).

(15, 21.74%) and *G. sputi* (13, 18.84%). The mean age of the patients was 53.10 years (Range: 4-92). There were 45 males (65.22%) and 24 females (34.78%). Main risk factors were patients with implanted CVC or other devices; any kind of IS (Immunosuppression), DM (Diabetes Mellitus) or prior oncological disease. It is notable that 9 of the 11 patients with prior history of diabetes were affected by *G. bronquialis*. Fisher exact test to evaluate the association between DM and the different *Gordonia* species yielded a significant difference (p 0.023). The most frequent presentation overall and in *G. bronquialis* infection was wound or skin infection (21.00, 30.43%; 15.00, 53.57% respectively). Most of the cases reported required further diagnostic testing in addition to a culture to achieve the diagnosis (54, 78.26%). Antibiotic regimens and duration were very heterogeneous. Long treatment regimens were preferred (median 21; IQR 21-56). Overall mortality was low (4.35%).

Discussion

This case represents the first case of VAD-associated mediastinitis by *Gordonia bronchialis*. Its importance relies on both it being an emergent pathogen, as well as on the fact that the number of patients who are supported by VADs continues to grow paralleled by the adverse events and complications they go through.

Epidemiology

Gordonia species are ubiquitous aerobic actinomycetes frequently isolated from soil and water. The genus *Gordonia* belongs to the family *Gordoniaceae*, the suborder *Corynebacterineae* and the order *Actinomycetales* [13]. There are around 50 species identified (some not yet validated), but only a few have been reported to cause human infections. Those include *G. aichiensis*, *G. araii*, *G. bronchialis*, *G. effusa*, *G. otitidis*, *G. polyisoprenivorans*, *G. rubripertincta*, *G. sputa*, *G. terrae*, *G. westfalica*, *G. iterans* and *G. Jacobaea*.

In the past, 69 cases of *Gordonia* spp. infections have been reported in medical literature [9,11,14-42]. Twenty-eight (40.60%) cases were caused by *G. bronchialis* and 57 (82.60%) were caused by three species (*bronchialis*, *terrae* and *sputi*). There were 45 males (65.22%) and 24 females (34.78%) with a median age of 59.00 years (IQR: 43.00-65.00). Further, there was a male predominancy in the *Gordonia* spp. cases (16, 57.14%) and median age of 59.00 years (IQR: 56.00-67.00).

Risk factors for the development of *Gordonia* infections are not well known. A previous medical history of Immunosuppression (IS) and implanted devices have been reported in most of the cases. In this review up to 40.58% of the cases had a CVC and 15.94% had some kind of IS. Regarding *G. bronchialis* infections, 10.7% of the cases were immunosuppressed. It is also of note that 32.14% of the *G. bronchialis* infections had DM as compared with 2 out of 41 cases (4.87%) among those with infections from other species (Fisher's exact test p=0.023) [43,44].

Clinical presentation

Gordonia spp. infections usually have a protracted clinical course featuring weakness and fever. From the reviewed literature, wound and other skin infections are the main clinical presentation (30.45%), followed by fever (23.19%). *Gordonia bronchialis*' main presentation is also wound and skin infection, accounting for 15 of the 28 reported cases (53.57%). Device-associated infections are also noteworthy, accounting for 5 of the 28 reported cases (17.86%).

Diagnosis

Gordonia are gram-positive, catalase-positive, weakly acid-fast, thinly beaded coccobacilli. However, accurate identification of these pathogens are difficult, and they have been frequently misidentified by traditional methods [8,10]. It is expected that the incorporation of genotypic methods like 16S rRNA gene sequencing or MALDITOF MS will improve identification, and this will lead to an increased frequency of diagnoses [45,46]. In the present review, most of the cases had negative culture results or were wrongly identified (54, 68.12%), requiring 16S rRNA gene sequencing, MALDI-TOF MS or PFGE in order to achieve the final diagnosis. The same was observed in *Gordonia bronchialis* cases (16, 57.15%). The present case was identified by conventional culture, but with a 22-day delay, which reinforces the idea that if a *Gordonia* spp. infection is suspected, further diagnostic tests should be performed early.

