IDCases 26 (2021) e01339

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases

Case report

The first case of *Janibacter hoylei* bacteremia in an adult

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ARTICLE INFO

Article history:
Received 9 November 2021
Received in revised form 13 November 2021
Accepted 13 November 2021
Available online xxxx

Keywords:
Bacteremia
Janibacter
Malignancy
Immunosuppression

ABSTRACT

The *Janibacter* species are Gram positive, coryneform bacteria that belong to the Actinobacteria phylum and have been linked to bacteremia in immunocompromised children. We present the first documented adult case of *Janibacter hoylei* bacteremia. The patient was a 52-year-old woman with a history of recurrent *Clostridioides difficile* infection, sinus tachycardia and high-risk AML who had been admitted one month prior to presentation for matched unrelated donor hematopoietic stem cell transplant with reduced intensity fludarabine-melphalan. Thirty days post-transplant, the infectious disease team was consulted because blood cultures grew *Janibacter hoylei*, from one of two blood cultures It took nine days to identify the species. She was treated with linezolid and imipenem. *Janibacter* are rarely implicated in human pathology, and therein, usually identified in the context of malignancy and relative immunosuppression. *J. hoylei* was only previously reported from the bloodstream of a previously healthy 8-week-old infant without underlying medical conditions. Antimicrobial susceptibility testing is challenging as only in vitro susceptibility testing of *Janibacter terrae* has been reported. Given these challenges, it is our hope to illustrate the clinical approach to diagnosis as well as subsequent recommendations for treatment in a particularly challenging case of bacteremia in an AML patient.

Introduction

Janibacter hoylei belongs to a genus of Gram positive, coryneform bacteria characterized as an actinomycete of the Actinobacteria phylum, originally isolated from an air sample in the upper atmosphere [1]. In humans, there is concern that this bacterium could represent an opportunistic pathogen. Previously identified cases of *Janibacter* bacteremia have been described in a setting of hematologic malignancies [2–5]. Otherwise, *Janibacter* species have been identified in vaginal secretions and heart valves [6,7]. Infection with *J. hoylei*, specifically, was described by Lim et al. in an 8-week-old infant without underlying medical conditions who presented with fevers without an obvious source of infection [2]. Herein, we present a case of *J. hoylei* bacteremia an adult with active malignancy and transplantation.

Case report

The patient was a 52 year old woman with for high risk AML and recurrent *Clostridioides difficile* infection who had been admitted for one month prior for match-unrelated donor hematopoietic stem cell transplant with reduced intensity fludarabine-melphalan. Afterwards, she was initiated on tacrolimus and methotrexate for graft-versus-host prophylaxis. Her hospital course had been complicated by sepsis, metabolic encephalopathy, chronic diarrhea, transaminitis, acute kidney injury, and eventual bone graft failure. She was seen by infectious diseases in consultation several times during her hospitalization (for febrile neutropenia, encephalopathy, and *Klebsiella* bacteremia) and eventually for evaluation of *J. hoylei* bacteremia.

On exam, she was afebrile and normotensive, her blood pressure was 143/104, pulse 104 beats per minute, respiratory rate 22 breaths per minute, and oxygen saturation 97% on room air. Physical exam was most remarkable for diffuse anasarca with bruising throughout

Abbreviations: AML, Acute myeloid leukemia; MIC, Minimum inhibitory concentration; MALDI-TOF MS, Matrix-assisted laser desorption ionization-time of flight mass spectrometry

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https://doi.org/10.1016/j.idcr.2021.e01339
2214-2509/

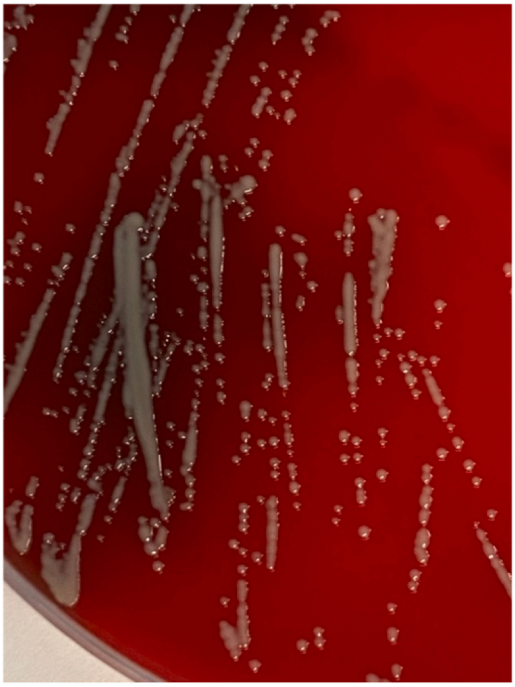

Fig. 1. Sheep blood agar plate after 48 h of aerobic incubation with 5% CO_2 at 37 °C. Colonies were small and cream-colored to yellow, with no hemolysis.

her extremities, bleeding gums and oral ulcers concerning for mucositis, course bilateral breath sounds, and hypoactive bowel sounds. Otherwise, her oral mucosa was without evidence of thrush and her left chest peripherally inserted central catheter (PICC) site appeared clean, dry and intact.

