

Rhizobium radiobacter bloodstream infection associated with long-term central venous access in an infant with Pompe disease

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SUMMARY

Rhizobium radiobacter (formerly *Agrobacterium tumefaciens*) is an environmental Gram-negative bacillus increasingly recognized as an opportunistic human pathogen, particularly in association with indwelling medical devices. Bloodstream infections (BSI) caused by this organism are rarely reported in children.

We describe a 10-month-old girl with infantile-onset Pompe disease undergoing weekly enzyme replacement therapy (ERT) via central venous catheter who presented with fever and clinical deterioration 72 hours after infusion. Initial inflammatory markers were not significantly elevated, and multiplex molecular assays were negative for bacterial pathogens. Blood culture obtained from the catheter became positive after 25 hours, yielding Gram-negative bacilli subsequently identified as *R. radiobacter*. The isolate showed susceptibility to aminoglycosides, carbapenems, and

fluoroquinolones, with intermediate susceptibility to piperacillin/tazobactam.

Targeted antimicrobial therapy led to rapid clinical improvement and clearance of bacteremia without catheter removal.

This case highlights both the pathogenic potential of uncommon environmental microorganisms in fragile children with long-term intravascular devices and the continuing diagnostic value of conventional blood cultures, particularly when rapid molecular assays are negative. Our experience also supports the possibility of catheter salvage in clinically stable patients responsive to appropriate antimicrobial therapy.

Keywords: Pompe disease, *Rhizobium radiobacter*, catheter-related bloodstream infection, central venous catheter, enzyme replacement therapy (ERT).

INTRODUCTION

Rhizobium radiobacter (*R. radiobacter*), formerly known as *Agrobacterium tumefaciens*, is a soil-dwelling Gram-negative aerobic bacillus belonging to the *Rhizobiaceae* family [1, 2]. Classically

regarded as a soil contaminant and a plant pathogen, *R. radiobacter* has emerged as an uncommon but clinically significant opportunistic pathogen in humans [3]. Human infections are most frequently associated with indwelling medical devices, particularly central venous catheters (CVC), and may occur in both immunocompetent and immunocompromised patients [4-6].

Here, we report a case of *R. radiobacter*-related sepsis associated with a CVC in an infant with infantile-onset Pompe disease receiving Enzyme Re-

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placement Therapy (ERT), highlighting the potential severity of this unusual pathogen.

■ CASE REPORT

We present the case of a ten-month-old girl with Pompe disease, diagnosed early in life following the identification of cardiologic abnormalities. Since the diagnosis, she has received ERT with recombinant human acid alpha-glucosidase (rh-GAA), administered once weekly via CVC. The last Port-type CVC had been placed approximately two months before the onset of symptoms to allow scheduled infusions. The patient was electively admitted in good clinical condition for the administration of her planned ERT in a day-hospital setting. Approximately 72 hours after the infusion, she developed high-grade fever at home, followed by progressive clinical deterioration, and was brought back to the hospital for urgent evaluation.

At admission, she was febrile (body temperature 38.8°C), tachycardic (heart rate 160 beats/min), and tachypneic (respiratory rate 50 breaths/min), with preserved oxygen saturation (98% on room air) and a capillary refill time of approximately two seconds. On objective examination, the patient appeared acutely ill and pale. The anterior fontanelle was tense. Cardiac exam showed sinus tachycardia with regular rhythm without pathological murmurs. Chest auscultation revealed symmetrical bilateral breath sounds. The abdomen was soft but mildly distended, with reduced peristaltic sounds. Peripheral pulses were weak but palpable. Neurological examination evidenced irritability and reduced responsiveness, without clear focal deficits. Laboratory findings revealed a white blood cell count of 4.770/uL (with 26.9% neutrophils), C-reactive protein (CRP) of 0.06 mg/dl (reference range 0.00-0.50 mg/dL), and procalcitonin (PCT) of 0.20 ng/mL (below <0.05 ng/mL). Blood culture was collected from CVC, while a multiplex polymerase chain reaction (PCR) assay for bacterial pathogens performed on peripheral blood (EuSepScreen Lattanti and EuSepScreen Plus, Eurospital) was negative. Unfortunately, peripheral blood culture was not obtained because of the patient's young age, fragile clinical condition, limited peripheral venous access, and the need to promptly initiate empirical antimicrobial therapy. A multiplex PCR assay for respiratory pathogens

detected parainfluenza virus. Nonetheless, the patient's rapid clinical deterioration, the presence of a long-term CVC, and her underlying medical fragility raised the suspicion of a catheter-related bloodstream infection. Empiric antimicrobial therapy with daptomycin (10 mg/kg every 24 h) and piperacillin/tazobactam (240 mg/kg/day, administered in three divided doses)

was therefore initiated, pending blood culture results.

