Case report

**Roseomonas mucosa** bacteremia in a neutropenic child: A case report and literature review

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**A B S T R A C T**

**Roseomonas** species are rarely found to be pathogenic to humans and there are few clinical cases that have been described in the literature. We report a case of **Roseomonas mucosa** bacteremia that involved a 9-year-old Japanese boy who was in a condition of febrile neutropenia caused by chemotherapy for cerebellar medulloblastoma. Conventional phenotyping failed to identify the organism; however, genetic analysis using 16S rDNA sequencing confirmed the pathogen to be *R. mucosa*. The patient recovered following treatment by meropenem without any complications. A literature review of pediatric cases of **Roseomonas** bacteremia identified 12 other documented cases, and these revealed that a common clinical situation for the infection is an immunocompromised state with malignancy and/or an indwelling intravenous catheter. Because of the low number of cases, the overall picture of **Roseomonas** bacteremia in children remains to be elucidated; however, the prognosis of the infection appears to be satisfactory.

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**Introduction**

Members of the genus **Roseomonas**, which was first reported by Rihs et al. in 1993 [1], are slow-growing, aerobic, non-fermentative Gram-negative bacteria, which appear as pink-pigmented colonies. More than 20 **Roseomonas** species have been isolated from environmental samples, including water, soil, and plants [2–5]. These species are opportunistic pathogens with low pathogenicity to humans; however, the occurrence of human infections has increasingly been reported over the last two decades, predominantly in immunocompromised patients [6–8]. These organisms frequently cause central line-associated bloodstream infections, but potentially give rise to respiratory, skin and soft tissue, peritoneal, and urinary tract infections, as well as spondylitis and subretinal abscesses [9–11].

The major human pathogens of **Roseomonas** species are **Roseomonas gilardii** subsp. *gilardii*, **Roseomonas gilardii** subsp. *rosea*, and **Roseomonas mucosa** [2,8,12]. Of these, *R. mucosa* appears to be the most frequently identified in clinical samples [8] and has the ability to cause infections in immunocompetent patients [8,13] and even life-threatening diseases [14]. However, the clinical picture of the infection caused by the pathogen remains to be fully elucidated because of the paucity of reported cases. Here, we report a case of *R. mucosa* bacteremia, with a literature review of pediatric cases of bacteremia caused by **Roseomonas** species.

**Case**

A 9-year-old Japanese boy (body weight, 27 kg) diagnosed with cerebellar medulloblastoma was admitted to our hospital. He had undergone cranial surgery for tumor resection and had subsequently undergone monthly cancer chemotherapy with a combination of cisplatin, cyclophosphamide, and vincristine. For the infusion of anticancer drugs, an indwelling central line catheter was placed. Three days subsequent to the third course, the patient developed febrile neutropenia, for which meropenem (2.7 g per day) was empirically initiated. His vital signs remained stable, but high fever accompanying diarrhea persisted. Whole-body tomography did not reveal any abnormal findings. Four days later, the patient’s laboratory findings revealed Grade 4 neutropenia (40 cells/μL), a mild elevation in C-reactive protein levels (2.77 mg/dL), and decreased serum gamma globulin levels (immunoglobulin G, 493 mg/dL). Following the collection of blood through the central line for culture, teicoplanin was administered. In addition, his stool specimen was positive for *Clostridium difficile* toxins, and treatment with intravenous metronidazole was initiated.
Blood was collected into in BD BACTEC™ Peds Plus/F culture vials (Becton Dickinson, Sparks, MD, USA) and was incubated in a BD BACTEC™ FX blood culture system (Becton Dickinson). After 48 h at 35 °C, there was a positive signal from the automated blood culture apparatus; however, no organisms were detected under microscopic examination. The fluid was centrifuged to collect bacteria, and Gram-negative plump coccoid rods were successfully confirmed (Fig. 1A). These were subcultured on trypticase soy agar with 5% sheep blood (Becton Dickinson) and on chocolate agar (Kyokuto Pharmaceutical Industrial, Tokyo, Japan) in 5% CO2 at 35 °C. Over subsequent days, colonies on the chocolate agar demonstrated a pink color (Fig. 1B). The organism, which was positive for catalase, oxidase, and urease in biochemical identification tests, could not be identified using Neg Combo Panel NNFCl (Beckman Coulter, Brea, CA, USA).

