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Roseomonas gilardii bacteremia in a patient with HbSβ0-thalassemia: clinical implications and literature review

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Abstract

Roseomonas gilardii is a gram-negative coccobacillus identified in immunocompromised pediatric patients. A 5-year-old male with a history of HbSβ^0 thalassemia status post-surgical splenectomy presented to the emergency department with fever. Blood cultures grew *R. gilardii* at 63 hours, but the patient had been discharged home at 48 hours. The patient was readmitted for repeat cultures and initiated on meropenem for 10 days as *Roseomonas spp*. are often resistant to third generation cephalosporins. *Roseomonas gilardii* is a rare cause of bacteremia in immunocompromised patients. Clinicians should consider *Roseomonas* in slow growing gram negative rod bacteremias, and consider meropenem as empiric coverage.

Keywords

Roseomonas gilardii; HbSβ^0 thalassemia; sickle cell disease; asplenia

BACKGROUND

Roseomonas gilardii is a gram-negative coccobacillus that is part of the *Roseomonas* genus. It was first identified in 1993 by Rihs et. al., and this classification was based off of DNA hybridization studies[1]. Only two of the 15 identified *Roseomonas* species have been found to be pathogenic in humans: *R. gilardii* and *R. mucosa*. These bacteria are slow growing in cultures, taking up to 7 days to identify [2]. Resistance patterns within this bacterial species is important in sickle cell populations as only 38% were susceptible to ceftriaxone and less than 5% were susceptible to ceftazidime or cefepime. In contrast, 100% of the reported

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cases were susceptible to amikacin, 99% to imipenem, two antibiotics that are not frontline therapies for managing febrile sickle cell patients.

CASE:

A 5-year-old African American male with a history of HbSβ^0-thalassemia status post-surgical splenectomy one year prior presented to the Children's of Alabama emergency department (ED) complaining of two days of dry cough and on day of fever to a maximum temperature of 38.1°C. He previously required a splenectomy secondary to multiple episodes of splenic sequestration, but he had no history of bacteremia. Other SCD complications included one episode of acute chest syndrome and 3 veno-occlusive crises. At the time of presentation to the ED, the patient's complete blood count (CBC) showed an elevated white blood cell (WBC) count of 43.85 (10^3/μL), a low hemoglobin/hematocrit (H/H) of 7.8 (g/dL) and 25.9 (%), and an elevated platelet count of 907 (10^3/μL). A chest radiograph was negative for any consolidation. Blood cultures were obtained, he received intravenous empiric ceftriaxone, and was admitted to hospital based on the leukocytosis per our institutional standard of care for febrile sickle cell patients[3]. The patient's fever resolved 12 hours into the admission and he remained hemodynamically stable throughout the hospitalization with no signs of sepsis. He was discharged home after 48 hours of negative blood cultures.

At hour 63 of monitoring his cultures, the aerobic bottle returned positive for growth of gram negative rods (GNRs). The patient's family was notified and he was brought back to the ED. He was afebrile on arrival to the ED and he had no new clinical symptoms. Repeat investigations showed a normal WBC (8.25 x 10^3/μL), stable anemia (Hemoglobin: 7.7 g/dL, hematocrit of 25.2 (%)), and a persistently elevated platelet count of 886 x 10^3/μL. A chest radiograph remained negative for any consolidation. Repeat blood culture was obtained and he was re-admitted to the hospital to await speciation from the initial sample. Ceftriaxone was administered with the addition of gentamicin for double coverage of GNRs. On the fifth day of growth for the first set of blood cultures, the speciation returned *Roseomonas gilardii*, with sensitivities listed in Table 1. In consultation with an infectious disease specialist, we changed the antibiotic management to a 10 day course of intravenous meropenem, as these microbes have high resistance patters to cephalosporins. The repeat blood cultures obtained on readmission remained negative for seven days..

DISCUSSION:

Roseomonas gilardii is a rare pathogen that has only been described in eight previous pediatric case reports (Table 2). This bacterium is thought to be an opportunistic infection in that it has only been cultured from children in immunocompromised states, mainly affecting patients with underlying malignancies. In specific context to pediatric patients, Kimura et al 2018 collected information on the clinical aspects from case reports *Roseomonas spp.* affecting children [4] This group found that the underlying diagnoses of those infected included prematurity, cystic fibrosis, various malignancies, and Pompe disease. Our patient represents the first reported case of *Roseomonas* bacteremia in a patient with Sickle Cell Disease (SCD). There is low morbidity associated with bacteremia from this pathogen, as

most patients who have been infected recovery quickly with antibiotics [5]. However, there are important clinical management issues in SCD that should be considered. First, *Roseomonas spp*. is often resistant to the traditional first line empiric antimicrobial coverages of third generation cephalosporins used in SCD [6]. Although this patient's fever defervesced while on ceftriaxone, the susceptibilities were consistent with previously published studies, which suggest that carbapenems are the antibiotic of choice for *Roseomonas g*. Therefore, clinicians caring for SCD patients with a slow growing GNR bacteremia should consider *Roseomonas* infection and initiate or switch to, carbapenems, rather than cephalosporins. Second, infection with this bacterium gives more credence to the idea that SCD is an immunocompromised state. Although the rate of overall mortality from infection in pediatric SCD patients has decreased with the introduction of prophylactic antibiotic use and vaccines against *Pneumococcus*, sepsis remains a major contributor to morbidity and all-cause mortality in this patient population [7], [8].