Treatment

The treatment of *Gordonia mediastinitis*, as that of mediastinitis of other etiologies, relies on two pillars: Appropriate antibiotic choice (regarding activity, pharmacokinetics, and duration) and appropriate surgical indication. There are no controlled studies to provide reliable and consistent recommendations relative to the antibiotic choice, duration, or indications for surgery. From the present review the following statements can be inferred:

1. Antibiotic choice and duration were heterogeneous. They

Table 1a: Data on gender, age, clinical features, diagnostic tests, surgical treatment, and survival from the 69 reviewed cases. Cases are grouped into the main three species reported (bronchialis, terrae and sputi) and the others. The continuous variables are summarized as mean and standard deviation and the categorical data using absolute counts and proportions.

AI: Autoimmune Disease; CVC: Venous Central Catheter; DM: Diabetes Mellitus; IS: Immunosuppression; HBV: Hepatitis B Virus; HIV: Human Immunodeficiency Virus; CSF-VP shunt: Cerebrospinal Fluid Ventriculoperitoneal Shunt; PD: Peritoneal Dialysis; rRNA: ribosomal Ribonucleic Acid; MALDI-TOF: Matrix-Assisted Laser Desorption/Ionization-Time of Flight; W: Wrong identification; PFGE: Pulsed-Field Gel Electrophoresis; IQR: Interquartile Range

Table 1b: Extend version of Table 1 with data on gender, age, clinical features, diagnostic tests, surgical treatment, and survival from the each of the 69 reviewed cases. The continuous variables are summarized as mean and standard deviation and the categorical data using absolute counts and proportions.

CVC: Venous Central Catheter; DM: Diabetes Mellitus; IS: Immunosuppression; HVB: Hepatitis B Virus; HIV: Human Immunodeficiency Virus; CSF-VP shunt: Cerebrospinal Fluid Ventriculoperitoneal Shunt; RNA: Ribo Nucleic Acid; MALDITOF: Matrix-Assisted Laser Desorption/Ionization-Time of Flight; W: Wrong Identification; PFGE: Pulsed-Field Gel Electrophoresis; IQR: Interquartile Range; AIDS: Acquired Immunodeficiency Syndrome

