Bacteremia Due to Imipenem-resistant Roseomonas mucosa in a Child With Acute Lymphoblastic Leukemia

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Summary: Roseomonas are described as opportunistic pathogens rarely involved in human infections. Their identification requires molecular methods and their antimicrobial susceptibility pattern varies according to the species. We report the first case of bacteremia due to Roseomonas mucosa in a child with leukemia and reviewed pediatric cases of Roseomonas infection, for which undoubted strain identification was available. Favorable outcome was observed despite resistance to numerous β-lactams that may account for delayed effective treatment, suggesting the low virulence of Roseomonas in children. Here, the strain also displayed unusual resistance to imipenem, highlighting the possible acquisition of additional resistance by this pathogen.

Key Words: Roseomonas mucosa, imipenem resistance, bacteremia, children, leukemia

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The genus Roseomonas includes slow-growing nonfermentative gram-negative coccobacilli with pink-pigmented colonies, mostly isolated from environmental samples. Roseomonas are opportunistic pathogens that have rarely been reported in human infections, although an increasing number of cases has been documented in the last decade. Infections mainly consisted of primary or health care-associated bacteremia in immunocompromised adult patients with or without indwelling devices, whereas pediatric cases have been rarely reported. Molecular-based methods were the most accurate to identify the isolates and the antimicrobial susceptibility pattern was variable depending on the species, Roseomonas mucosa being the most resistant one.

Here, we report the first case of R. mucosa infection in a child with malignancy and the second imipenem-resistant R. mucosa isolate. A review of pediatric cases including molecular-based identification of the isolates is also presented.

CASE REPORT

A 3-year-old child on maintenance therapy for B-lineage acute lymphoblastic leukemia (ALL) was admitted for febrile aplasia 1 year after ALL diagnosis. The patient had a Broviac catheter for 1 year. Two episodes of febrile aplasia of unknown etiology occurred during hospital stay for intensification therapy in the past year, with a favorable evolution under treatment with piperacillin-tazobactam and amikacin with or without vancomycin. On admission, the patient showed a temperature of 38.5°C with a good general condition and clear rhinitis without other particularity. No evidence of inflammation was observed at the catheter insertion site. Laboratory investigation confirmed aplasia diagnosed 2 days before with a white blood cell of 2300/mm² and an absolute neutrophil count (ANC) of 385/mm³. Increasing C-reactive protein level was noted (from 11.3 mg/L on the day of hospitalization to 50 mg/L on day 2), whereas procalcitonine level remained within normal range (0.28 ng/mL). Urine and 7 BacT/Alert pediatric blood culture bottles drawn from the Broviac catheter line within a 72-hour period were collected for bacteriological analysis. Two of them were sampled before starting empirical treatment with piperacillin-tazobactam. Five vials were positive for a gram-negative coccobacillus after 2 to 3 days of incubation, and pink, mucoid colonies were observed after 2 to 3 days of subculture. Urines remained negative. In the meantime, the treatment was switched to imipenem and amikacin because of persistent fever despite 4 days of empirical treatment, and the catheter was removed yielding negative cultures. On day 7 of hospitalization, the patient became apyretic, the C-reactive protein level decreased to 28.4 mg/L, and white blood cell count was 7900/mm³. Urine and 7 BacT/Alert pediatric blood culture bottles drawn from the Broviac catheter line within a 72-hour period were collected for bacteriological analysis. Two of them were sampled before starting empirical treatment with piperacillin-tazobactam. Five vials were positive for a gram-negative coccobacillus after 2 to 3 days of incubation, and pink, mucoid colonies were observed after 2 to 3 days of subculture. Urines remained negative. In the meantime, the treatment was switched to imipenem and amikacin because of persistent fever despite 4 days of empirical treatment, and the catheter was removed yielding negative cultures. On day 7 of hospitalization, the patient became apyretic, the C-reactive protein level decreased to 28.4 mg/L, and white blood cell count was 7900/mm³. The patient was discharged home before availability of antimicrobial susceptibility testing results with an oral treatment with cefixime for 1 week. He had an uneventful follow-up.

Regarding microbiological investigations, 16S rRNA gene sequencing identified R. mucosa (100% sequence identity to R. mucosa, GenBank accession number EU934085), whereas phenotypic identification using API 20NE strips (bioMérieux, Marcy l’Étoile, France) misidentified the oxidase-positive isolates as Methylobacterium mesophilicum. Antimicrobial susceptibility testing performed according to standards for nonfermentative gram-negative bacilli revealed resistance to multiple antibiotics including piperacillin-tazobactam, heterogenous resistance to imipenem, and susceptibility to amikacin (Table 1). The hematology-oncology unit displayed a highly controlled environment with terminal filters producing bacteriologically controlled water at the points of use and was controlled semianually for microbial contamination of air, water, and surfaces. The routine sampling performed before and after the case did not reveal Roseomonas sp.