On the second day of hospitalization, laboratory tests revealed markedly elevated aspartate aminotransferase and alanine aminotransferase levels (207 U/L and 262 U/L, respectively), along with increased CRP (7.23 mg/dL) and PCT (20.55 ng/L). Real time-PCR for CMV, EBV, HHV6 DNA on blood samples were negative. CVC blood culture became positive after 25 hours of incubation in Bactec FX system (Becton Dickinson). Gram staining detected Gram-negative bacilli. Multiplex PCR assay performed on positive blood culture (Biofire FilmArray BCID2 panel, BioMerieux) was negative. Culture on blood agar, chocolate agar, and McConkey agar led to the growth of lactose-fermenting Gram-negative bacteria with mucoid colonies. Matrix-Assisted Laser Desorption Ionization Time-of-flight Mass Spectrometry (MALDI-TOF MS Biotyper MBT SMART, Bruker) led to the identification of the proteomic profile of *R. radiobacter*. Antibiotic susceptibility profile was tested by automated system (BD Phoenix, Becton Dickinson) and was interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines for "other non-Enterobacteriales" as specific EUCAST breakpoints for *R. radiobacter* were not available. The strain was identified as susceptible to amikacin, imipenem, meropenem and fluoroquinolones, with intermediate susceptibility to piperacillin/tazobactam. The dosage of piperacillin/tazobactam was therefore increased to 300 mg/kg/day administered in three doses and the patient showed a favorable response to antibiotic therapy, with rapid clinical and laboratory improvement. This distinction supported the decision to attempt port-a-cath salvage under close monitoring.

The CVC was preserved, and no persistent bacteremia was documented.

After 10 days of intravenous antimicrobial treatment, a subsequent blood culture taken at discharge revealed no growth. No oral step-down

therapy was administered after discharge and no additional microbiological follow-up cultures were available thereafter.

■ DISCUSSION

R. radiobacter is primarily recognized as a phytopathogen capable of inducing neoplastic transformation in plant cells [1, 2]. It has been shown to survive and replicate within free-living amoebae such as *Acanthamoeba polyphaga*, which share environmental niches with the bacterium, including soil and freshwater reservoirs, potentially contributing to environmental persistence and human exposure [7]. Beyond its well-established role in plant pathology, *R. radiobacter* has increasingly been reported as an opportunistic human pathogen, implicated in a variety of clinical syndromes, including peritonitis, endocarditis, urinary tract infections, myositis, pneumonia, and soft tissue infections, with bacteremia representing the most frequently reported manifestation. To date, no definitive mode of transmission has been identified [8–12]. Most reported cases lack a clear history of direct exposure to plants or soil, and infections have been described as either community-acquired or nosocomial [10]. The organism's ability to adhere to synthetic surfaces plays a central role in its pathogenesis. Infections have been associated with a wide range of foreign bodies, including long-term central venous access devices, prosthetic cardiac valves, urinary catheters, nephrostomy tubes, intraperitoneal catheters, and tunneled cuffed hemodialysis catheters [13, 14]. Most published pediatric cases involve children with significant underlying conditions, including hematologic malignancies, bone marrow transplantation, chronic renal failure, cystic fibrosis, and HIV infection [5, 8, 15, 16]. In our case, the patient was immunologically fragile due to infantile-onset Pompe disease, a multisystem metabolic disorder associated with progressive organ involvement and long-term dependence on central venous access for ERT. Although *R. radiobacter* possesses lipopolysaccharides (LPSs), the rhizobial LPSs exhibit unique structural characteristics that modulate Toll-like receptor signaling, potentially leading to a diminished pro-inflammatory response when compared to classical enterobacterial endotoxins [17, 18]. This attenuated inflammatory signaling could explain the lack of a marked rise in inflam-

matory markers at the onset of infection in our case. In this context, especially in children with long-term CVCs, a subtle clinical picture may delay the recognition of catheter-related bloodstream infections (CRBSIs).

CRBSIs are laboratory-confirmed bloodstream infections occurring in patients with an intravascular catheter in place or within 48 hours since the onset of bacteremia, with no alternative source identified [19]. They may be caused by common nosocomial pathogens and by uncommon or environmental microorganisms, such as *R. radiobacter*, which can be difficult to detect using rapid molecular panels.

Considering the inability of rapid molecular tests to identify rare pathogens not included in the diagnostic panels, blood cultures remain essential for accurate microbiological diagnosis and continue to represent the diagnostic reference method for clinicians in the suspicion of sepsis.