Sno	Author	Year	Sex	Age	Immunity	Other risk factors	Clinical presentation	Diagnostic Test	Cepa	Antibiotic	Days	Death
1	Thomas	2017	F	44	Intravenous immunoglobulins	No	Fever	Culture (+): Wrong ID MALDI TOF (+) RNA 16s (+)	G aichiensis	Linezolid ev(4) -> Amoxicillin ev(4) -> Amoxicillin vo (8)	16	No
2	Gueneau	2020	M	30	No	No	Mycetoma	Culture (-) RNA 16s (+)	G westfalica	Clotrimoxazol Rifampicina	30	No
3	Guiraud	2021	F	74	Chron disease, Rheumatoid Arthritis, long term IS	CVC	Septic Arthritis	Culture (+): WrongID MALDI TOF (-) RNA 16s (+)	G jacobaea	RO Ceftriaxona Levofloxacino Clotri moxazol	90	No
4	Ma	2014	M	61	No	CVC	Peritoneal dialysis-associated peritonitis	Culture (+)	G terrae	Vancomycin	14	No
5	Ma	2014	M	60	No	CVC	Peritoneal dialysis-associated peritonitis	Culture (+)	G terrae	Meropenem	28	No
6	Ma	2014	M	45	No	CVC	Peritoneal dialysis-associated peritonitis	Culture (+)	G terrae	Vancomycin	21	No
7	Nicodemo	2014	F	55	Renal transplantation under IS treatment	No	Pneumonia	Culture (+): WrongID RNA 16s (+)	G terrae	Ciprofloxacin Rifamp -> Imipenem -> Levofloxacin	84	No
8	Pham	2003	M	28	Haematological cancer splenectomy	CVC	Fever	Culture (+): WrongID ARN 16s (+)	G terrae	Vancomycin ceftacidime	>28	No
9	Pham	2003	F	44	Brain tumor	CVC	Fever	Culture (+): WrongID RNA 16s (+)	G terrae	Vancomycin ceftacidime	>28	No
10	Pham	2003	F	54	Haematological cancer	CVC	Fever	Culture (+): WrongID RNA 16s (+)	G terrae	Imipenem Levofloxacin	>28	No
11	Pham	2003	F	46	Unknown primary cancer	CVC	Fever	Culture (+): WrongID RNA 16s (+)	G terrae	Erythromycin -> Vancomycin Imipenem	>28	No
12	Pham	2003	M	60	Thyroid cancer with	CVC	Fever	Culture (+): WrongID RNA 16s (+)	G terrae	Aztreonam -> Clindamycin Azithromycin	>28	No
13	Guerrero	2014	M	19	Borrow Narrow transplant	CVC	Catheter related bacteremia	Culture (+): WrongID RNA 16s (+)	G terrae	Teicoplanin	14	Yes
14	Lai	2010	M	75	No	No	Primary bacteraemia	Culture (+): WrongID RNA 16s (+)	G terrae	Vancomycin + ciprofloxacin	¿?	No
15	Lai	2010	M	30	No	HBV	Wound infection.	Culture (+): WrongID RNA 16s (+)	G terrae	Amoxicillin - clavunalate	¿?	No
16	Lai	2010	M	48	No	No	Celulitis	Culture (+): WrongID RNA 16s (+)	G terrae	Amoxicillin - clavunalate	¿?	No
17	Lai	2010	M	23	Borrow Narrow transplantation	No	Fever	Culture (+): WrongID RNA 16s (+)	G terrae	Vancomycin + Imipenem	¿?	No
18	Ramanan	2015	F	81	DM	CVC	Peritoneal dialysis-associated peritonitis	Culture (+): WrongID RNA 16s (+)	G terrae	Vancomycin + Cefepime	3	No
19	Kang	2014	M	48	No	No	Pneumonia	ulture (+) RNA 16s (+)	G iterans	¿?	¿?	¿?
20	Jannat-Khah	2009	M	27	No	Femoral fixation	Orthopedic device associated infection	Culture (+) RNA 16s (+)	G araii	TMP - SMX + surgical treatment	31	No