DISCUSSION

The genus Roseomonas includes strains successively designed as Gilardi pink-pigmented unnamed taxon and Centers for Disease Control pink coccoid group. This confusing designation probably accounted for the variable
TABLE 1. Clinical and Biological Review of the 7 Pediatric Cases of *Roseomonas* sp. Infection With Molecular-based Identification of the Isolates

<table>
<thead>
<tr>
<th>Patients</th>
<th>Underlying Condition or Background</th>
<th>Indwelling Device</th>
<th>Fever at <em>Roseomonas</em> Isolation</th>
<th>Antimicrobial Treatment</th>
<th>Clinical Outcome</th>
<th>Species</th>
<th>Positive Samples (Delay in Days)*</th>
<th>Biological Data</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (1 y/F)</td>
<td>Bacteremia</td>
<td>None</td>
<td>No</td>
<td>NA</td>
<td>SAM</td>
<td>Cured</td>
<td><em>Roseomonas</em> genospecies 5</td>
<td>Blood (NA)</td>
<td>ATM, CAZ, FEP, IPM, TIM, TZP, AMK, GEN, CIP, LVX, GEN, CIP, MIN</td>
</tr>
<tr>
<td>2 (16 y/F)</td>
<td>Arthritis</td>
<td>Knee surgery</td>
<td>No</td>
<td>NA</td>
<td>CRO, DOX</td>
<td>Cured</td>
<td><em>R. gilardii</em></td>
<td>Knee fluid aspiration (2 d)</td>
<td>1 of 2 blood cultures (4 d)</td>
</tr>
<tr>
<td>3 (18 y/M)</td>
<td>Central-line-related bacteremia</td>
<td>Chronic total nutrition dependence (colectomy)</td>
<td>Yes</td>
<td>CIP</td>
<td>Cured</td>
<td><em>R. mucosa</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 (8 m/M)</td>
<td>Soft tissue infection</td>
<td>Tethered cord with dermal tract</td>
<td>No</td>
<td>NA</td>
<td>CTX, VA</td>
<td>Cured</td>
<td><em>R. mucosa</em></td>
<td>Soft tissue (NA)</td>
<td></td>
</tr>
<tr>
<td>5 (3 y/F)</td>
<td>Bacteremia</td>
<td>Pompe disease</td>
<td>No</td>
<td>NA</td>
<td>SAM</td>
<td>Cured</td>
<td><em>R. mucosa</em></td>
<td>Blood (NA)</td>
<td></td>
</tr>
<tr>
<td>6 (19 y/M)</td>
<td>Recurrent peritonitis</td>
<td>HIV, chronic renal failure, peritoneal dialysis</td>
<td>Yes</td>
<td>CIP, GEN, VA</td>
<td>Cured</td>
<td><em>R. mucosa</em></td>
<td>3 peritoneal dialysate fluid samples (3-5 d)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 (3 y/M)</td>
<td>Bacteremia</td>
<td>ALL</td>
<td>Yes</td>
<td>CIP, then IMP, AMK</td>
<td>Cured</td>
<td><em>R. mucosa</em></td>
<td>5 of 7 blood cultures (2-3 d)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>*For blood cultures, the number of positive blood cultures out of the total number of blood cultures sampled is indicated where available.</sup>

<sup>†Peritoneal catheter was removed after *Roseomonas* infection resolution.</sup>

<sup>‡No evidence of inflammation of CVC insertion site, catheter was removed yielding negative cultures.</sup>

<sup>| CVC, central venous catheter; F, female; HIV, human immunodeficiency virus; M, male; NA, not available; *R. gilardii*, *Roseomonas gilardii; R. mucosa*, *Roseomonas mucosa.*</sup>

*Antimicrobial drugs (indicated by class, ie, β-lactams, aminoglycosides, fluoroquinolones, cyclines, and others, and then by alphabetical order of the abbreviation): β-lactams: AMC indicates amoxicillin-clavulanic acid; AMP, ampicillin; AMX, amoxicillin; ATM, aztreonam; CAZ, ceftazidime; CEF, cefalothin; CFM, cefotaxime; CFZ, cefazolin; CPD, cefpodoxime; CPO, cefpirome; CRO, ceftriaxone; CTX, cefotaxime; FEP, cephepine; FOX, cefoxitin; IPM, imipenem; MEM, meropenem; MOX, moxalactam; SAM; ampicillin-sulbactam; TIM, ticarcillin-clavulanic acid; TZP, piperacillin-tazobactam.