In suspected CRBSI, obtaining paired blood cultures from both the device and a peripheral vein may help to support the clinical significance of the isolate by distinguishing true bacteremia from possible contamination and may also contribute to defining the relationship between the bloodstream infection and the intravascular device through differential time to positivity (DTP) analysis, a key criterion for CRBSI diagnosis in children [19, 20]. In our case, although contamination cannot be definitively excluded, several findings supported the clinical significance of the isolate, including the patient's acute clinical deterioration, the subsequent marked increase in inflammatory markers, the presence of a long-term intravascular device, and the patient's underlying medical fragility. Furthermore, the rapid clinical improvement following targeted antimicrobial therapy and the absence of bacterial growth in the follow-up blood culture obtained after completion of treatment supported the interpretation of *R. radiobacter* as the causative pathogen rather than a contaminant.

The absence of simultaneous peripheral blood cultures also prevented calculation of differential time to positivity and therefore did not allow definitive confirmation of a port-a-cath-related bloodstream infection. However, given the presence of a long-term intravascular device and the lack of an alternative identifiable source of infection, the episode was considered consistent with a presumptive port-a-cath-associated bloodstream

infection. Clinical management of suspected CVC-related sepsis is challenging and requires careful evaluation of the need for catheter removal versus salvage, balancing the risks of persistent infection against the difficulties of obtaining new vascular access [15, 16]. While some authors recommend catheter removal in cases of persistent fever or bacteremia beyond 48 hours of optimized antimicrobial therapy [21], others have reported successful catheter salvage in clinically stable patients without persistent bacteremia [4, 6, 16, 22]. In our case, given the hemodynamic stability, the rapid response to antimicrobial therapy, and the critical need to maintain long-term vascular access for ERT, a carefully monitored catheter-salvage approach was adopted.

According to literature data, *R. radiobacter* is usually susceptible to ticarcillin, piperacillin/tazobactam, fluoroquinolones, and carbapenems, despite reports of resistance to cephalosporins due to the production of inducible AmpC beta-lactamases. A variable susceptibility is also reported for aminoglycosides [10, 23]. In our case, susceptibility to carbapenems and fluoroquinolones suggested the absence of more complex acquired resistance mechanisms such as carbapenemase production or efflux pump overexpression.

Overall, outcomes of *R. radiobacter* infections in both pediatric and adult populations are generally favorable, with no reports of mortality directly attributable to the organism in the literature [9]. Severe complications and long-term sequelae are uncommon, and catheter removal is rarely required unless sepsis persists or antimicrobial therapy fails. Catheter-related bloodstream infections may recur, particularly when catheters are manipulated or replaced shortly after treatment completion [21]. In our patient, no recurrence of *R. radiobacter* bacteremia was observed during follow-up, supporting the appropriateness of catheter salvage in the context of a favorable clinical response.

■ LIMITATIONS OF THE STUDY

Some limitations should be acknowledged. First, only a port-a-cath blood culture was obtained, and no simultaneous peripheral blood culture was available at admission; therefore, differential time to positivity could not be calculated, and a definitive diagnosis of CRBSI cannot be established. For this reason, we describe the episode as a presump-

tive port-a-cath-associated bloodstream infection. Second, only one initial blood culture was positive, while multiple paired cultures would have strengthened diagnostic certainty, therefore limiting the ability to fully exclude contamination. Nevertheless, the patient's clinical deterioration, subsequent inflammatory response, risk profile, response to antimicrobial therapy, and negative follow-up culture support the clinical relevance of the isolate.

■ CONCLUSIONS

This case report exemplifies the importance of considering atypical, opportunistic pathogens, which may not be captured by routine or rapid diagnostic tests alone, when managing cases of suspected sepsis in fragile or immunocompromised patients.

Despite the importance of rapid multiplex molecular panels, blood cultures are essential for the identification of rare but potentially dangerous bacterial pathogens and enable antimicrobial susceptibility assessment with subsequent treatment adjustments.

Early initiation of appropriate antimicrobial treatment is crucial to prevent organ dysfunction and mortality, especially in vulnerable pediatric patients.

Catheter removal should be considered when fever or bacteremia persist despite adequate antimicrobial therapy, while catheter salvage may be feasible in clinically stable patients who show a timely response to treatment. Prompt recognition of uncommon pathogens remains essential in fragile pediatric patients with long-term vascular devices, particularly when rapid molecular assays are negative.

Although traditionally considered an environmental microorganism, *R. radiobacter* should be considered a potential nosocomial pathogen, given its documented presence in hospital environments, including in total parenteral nutrition solutions, sample collection systems, sinks, and fluid dispensers [1,10]. In this context, careful handling and maintenance of vascular access devices remain important to reduce the risk of opportunistic device-associated infections.

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Conflict of interest

None

Informed consent

This study was conducted in accordance with the ethical standards of the responsible institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments. All data included in this manuscript have been fully anonymized.

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