21	Muñoz-Peña	2016	M	74	Chronic hepatopaty	No	Skin infection	Culture (+): WrongID RNA 16s (+)	G araii	Ciprofloxacin, cotrimoxazol	21	No
22	Kempf	2004	F	26	Allogeneic transplantation of peripheral blood	CVC	Fever	Culture (+) RNA 16s (+)	G polyisoprenivorans	Piperacillin-tazobactam (3) Ciprofloxacin, amoxicillin (7phapham)	10	No
23	Ding	2017	M	37	AIDS related lymphoma under chemotherapy	CVC	Catheter related bacteremia	Culture (+): WrongID MALDITOF (+) RNA 16s (+)	G polyisoprenivorans	Imipenem (5) -> then oral (85)	85	Yes
24	Ramanan	2015	M	48	Allogeneic transplantation of peripheral blood	CVC	Fever	Culture (+): WrongID RNA 16s (+)	G polyisoprenivorans	Vancomycin + Cefepime	21	No
25	Lai	2010	F	62	No	No	Conjunctivitis	Culture (+): WrongID RNA 16s (+)	G sputi	Topical sulfamethoxazole	¿?	No
26	Lai	2010	M	49	Gastric cancer	No	Fever	Culture (+): WrongID RNA 16s (+)	G sputi	Cefoxitin	¿?	No
27	Brust	2009	M	60	No	No	Pneumonia	Culture (+)	G sputi	Levofloxacine	¿?	No
28	Brust	2009	M	43	Lupus erythematosus	CVC	Fever	Culture (+)	G sputi	Vancomycin + Imipenem	¿?	No
29	Martín	2017	M	82	DM	CSF ventriculo peritoneal shunt	Fever	Culture (+): WrongID MALDITOF (+) RNA 16s (+)	G sputi	Ampicillin + Vancomycin (28) -> Linezolid (90)	118	No
30	Zhang	2015	F	31	No	Augmentation mammoplasty	Skin infection	Culture (+): WrongID RNA 16s (+)	G sputi	Cefmetazole metronidazole Surgical treatment	¿?	No
31	Villanueva	2016	M	91	No	CVC	Catheter related bacteremia	Culture (+)	G sputi	Vancomycin	21	No
32	Eribi	2020	M	50	HIV	No	Brain Abscess	Culture (+): WrongID RNA 16s (+)	G sputi	Meropenem + Vancomycin + Rifampicin	30	Yes
33	Renvoise	2009	M	69	Cancer under chemotherapy treatment	CVC	Fever	Culture (+): WrongID RNA 16s (+)	G sputi	Ticarcillin - clavulanate (3) -> Ciprofloxacin (12d)	15	No
34	Lai	2010	F	14	No	CVC	Cathether related bloodstream infection	Culture (+): Wrong ID RNA 16s (+)	G sputi	Imipenem amikacin	¿?	No
35	Lai	2010	M	13d	No	No	Conjunctivitis	Culture (+): Wrong ID RNA 16s (+)	G sputi	Topical sulfamethoxazole	¿?	No
36	Lam	2015	M	65	No	CVC	Dialysis catheter related bacteremia	Culture (+): WrongID ARN 16s (+)	G sputi	Imipenem-cilastin + amikacin	42	No
37	Lam	2015	M	67	No	CVC	Dialysis catheter related bacteremia	Culture (+): WrongID ARN 16s (+)	G sputi	Imipenem-cilastin + amikacin	21	No
38	Villanueva	2016	M	82	No	CVC	Dialysis catheter related bacteremia	Culture (+)	G rubropertincta	Meropenem	42	No
39	Ramanan	2015	M	38	Allogeneic peripheral	No	Fever	Culture (+): Wrong ID RNA 16s (+)	G otiditis	Vancomycin	7	No
40	Lam	2015	M	52	No	No	Dialysis catheter related bacteremia	ARN 16s (+)	Gordonia sp	Vancomycin + amikacin	21	No
41	Ramanan	2015	F	4	Acute lymphoblastic leukemia	CVC	Fever	Culture (+): Wrong ID RNA 16s (+)	Gordonia sp	trimethoprim - sulfamethoxazole	14	No
42	Brust	2009	M	67	short course of oral steroids	CVC	Fever	Culture (+)	G bronchialis	¿?	¿?	No
43	Siddiqui	2012	F	22	No	No	Osteomyelitis	Culture (+): WrongID ARN 16s (+)	G bronchialis	Vancomycin (14) -> Ciprofloxacin (28) è debridement	42	No
44	Sukackiene	2017	M	32	No	CVC	Peritoneal dialysis-associated peritonitis	Culture (+): WrongID MALDITOF (+) WrongID ARN 16s (+)	G bronchialis	Vancomycin (21) -> Ciprofloxacin (14)	35	No
45	Bartolomé-Alvarez	2016	F	50	No	Self injection	Skin infection	Culture (+): WrongID RNA 16s (+)	G bronchialis	Amoxicillin - clavulanate	10	No
46	Ma	2014	M	70	DM	CVC	Peritoneal dialysis-associated peritonitis	Culture (+)	G bronchialis	Amikacin + Imipenem/cilastin	14	No
47	Akrami	2017	M	69	DM	No	Sternal wound infection	Culture (+) MALDI TOF (+) RNA 16s (+)	G bronchialis	Ceftaroline	56	No

