Case Report

Hickman catheter-related bacteremia caused by *Gordonia sputi* in a patient with breast cancer

Diamantis P. Kofteridis[1], Antonios Valachis[1], Efstathia Scoulica[2], Athanasia Christidou[2], Sofia Maraki[2], George Samonis[1]

Departments of Internal Medicine[1] and Clinical Microbiology[2], University Hospital of Heraklion, Crete, Greece

Abstract

The case of a Hickman catheter-related bacteremia caused by *Gordonia sputi* in a patient with breast cancer is presented. Blood cultures grew a Gram-positive rod, susceptible to several antimicrobials, subsequently identified by 16S rRNA gene sequencing as *Gordonia sputi*. The infection resolved after successful treatment with antibiotics and catheter removal.

Key words: *Gordonia sputi*; central venous catheter; bacteremia

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Introduction

The bacterial genus *Gordonia* includes 28 species of mycolic acid-containing actinomycetes [1]. The taxonomy of this group is confusing because of reclassification of some strains from the genus *Rhodococcus* or *Nocardia* to the genus *Gordonia* [2,3]. These bacteria are generally isolated from environmental sources, including soil and water, and many of them are capable of degrading xenobiotics and environmental pollutants [4].

Gordonia species are increasingly recognized as pathogens, causing human infections in both immunocompromised and immunocompetent individuals. The major pathogenic *Gordonia* species are *Gordonia sputi*, *Gordonia bronchialis* and *Gordonia terrae* [4,5]. It is believed that their potential in causing human infections is underestimated, because their identification by conventional microbiological and biochemical methods is very difficult. Therefore, the application of 16S rRNA gene sequencing for the precise identification is extremely important [2].

We present a case of a breast cancer patient with *Gordonia sputi* catheter-related bacteremia identified by 16S rRNA gene sequencing.

Case report

A 70-year-old woman was admitted to the hospital because of fever (39°C) and malaise that started two days earlier. The patient had been diagnosed with breast cancer five years earlier. At that time she underwent surgery and was treated with radiation therapy and adjuvant chemotherapy. The disease recurred two years after initial therapy and progressed despite three lines of chemotherapy. At that time she suffered liver and brain metastases and was treated with gemcitabine and trastuzumab, as a fourth-line treatment. Chemotherapy had been completed twenty days prior to the present admission. She had a Hickman central venous catheter (CVC), which had been inserted six months earlier for the administration of chemotherapy.

On admission, the patient was febrile (38.7°C) but not acutely ill. Examination of the head, neck, chest and abdomen was unremarkable. There was no pain, erythema or exudate at the CVC insertion site.

Methodology

Blood cultures

Two samples of blood, one from a peripheral vein and the other through the CVC (each 11 ml in volume) and a urine specimen were obtained for culture. The patient was empirically treated with ceftriaxone, teicoplanin and amikacin. Blood samples were processed as follows: a volume of 10 ml was equally divided and inoculated into a set of aerobic and anaerobic bottles for the BacT/Alert (bioMérieux, Marcy L' Etoile, France) automated

blood culture system and the remaining 1 ml was inoculated into the Isolator 1.5 (Oxoid LTD, Basingstoke, England) lysis system for quantitative blood culture determination. A volume of 200 μl of this sample was inoculated onto each of three chocolate and two Columbia blood agar plates and incubated at 36^{o}C in 5% CO_2 atmosphere.

16S rRNA gene sequencing

For identification of the strain we sequenced 1,263 bases of the 16S rRNA gene. Genomic DNA was extracted from the cultured bacteria strain using the QIAamp DNA mini kit (Qiagen, Hilden, Germany). The 16S rRNA gene was amplified using the primers BACT 5′ CAGGCCTAACACATGCAAGTC 3′ and UNI1390 5′ GACGGGCGGTGTGTACAA 3′. The PCR product was purified by the JETquick kit (Genomed, Löhne, Germany) and sequenced using the amplification primers in combination with the primers 515F 5′ CCAGCAGCCGCGGTAATA 3′ and 806 R 5′ ACTACCAGGGTATCTAAT 3′. Sequencing was performed using a LI-COR 4200 automated sequencer (LI-COR Inc., Lincoln, NV, USA) and the assembled nucleotide sequence was blasted against the NCBI nucleotide database with the software provided at the website www.ncbi.nlm.nih.gov [6].

Antimicrobial susceptibility tests

The antimicrobial susceptibility test that was performed on the isolate was the E-test method (bioMérieux) which provides minimum inhibitory concentrations (MICs). The tests were performed and the MICs were interpreted according to the CLSI guidelines for *Nocardia* species and other actinomycetes [7].

Results

Laboratory results revealed a white blood cell count of 8000 cells/μL, with 89% granulocytes and haemoglobin level of 10.4 g/dl. On admission all of the remaining biochemical laboratory tests such as urea nitrogen and creatinine levels as well as liver function tests, AST, ALT, γ-GT, ALP and urine analysis were within normal ranges.

Gram-positive bacilli were recovered from the initial blood samples; the urine culture resulted in no microbial growth. A second set of blood cultures, taken five days after admission also grew Gram-positive bacilli, indicating its role as a pathogen in this patient. The quantitative Isolator assays resulted in greater than 5,000 colony-forming units (CFU)/ml (CVC) versus 516 CFU/ml (peripheral line) from the first blood culture set and 1000 CFU/ml (CVC) versus 76 CFU/ml (peripheral line) from the second set.