Full-base 16S rDNA polymerase chain reaction analysis was conducted and 1,411 base pairs of the targeted gene were amplified using the universal primers 8U (5’-AGA GTT TAC TGG TCT CAC-3’) and 1485B (5’-TAC GGT TCT CTT GGG AGC-3’). The sequence data were analyzed using BLAST sequence homology search programs (GenBank, EzBioCloud, and leBIBI), and the pathogen was finally confirmed to correspond with the type strain of R. mucosa (ATCC BAA-692; accession number AF538712) with an accuracy of 100%. The organism was also identified as R. mucosa by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry using a MALDI Biotyper (Bruker Daltonics, Bremen, Germany), with a score of 2.378. The isolate showed resistance to piperacillin, aztreonam, and cefazidime, and was susceptible to carbapenems, aminoglycosides, minocycline, fluoroquinolones, and trimethoprim/sulfamethoxazole (Table 1).

The patient gradually recovered from the neutropenia, and a subsequent blood culture examination was negative. He was treated with meropenem for 2 weeks with a satisfactory clinical course.

Discussion

Because of their low pathogenicity, Roseomonas species rarely cause infections in humans; thus, its clinical features are not yet fully understood. To elucidate the clinical characteristics of Roseomonas bacteremia in children, we reviewed previous literature (Table 2) [8,9,14–18]. A search of MEDLINE from its inception in 1996 revealed only 12 such cases. Of the 13 cases, including our patient, the majority of cases had any underlying diseases (11 cases, 84.6%); almost half of the cases had malignancies (6 cases, 46.2%) and neutropenia was observed in at least three cases (23.1%). Only one child was free from any underlying disease [8]. Since the characterization of R. mucosa in 2003 [12], this species has accounted for the majority of clinical cases (6/8 cases, 75%). According to a 16S rDNA-based study in Taiwan, R. mucosa was the most prevalent strain among various Roseomonas species [8]. Central lines appear to be common infectious sites for Roseomonas bacteremia in children, as has been described in adult cases [7–9,16]. A recent investigation found that opportunistic infections due to R. mucosa are associated with skin microbiota rather than the environment [2]. Considering these findings, Roseomonas bacteremia may occur as a result of the direct invasion of the pathogen through a catheter penetration site, particularly when the patient’s neutrophil immunity has decreased. All of the pediatric patients were reported to be recovered from the infection, suggesting a preferable prognosis for cases of Roseomonas bacteremia.

The choice of treatment for Roseomonas species is difficult as there is no standard laboratory method at present, and drug susceptibility varies between species. Of note, the majority of previously reported isolates were not susceptible to third- or fourth-generation cephalosporins [12], as was the case in the patient described here. Among the Roseomonas species, R. mucosa, the most frequent isolate in clinical settings, exhibits the highest antimicrobial resistance [8,12]. The result of whole-genome sequencing for a clinical isolate of R. mucosa in a previous study indicated that the organism possesses innate antimicrobial-resistant characteristics [19]. However, Roseomonas species usually show in vitro susceptibility to other antimicrobial classes, such as carbapenems, aminoglycosides, and fluoroquinolones, and the clinical outcome with these antimicrobials has been reported to be satisfactory in adult cases [8].

| Table 1 |
| --- |
| **Antimicrobial susceptibility testing of the pathogen after 48-h incubation in ambient air at 35 °C** |
| | MIC (µg/mL) | Susceptibility |
| Piperacillin | >64 | R |
| Ceftazidime | >16 | R |
| Cefepime | 16 | 1 |
| Imipenem | ≤1 | S |
| Meropenem | ≤1 | S |
| Aztreonam | >16 | R |
| Gentamicin | ≤2 | S |
| Tobramycin | ≤2 | S |
| Amikacin | ≤5 | S |
| Minocycline | ≤2 | S |
| Ciprofloxacin | 0.5 | S |
| Levofloxacin | ≤0.5 | S |
| Trimethoprim/sulfamethoxazole | ≤2 | S |

MIC, minimum inhibitory concentration. Antimicrobial susceptibility was interpreted on the basis of Clinical & Laboratory Standards Institute Guideline (M100-S27, other non-Enterobacteriaceae).