Aminoglycosides: AMK indicates amikacin; GEN, gentamicin; TOB, tobramycin.

Fluoroquinolones: CIP indicates ciprofloxacin; LVX, levofloxacin.

Cyclines: DOX indicates doxycycline; MIN, minocycline; TET, tetracycline.

Others: CHL indicates chloramphenicol; CST, colistin; FOF, fosfomycin; SXT, trimethoprim-sulfamethoxazole; VA, vancomycin.

*Existence of inflammation of CVC insertion site and removal or not of the catheter were not reported.

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number of *Roseomonas* reported from clinical samples, at least 300 cases by Nolan et al in 2005 and only 61 cases by Tsai et al in 2012. In addition, phenotypic methods were shown inaccurate for both *Roseomonas* genus identification, several studies reporting misidentification of *Roseomonas* notably as *Methylobacterium*, and species identification within the genus (see references and this study). The few studies characterizing collections of *Roseomonas* spp. identified by 16S rRNA gene sequencing revealed (i) that *R. mucosa* is the most prevalent species in clinical samples (61% to 90% of the strains), (ii) heterogeneity in antimicrobial susceptibility patterns, *R. mucosa* being the most resistant species.

In children, only few sporadic cases of *Roseomonas* isolation have been reported, some being incompletely documented or corresponding to transient colonization. In 2006, McLean et al reviewed 7 pediatric cases of catheter-related bacteremia involving *Roseomonas gilardii* (n = 3), *Roseomonas* sp. (n = 3), and *Roseomonas fauriae* (n = 1) identified by phenotypic methods. The case due to *R. fauriae* should not be considered anymore, as the species is now designed as *Azospirillum brasilense*. Thus, pediatric cases of *Roseomonas* infection including undoubted identification of the isolates remain rarely documented and a review of clinical and biological features of the 7 available cases is given in Table 1. *R. mucosa* and bacteremia were the most frequently identified species and infection (5 and 4 cases, respectively). Infection mostly occurred in immunocompetent patients. Two bacteremia occurred in patients with central venous catheter (CVC), and in 1 case the bacteremia was related to the catheter. Outcome was favorable in all cases reviewed here (Table 1) or reported by McLean et al whatever the antimicrobial treatment and the removal of the catheter, suggesting low virulence of *Roseomonas* in children. However, Boyd et al recently reported a case of recurrent peritonitis that induced scarring of the peritoneal cavity leading to peritoneal dialysis precluding.

In children with ALL, 3 cases of *Roseomonas* bacteremia have been previously reported and attributed to an unidentified species (n = 1) and to *R. gilardii* (n = 2). Common features were the fever upon *Roseomonas* isolation and the favorable outcome under treatment including an association of ceftriaxone (68% of the isolates) and trimethoprim-sulfamethoxazole (77%) but full susceptibility to aminoglycosides (amikacin, gentamicin) and fluoroquinolones (levofloxacin, ciprofloxacin), and usual susceptibility to ticarcillin-clavulanate (77%) and imipenem (95%). Here, the strain displayed resistance to piperacillin-tazobactam used for empirical treatment and heterogenous resistance to imipenem used as a second-line β-lactam in association with an aminoglycoside. Resistance to imipenem is a rare finding in *Roseomonas*, which has only been reported in 2 clinical isolates belonging to *R. gilardii* subsp. roseus and *R. mucosa*. In the present case, improvement was only observed when effective antimicrobial therapy with amikacin was started and the CVC removed, although we cannot evaluate the relative contribution of each measure to the clinical outcome.

In conclusion, *Roseomonas* are usually considered as pathogens with low virulence for humans and remain a rare finding in the pediatric population. Here, we reported the first clinically and microbiologically well-documented case of bacteremia due to *R. mucosa* in a child showing that *R. mucosa* can be responsible for persistent fever and bacteremia in children with leukemia unless catheter is removed and/or adequate antimicrobial therapy is started. Resistance to β-lactam agents administered in immunocompromised children with bacteremia may result in delayed effective treatment against *Roseomonas*. It supports the importance of including an aminoglycoside for the treatment of pediatric febrile neutropenia when clinical condition is not improved under β-lactam monotherapy and when gram-negative rods are found by Gram stain examination of blood cultures pending susceptibility testing results.

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**REFERENCES**