The Gram-positive bacilli were identified as *Gordonia sputi* by molecular methods. The antimicrobial susceptibility results of the isolate tested against 27 antimicrobial agents (Table 1) showed resistance only to cefoxitin and rifampicin.

The patient became afebrile 48 hours after initial antimicrobial treatment had been started showing gradual improvement of her general clinical condition. After the microbiological results became available, antimicrobial therapy was changed to teicoplanin and meropenem to which the organism was susceptible. The catheter was removed. She was discharged 19 days after admission, with instructions to continue oral amoxicillin/clavulanic acid for 10 days.

She was readmitted 40 days later with extreme weakness without signs and symptoms of infection. She was afebrile. Clinical examination revealed oedema of her extremities. Blood cultures obtained repeatedly resulted in no growth. There was no evidence of recurrence of the *Gordonia sputi* infection. However, she died after 10 days apparently due to progression of her neoplastic disease.

Discussion

To our knowledge, only a limited number of infections caused by *Gordonia* species have been described in the literature. These include cases of bacteremia, native valve endocarditis, sternal wound infections and mediastinitis after coronary artery by-bass, brain abscess, lung and pleural fluid infection, skin infection with lymphadenitis, granulomatous mastitis, mycetoma, keratitis, conjunctivitis and medical device associated septic arthritis [4,5,8-11]. Most case reports of *Gordonia* infection in both adults [9] and children [12] have involved patients with immune dysfunction, mainly suffering from malignant diseases as indicated in the present case.

Quantitative blood cultures with a ratio of ≥ 3:1 CFU/mL of blood (CVC versus peripheral blood) are the most accurate method to diagnose a catheter-related bloodstream infection (BSI) [13]. This was the case with the present patient. The organism was cultured from four blood samples, two from the CVC and two from a peripheral vein, meeting the criteria for quantitative blood cultures for catheter-related

Table 1. MICs* of isolated *Gordonia sputi* as determined by E-test

Antimicrobial Agent	MIC (μg/ml)	Interpretation*
Amikacin	0.25	S
Amoxicillin	0.25	S
Amoxicillin/clavulanic acid	0.25	S
Cefotaxime	0.25	S
Cefoxitin	32	R
Ceftriaxone	0.5	S
Ciprofloxacin	0.125	S
Clarithromycin	0.25	S
Erythromycin	1.5	I
Gentamicin	0.25	S
Imipenem	0.125	S
Levofloxacin	0.125	S
Linezolid	1	S
Meropenem	0.125	S
Norfloxacin	1.5	S
Penicillin	0.125	S
Piperacillin	0.5	S
Piperacillin/tazobactam	0.5	S
Rifampicin	16	R
Teicoplanin	1	S
Tetracycline	4	I
TMP/SMX*	0.004	S
Tobramycin	0.25	S
Vancomycin	0.75	S

Abbreviations: MICs, minimum inhibitory concentrations; S, susceptible; R, resistant; I, intermediate, TMP/SMX, trimethopr

bloodstream infections. Furthermore, the patient had no other apparent source of BSI [13].

Only 11 cases of BSI caused by *Gordonia sputi* have been reported in the literature [8,10,11]. The use of medical devices such as CVCs have been shown to be a major risk factor for acquiring BSI, as exemplified in this case report [4,5,8,10]. The ability of *Gordonia* species to inhabit skin among the normal flora, and its propensity to form biofilms, may contribute to its infectious potential [3].

A review of reported cases of *Gordonia* species BSI showed a high cure rate, suggesting low virulence of this genus [4,5,8-12]. However, the slow growth of *Gordonia* species in the culture media (more than 48 hours) in combination with the often inconclusive results by routine biochemical identification tests may contribute to an underestimation of its pathogenic role [11]. Moreover, *Gordonia* can be confused with other species, such as coryneform bacteria [3] and may require the use of molecular techniques to secure an accurate identification to species level. In this respect, 16S rRNA gene sequencing for precise identification is an extremely useful diagnostic tool to avoid misdiagnosis [2,11].

The antimicrobial susceptibility profiles of *Gordonia* species that were reported in the literature as most effective were carbapenems, ciprofloxacin, gentamicin, amikacin, and vancomycin [5,12]. On the other hand, trimethoprim-sulfamethoxazole, a drug often used to treat *Nocardia* infections [14], was not active in one study [15] and only 65% susceptible in another report [12]. In the present case, the *Gordonia sputi* isolate was susceptible to all these agents, including trimethoprim-sulfamethoxazole. Antimicrobial therapy with teicoplanin and carbapenem along with removal of the catheter was proven successful, although the catheter removal remains a controversial issue [9,12]. The primary care physicians, having oncology experience, had chosen this regimen based upon the MIC results of meropenem, as well as on previous successful clinical experiences using broader antimicrobial coverage when treating immunocompromised cancer patients. Additionally, they considered that although the

organism was susceptible to the antimicrobials previously prescribed, *Gordonia* persisted in the blood.

In conclusion, *Gordonia sputi* should be added to the list of pathogens that cause catheter-related bacteremia, particularly in immunocompromised patients. Since these bacteria are difficult to identify to the species level in routine laboratories, molecular methods are recommended for accurate diagnosis. Further studies regarding the identification, antimicrobial susceptibility profile, and treatment options available for patients with *Gordonia* infections are needed to clarify and improve our knowledge for patient management.

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Corresponding author

Diamantis P. Kofteridis, MD
Department of Internal Medicine
University Hospital of Heraklion
PO Box 1352
71110 Heraklion, Crete, Greece
Telephone: (+30) 2810 392688
Fax: (+30) 2810 392359
Email: kofterid@med.uoc.gr

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