Rhizobium radiobacter recovered from blood of a pediatric patient with stem cell transplantation: a case report and characterization of antimicrobial susceptibility profile

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ABSTRACT

Rhizobium radiobacter is an uncommon agent of infection and has been associated with indwelling intravascular devices such as catheter in immunocompromised patients. Here, we report a case of R. radiobacter recovered from blood cultures in stem cell transplantation in a pediatric patient and present an extensive characterization of its antimicrobial susceptibility profile. The isolate presented low MICs to many antimicrobial agents, but high MICs to ceftazidime, piperacillin-tazobactam, aztreonam, and fosfomycin.

Keywords: *Transplantation; antimicrobial agents*

Species of Rhizobium (formerly named Agrobacterium, which was reclassified based on 16S rDNA analysis) are aerobic, non-spore forming, oxidase- and catalase-positive, gram-negative microorganisms, affecting a wide variety of plants, making it an important concern for agriculture industry. Among the Rhizobium species, R. radiobacter is the most common agent of infection in humans[1,2]. Cases of bacteremia, prosthetic valve endocarditis, urinary tract infection, peritonitis, and pneumonia have been reported[1,2]. Immunocompromised hosts, especially patients with hematological malignancy, bacteremia, and catheter-related bloodstream infection are the most prevalence cases[2]. Bacteremia due to R. radiobacter is frequently associated with the presence of an indwelling device such as a central venous catheter, probably due to its ability for slime production on the surfaces[3,4]. The outcome of device-associated infection due to R. radiobacter is generally favorable compared with other pathogens, such as *Staphylococcus aureus* and *S. epidermidis*[5].

Here, we report a case of bacteremia due to R. radiobacter in a stem cell transplantation patient and we discuss the identification and antimicrobial susceptibility profile of the isolate.

Case

A 7-year-old male patient, diagnosed with hepatosplenic lymphoma, underwent chemotherapy and autologous bone marrow transplantation. Accomplished pre-transplant conditioning with carmustine, etoposide, cytarabine, and melphalan, he developed severe neutropenia. According to the protocol of febrile neutropenia, we introduced cefepime (administrated during a week), piperacillin/tazobactam (for 2 days), meropenem, and vancomycin. As an

antifungal agent, amphotericin B was subsequently replaced by micafungin due to toxicity. The patient evolved with improved thermal curve, microbial cultures without growth of microorganisms, completing 14 days of antimicrobial treatment.

After 2 days of stopping the treatment, the patient had fever again, and therefore the antimicrobial treatment was restarted with meropenem and vancomycin. From a couple of blood samples (one from peripheral blood and another from catheter) it was verified the presence of rod-shaped, gram-negative bacteria, presenting oxidase-positive reaction and growth on MacConkey's and blood agar after 24 h of incubation at 35ºC. This microorganism was submitted to VITEK 2 (bioMérieux, France) and MALDI-TOF (Becton Dickinson, USA) automated systems, being identified as Rhizobium radiobacter by both methods.

According to the results of antimicrobial susceptibility profile performed by Etest (bioMérieux, France), this isolate presented low minimal inhibitory concentrations (MICs) to ampicillin/sulbactam, ciprofloxacin, ceftriaxone, and carbapenems (table). It is of note that a possible catheter-related infection was evidenced, according to the time of positivity between peripheral blood and blood collected via catheter. The catheter was removed and the treatment was completed in 14 days with 10 mg\Kg meropenem. The patient evolved with improved clinical parameters, such as decreased inflammatory markers (procalcitonin and C-reactive protein), and immune (normal leukocyte blood count) reconstitution. A new couple of blood cultures were collected and did not show bacterial growth, verifying the clearance of the Rhizobium infection.

Table: MICs for the different antimicrobial agents tested for the R. radiobacter isolate.

Antimicrobial agents	MIC (µg/mL)
Ampicillin/Sulbactam	≤ 0.16
Ciprofloxacin	0.25
Gentamicin	3
Amikacin	8
Cefuroxime	8
Ceftriaxone	0.75
Ceftazidime	16
Cefepime	2
Piperacillin/Tazobactam	32
Meropenem	2
Ertapenem	≤0.5
Doripenem	0.094
Imipenem	≤0.5
Polymyxin B	<0.125
Colistin	0.25
Aztreonam	64
Tigecycline	0.5
Fosfomycin	>1024
Chloramphenicol	2

DISCUSSION

Rhizobium radiobacter has been implicated in infections involving prosthetic valve, central venous catheter, and other types of medical devices. On the other hand, a few studies have pointed R. radiobacter as a "true" agent of infection. In fact, this microorganism should be included in the list of pathogens that cause infection, mainly cases of bacteremia, when immunocompromised patients are affected, especially in the presence of an intravenous catheter.

Additionally, other two situations should be considered in cases involving R. radiobacter: 1) given the very small number of clinical isolates of R. radiobacter encountered in clinical laboratories, there are limited data on which to judge how well the manual and automated bacterial identification systems identify it; and 2) there is no susceptibility breakpoints defined for these organisms so far, and there are few studies in which R. radiobacter has a full characterization of its antimicrobial susceptibility by the determination of the MIC[3,5-8]. In fact, most isolates are susceptible to broad-spectrum cephalosporins, carbapenems, tetracyclines, and gentamicin but not tobramycin[8,9].Testing of individual isolates is recommended for clinically significant cases once that it is unknown the intrinsic mechanisms of resistance for the rhizobia species.

Some studies have pointed that R. radiobacter presents low MICs (inferior to 1 µg/mL in most of cases) to the third generation cephalosporins, cephamycins, carbapenems, fluoroquinolones, tetracycline, nitrofurantoin, and aminoglycosides, but high MIC (superior to 8 µg/mL have been reported) to penicillins, penicillin/enzyme inhibitors, beta-lactam, aztreonam, and fosfomycin[3,6,7]. In this report, the isolate showed low MICs for many antibiotics and presented a high MICs for others, mainly aztreonam and fosfomycin (table). For therapeutic approaches, cephalosporins (mainly cefepime) and ciprofloxacin have been used successfully to treat Rhizobium infections[6,7,9]. Lai et al.[2] reported in their study a very lower MICs for carbapenem agents in comparison to our isolate, mainly for meropenem (2 µg/mL for our isolate against a range from 0.03 to 0.06 µg/mL for 18 isolates tested in Lai's study). For imipenem, a similar MIC value was obtained in comparison with the findings of Lai et al.[2] It is of note that, based on a few reports to date, antimicrobial susceptibilities for R. radiobacter is variable. There is no consensus for type or length of treatment or optimum therapy, owing to the small number of cases described to date, and these may logically be dictated by the clinical response, degree of underlying illness, status of the host immune system, and whether microbiologic eradication can be documented. Also, it is not uncommon to recover R. radiobacter from sites of body without obvious pathologic effects and thus it may be present simultaneously with other bacterial species in mixed flora. It is important to note that R. radiobacter should be added to the list of pathogens that induce infections conditions in patients with malignancy, but mainly in pediatric patients. For an empirical and definitive antibiotic therapy, it has been considered the use of cefepime 2 g intravenously every 8 hours for a total of 8-10 days[9]. In conclusion, we present an unusual case of R. radiobacter bacteremia in a stem cell transplant patient. The isolate presented low MICs to many antimicrobial agents, but high MICs to ceftazidime, piperacillin-tazobactam, aztreonam, and fosfomycin. Further studies are required to characterize the antimicrobial susceptibility profile and the underlying resistance mechanisms of this pathogen.

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