Fig. 1. Gram staining of blood culture fluid (A) and pink-pigmented colonies on a chocolate agar plate (B). A, stained following centrifugation. B, incubated in 5% CO2 at 35 °C for 2 days.
Table 2
Summary of Roseomonas species bacteremia in pediatric cases.

| No | Age | Sex | Underlying diseases | Neutropenia at the onset | Species | Infectious sites | Treatment | Prognosis | year | Ref |
|----|-----|-----|---------------------|-------------------------|---------|----------------|-----------|-----------|------|-----|
| 1  | 1m | n. | Premature d. | n.d. | R. gilardii | n.d. | n.d. | n.d. | 1996 | 9 |
| 2  | 2m | n. | none d. | n.d. | Roseomonas (not identified) | n.d. | n.d. | Transient Colonization | 1996 | 9 |
| 3  | 6y | F | Cystic fibrosis | n.d. | Roseomonas (not identified) | n.d. | n.d. | Transient Colonization | 1996 | 9 |
| 4  | 15y | F | ALL | <100 /μL | Roseomonas (not identified) | n.d. | GM, CAZ | "Response was positive" | 1996 | 9 |
| 5  | 2y | M | ALL | No | R. gilardii | CVC | AMK, CAZ | Recover | 2001 | 15 |
| 6  | 11m | M | ALL | No | R. gilardii | CVC | GM, CAZ | Recover | 2006 | 16 |
| 7  | 18y | M | TPN dependence | n.d. | R. mucosa | CVC | CPFX | Recover | 2010 | 14 |
| 8  | 8m | M | Tethered cord syndrome with dermal tract | No | R. mucosa | Soft tissue infection | CTX | Recover | 2012 | 8 |
| 9  | 1y | F | none | No | Roseomonas genomospecies 5 | Primary bacteremia | ABPC/SBT | Recover | 2012 | 8 |
| 10 | 3y | F | Pompe disease | No | R. mucosa | Primary bacteremia | ABPC/SBT | Recover | 2012 | 8 |
| 11 | 3y | n. | ALL | 385 /μL | R. mucosa | Probably CVC | IPM, AMK | Recover | 2014 | 17 |
| 12 | 17y | M | AML | | R. mucosa | Probably CVC | carbenapen | Recover | 2016 | 18 |
| 13 | 9y | M | Cerebellar medulloblastoma | 40 /μL | R. mucosa | Probably CVC | MEM | Recover | 2017 | Present case |

ABPC/SBT, ampicillin/sulbactam; ALL, acute lymphoblastic leukemia; AMK, amikacin; AML, acute myeloid leukemia; CAZ, ceftazidime; CPFX, ciprofloxacine; CTX, cefotaxime; CVC, central venous catheter; GM, gentamicin; IPM, imipenem; MEM, meropenem; NB, neuroblastoma. n.d., not described; TPN, total parenteral nutrition.

Roseomonas organisms form characteristic pink-pigmented colonies on agar plates [11], which show positive reactions to catalase and urease, and thus identification at the genus level is not such difficult. However, commercial microbiologic kits using a phenotypic approach may result in misidentification, and accurate bacterial identification of the organisms at the species level requires genetic techniques. As in previous cases [14,17,20], we identified the R. mucosa strain using ISS rDNA sequencing.

To conclude, we described a case of R. mucosa bacteremia in a Japanese boy with febrile neutropenia following chemotherapy for cerebellar medulloblastoma. A literature review revealed that a common clinical feature of bacteremia caused by Roseomonas in children is a healthcare-associated catheter-related infection in an immunocompromised child with an underlying disease, particularly a malignancy. Roseomonas species are comparatively resistant to various antimicrobials; however, good outcomes can be expected, even in pediatric cases.

Declarations of interest
None.

Consent
Written informed consent was obtained from the parents for publication. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Contribution
Writing, H. Hagiya and K. Kimura. Supervision, I. Nishi, H. Yoshida, and K. Tomono.

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