Thirty days post-transplant, one aerobic blood culture grew *J. hoylei* after 2 days and 20 h of incubation. This culture was drawn from a peripheral line during an episode of decompensation. The patient had active oral mucositis hemorrhage and was transferred to the intensive care unit for airway management. The organism grew on sheep blood agar after 48 h of aerobic incubation at 37°C with the addition of 5% CO_2 (Fig. 1). The morphology was Gram-positive and coryneform. Final identification was achieved by MALDI-TOF MS (research use only database) and confirmed with 16S ribosomal RNA gene PCR/sequencing.

At the time of her bacteremia, she had been receiving intravenous cefepime and vancomycin for 8 and 11 days, respectively. She was empirically transitioned to imipenem and linezolid for 7 days. Subsequent susceptibility results demonstrated the following MICs: ceftriaxone (>2 μg/mL), meropenem (≤0.25 μg/mL), penicillin (2 μg/mL), and vancomycin (≤1 μg/mL). Follow-up blood cultures remained negative. Unfortunately, her pancytopenia worsened over the following weeks. Repeat bone marrow biopsy showed severely aplastic bone marrow without any signs of leukemia. Given her poor prognosis, as well as significant deterioration in functional status, she elected for comfort and hospice care and died a few days later.

Discussion and conclusion

J. hoylei belongs to the *Actinomycetales* order of microorganisms, which are characterized as aerobic, gram positive rods of irregular morphology [4]. The species was first identified by upper atmosphere balloon collection in 2009 [8], with subsequent genomic identification of the atmospheric strain available by 2012 [1]. *J. hoylei* bacteremia remains a rare clinical finding, with only a handful of case reports to date. *J. hoylei* is not included in the databases of phenotypically based identification systems. Because of this, definitive identification using both MALDI-TOF and 16S rRNA sequencing was performed in this case. The previous literature has shown clinical relevance in patients with hematologic malignancies, prompting concerns of opportunistic infection in immunocompromised individuals [4].

This certainly appears to be the case with our patient, who suffered from AML status post completion of a peripheral blood stem cell transplant with chemotherapy, resulting in a prolonged period of profound immunosuppression. In this setting, she was subjected to various, prophylactic anti-infectives, including acyclovir, inhaled pentamidine, levofloxacin, oral vancomycin, as well as both fluconazole and voriconazole. Additionally, she had been treated with courses of parenteral vancomycin, piperacillin-tazobactam, aztreonam, and levofloxacin for concerns of febrile neutropenia, over time. Such advanced illness and an extended period of immunocompromise can predispose to a variety of opportunistic infection.

The previous literature on *Janibacter* bloodstream infections cite environmental isolation with introduction to the host via breaks in skin integrity (injury, insect bite, etc.) [3]. In our case, the patient had a PICC in place, at least one peripheral IV access, as well as an indwelling urinary catheter, all of which can represent potential sites for inoculation, particularly with long-standing, profound neutropenia. Though the possibility of contamination cannot be effectively ruled out, in such a setting, and given the rarity of the offending microorganism, we believe that its presence constitutes true infection.

Similarly, given the paucity of data in the literature, the optimal course and duration of antimicrobial therapy has not been established. It was our recommendation that the patient receive intravenous treatment for seven days, bearing in mind the antibiotics she was on, beforehand. Initially, our decision to empirically treat our patient with imipenem and linezolid, pending susceptibility testing, was based on the article by Natal et al., which identified microbiological susceptibilities of four *J. terrae* isolates [5]. Therein, imipenem and linezolid MICs of <0.25 and <1 μg/mL, respectively, were reported for all four isolates.

Infections from the *Janibacter* species in immunocompromised patients might reflect true infection rather than contamination. Further clinical studies and consultation with the microbiology laboratory and infectious diseases would be recommended given the rarity of this organism.

Funding

The authors declare that they have no source of funding.

CRediT authorship contribution statement

All authors contributed equally to the writing of this manuscript. This includes Conceptualization, Investigation, Resources, Data curation, Supervision, Writing – original draft, Writing – review & editing.

Data availability

Not applicable.

Acknowledgements

We would like to acknowledge the staff of the Mayo Clinic microbiology laboratory for their assistance in this case.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of

the written consent is available for review by the Editor-in-Chief of this journal on request.

Competing interests

Dr. Patel reports grants from Merck, ContraFect, TenNor Therapeutics Limited and Shionogi. Dr. Patel is a consultant to Curetis, Specific Technologies, Next Gen Diagnostics, PathoQuest, Selux Diagnostics, 1928 Diagnostics, PhAST, and Qvella; monies are paid to Mayo Clinic. Dr. Patel is also a consultant to Netflix. In addition, Dr. Patel has a patent on *Bordetella pertussis/parapertussis* PCR issued, a patent on a device/method for sonication with royalties paid by Samsung to Mayo Clinic, and a patent on an anti-biofilm substance issued. Dr. Patel receives an editor's stipend from IDSA, and honoraria from the NBME, Up-to-Date and the Infectious Diseases Board Review Course. All other authors declare that they have no competing interests.

Authors' contributions

All authors contributed equally to the development, writing, and editing of this manuscript.

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