48	Rodriguez Lozano	2016	F	64	No	No	Sternal wound infection	Culture (+): WrongID MALDI TOF (+) RNA 16s (+)	G bronchialis	Teicoplanin ciprofloxacin, rifampicin (14) -> ciprofloxacin, rifampicin (42)	56	No
49	Wright	2014	M	68	DM	No	Sternal wound infection	Culture (+) PFGE (+)	G bronchialis	Imipenem + others + debridement and flap grafts	60	No
50	Wright	2014	M	68	DM	No	Sternal wound infection	Culture (+) PFGE (+)	G bronchialis	Imipenem + others + debridement and flap grafts	60	No
51	Wright	2014	M	68	No	No	Sternal wound infection	Culture (+) PFGE (+)	G bronchialis	Imipenem+other evs + debridement and flap grafts -> moxifloxacin + linezolid, + minocycline oral	116	No
52	Bruno	2022	F	13	No	CVC	Peritoneal dialysis-associated peritonitis	Culture (+) ARN 16s (+)	G bronchialis	Vancomycin+Ciprofoxacin 3)	35	No
52	Choi	2019	F	63	DM	no	Endophthalmitis	Culture (+): Wrong ID MALDI TOF (+) RNA 16s (+)	G bronchialis	Moxifloxacin	21	No
53	Choi	2019	F	61	No	Acupunture	Skin infection	Culture (+): Wrong ID RNA 16s (+)	G bronchialis	Cefpodoxime	42	No
54	Werno	2005	F	43	No	No	Skin infection	Culture (+): WrongID RNA 16s (+)	G bronchialis	¿?	¿?	No
55	Richet	1991	M	59	No	No	Sternal wound infection	Culture (+)	G bronchialis	Ciprofloxacin	74	No
56	Richet	1991	M	59	Steroid treatment	No	Sternal wound infection	Culture (+)	G bronchialis	Trimethoprim – sulfamethoxazole	122	No
57	Richet	1991	M	59	Prostate cancer	No	Sternal wound infection	Culture (+)	G bronquialis	ceftriaxone and oral ciprofloxacin	156	No
58	Richet	1991	M	59	DM	No	Sternal wound infection	Culture (+)	G bronquialis	¿? + surgical treatment	¿?	No
59	Richet	1991	M	59	No	No	Sternal wound infection	Culture (+)	G bronquialis	¿?+surgical treatment	¿?	No
60	Richet	1991	M	59	No	No	Sternal wound infection	Culture (+)	G bronquialis	¿?+ surgical treatment	¿?	No
61	Richet	1991	M	59	No	No	Sternal wound infection	Culture (+)	G bronquialis	¿?+ surgical treatment	¿?	No
62	Lai	2019	M	63	No	No	Endophtalmitis	Culture (-) ARN 16s (+)	G bronquialis	Amikacin	15	No
63	Johnson	2011	F	52	Hodgkin's lymphoma, splenectomy	No	Pneumonia	Culture (+): WrongID ARN 16s (+)	G bronquialis	Ciprofloxacin vo (90)	90	No
64	Sng	2004	F	58	DM	No	Pneumonia	Culture (+): WrongID ARN 16s (+)	G bronquialis	Vancomycin(95) Ceftriaxone(75) -> amoxicillin - clavunalate(42) Surgical treatment	137	No
65	Titécat	2014	M	92	No	Pace marker	Endocarditis	Culture (+): WrongID MALDI TOF (+) ARN 16s (+)	G bronquialis	Amoxicillin	42	No
66	Lam	2015	F	64	No	CVC	Dialysis catheter related bacteremia	Culture (+): Wrong ID ARN 16s (+)	G bronquialis	Meropenem -> levofloxacin	49	No
67	McCormick	2022	F	56	DM, high grade B-cell lymphoma under chemotherapy and steroidtreatment	CVC	Fever	Culture (+): WrongID MALDI TOF (+) ARN 16s (+)	G bronquialis	trimethoprim - sulfamethoxazole + imipenem -> imipenem + cilastina	28	No
68	Ramanan	2015	F	67	DM, autoimmune thyroiditis	No	Encephalitis	Culture (+): Wrong ID RNA 16s (+)	G bronquialis	Cefepime + vancomycin + piperacillin - tazobactam + cefazolin	10	No

depended on the antimicrobial susceptibility tests and on the type of infection, but long treatment regimens were preferred (median 21; IQR 21-56). Sternal wound and device-associated infections have been treated for long periods as long treatment regimens were selected. In the present case, antibiotic treatment was selected based on antimicrobial susceptibility tests and the overall duration reached several months due the unfavorable course.

2. Wound care with PICO (negative pressure wound therapy) and VAC (Vacuum-Assisted Closure) systems have also been reported to both be effective methods to treat post-sternotomy mediastinitis [47-49]. In patients who have undergone VAD implantation there is only anecdotal experience [50]. In this case they were able to partially control the infection, but even the combination of long-term broad-spectrum antibiotics, surgical revision and negative pressure was not enough to eradicate it.

3. Surgical indication depends on the type of infection. Regarding sternal wound infections, 10% of the cases underwent surgical debriding successfully [4]. Complex surgical strategies such as omentoplasty have been elected in previous reports of VAD-related mediastinitis caused by other bacteria. In the presented case, the protracted course and the need for several surgical debridement's, including bone, led to the necessity of a delayed closure, and pectoral

muscle plastia that was successfully performed.

Prognosis

The prognosis of *Gordonia* infections, including mediastinitis, seems favorable with an overall mortality of 4.35%. No mortality secondary to *Gordonia bronquialis* has been reported. The present case is exceptional for being the first reported in a VAD patient. Despite an unfavorable course because of all the prosthetic materials that were probably responsible for the relapsing course of the infection, the patient underwent cardiac transplantation recovering from the infection.

Conclusion

Bacteria of the genus *Gordonia* are rare but emerging human pathogens that can cause a variety of infections. A high index of suspicion is necessary for progressing in selecting the appropriate diagnostic tests in culture-negative infections; given the poor yield of standard microbiological techniques in the identification of *Gordonia* spp. 16s RNA seems likely to replace culture in this setting. There is no defined treatment for *Gordonia* infections. Therefore, the choice of an antimicrobial regimen should be guided by *in vitro* susceptibility test results with a treatment duration adjusted according to specific individual characteristics. The clinical course is subacute or chronic and most of the reported cases have had good outcomes. Nevertheless, in specific scenarios such as patients undergoing VAD therapy the course could be not so indolent since eradication becomes difficult despite long term antibiotic and repeated surgeries.

Highlights

1. Bacteria of the genus *Gordonia* are rare but emerging human pathogens that can cause a variety of infections.

2. Standard microbiological techniques have poor yield for the identification of *Gordonia* spp. Therefore, more precise alternatives, such as 16s RNA sequencing, are needed to replace culture in this setting.

3. There is no defined treatment for *Gordonia* infections. Therefore, antimicrobial regimen should be chosen according to vitro susceptibility-test results.

4. The clinical course of *Gordonia* spp. infections has been reported to be subacute or chronic and most cases have a had good outcome.

5. In patients harboring devices, such as a Ventricular-Assist Device, eradication is more challenging and prognosis may be worse.

Limitations

As any literature review, the one presented here relies on data not collected for research and consequently in many cases some data of interest for us have not been reported. This fact limits the possibility to establish relationships and to generalize and it also implies danger of over-interpretation. Because of the nature of the study, there is also a risk of publication risk.

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