Our understanding of the immunocompromised state of patients with SCD is limited. Although autoinfarction of the spleen may play a major role in infection risk, more research needs to evaluate other mechanisms for immune dysregulation that place SCD patients at risk for opportunistic infections. Currently, the literature would suggest four aspects of immune dysfunction. First, the loss of splenic function affects specific IgM memory B-cells that help produce anti-polysaccharide antibodies that typically help with opsonizing encapsulated organisms. Thus, with fibrosis of the spleen from sickled red blood cells, there is loss of these memory B-cells and an increase in the likelihood of infections from encapsulated microbes [9]. Second, ischemia and reperfusion injuries of microvasculature leads to increased risk of infections in end-organ tissue, including the intestines, lungs, and bones. For example, infections from gut microbes may occur secondary to this repeated damage to the endothelial lining of the stomach and intestines[10]. Also, necrosis at the end of long bones can serve as a nidus for infection, increasing the likelihood of osteomyelitis, especially with gut microbes (i.e. *Salmonella spp*.) In addition, the hyperinflammatory state induced by ischemia and reperfusion injury may increase the receptors responsible for infections to enter the bloodstream [11].Acute chest syndrome is associated with sickling in the capillaries of the lungs, leading to fluid collection in the alveolar space which provides an environment that is conducive for infectious microbes to proliferate [12].Third, iron overload is thought to play a critical role as an iron-rich environment is considered beneficial for the proliferation of microbes, including protozoa, fungi, gram positive and gram negative bacteria [13]. Finally, there has been further research assessing the genetic makeup of immune effector cells. There are studies evaluating immune cell migration abnormalities secondary to adhesion protein dysfunction on chronically activated endothelial cells of the microvasculature along with defective phagocytosis, and dysregulation of inflammatory mediators [14].

CONCLUSION:

Roseomonas is a rare gram negative coccobacillus that causes bacteremia in immunocompromised patients. Our patient with HbSβ^0 thalassemia admitted for fever associated with this specific bacterium. This case highlights the importance of identification

of this pathogen as it is resistant to cephalosporins along with bringing to light that this patient population is immunocompromised.

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Abreviations:

CBC	complete blood count
WBC	white blood cell
ED	emergency department
SCD	sickle cell disease
GNR	gram negative rod
H/H	hemoglobin and hematocrit

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Table 1.

Susceptibility Profile

Antibiotic	MIC in μg/mL	Susceptibility
Amikacin	≤ 8	S
Aztreonam	4	S
Cefepime	8	S
Ceftazidime	> 16	R
Ciprofloxacin	≤ 0.5	S
Gentamycin	≤ 2	S
Imipenem	≤ 0.5	S
Levofloxacin	≤ 1	S
Meropenem	≤ 0.5	S
Piperacillin/tazobactam	> 128	R
Trimethoprim/sulfamethoxazole	≤ 2	S
Ticarcillin/clavulanic acid	≤ 8	S
Tobramycin	≤ 2	S

Abbreviations: MIC, minimal inhibitory concentration. Colonies were identified using Gram-Negative identification cars on Vitk2 XL system (BioMerieux, Marcy l'Etoile, France) S, sensitivity, R, resistant

Table 2.

Literature review of Roseomonas infections in the pediatric population.

Underlying Disease	Strain of Roseomonas	Time to ID	Resistance	Sensitivities	Treatment	Outcome	Prior Studies
ALL	Not identified	n.d.	n.d.	n.d.	V, CAZ, GEN	Full recovery	[2]
Prematurity	*R. gilardii*	n.d.	n.d.	n.d.	n.d.	n.d.	[2]
Cystic fibrosis	Not identified	n.d.	n.d.	n.d.	n.d.	Transient colonization	[2]
None	Not identified	n.d.	n.d.	n.d.	n.d.	Transient colonization	[2]
ALL	*R. gilardii*	48hr	CEF, PEN, CAZ	AMK, GEN, MER	CAZ, AMK	Full recovery	[15]
ALL	*R. gilardii*		TMP/SMX, AMP	GM, CAZ, PT, MER	GEN, CAZ	Full recovery	[16]
NB	*R. fauriae*	7 days	CAZ, AMP, PT	GM, AMK, CIP, TMP/SMX, MER	GM, MER	Full recovery	[16]
TPN depend	*R. mucosa*	5 days	CEF, CAZ, PT, TMX/SMX	AMK, CIP, GM, TOB, MER	CIP	Full recovery	[17]
Tethered Cord	*R. mucosa*	n.d.	n.d.	n.d.	V, CTX	Full recovery	[18]
Pompe disease	*R. mucosa*	n.d.	n.d.	n.d.	AMP-SB	Full recovery	[18]
None	*R.* geno 5	n.d.	n.d.	n.d.	AMP-SB	Full recovery	[18]
ALL	*R. mucosa*	72hr	AZT, CAZ, CTM, CEF, PT, TMP/SMX	AMK, GEN, TOB, LEVO, CIP, TET	MER, PT, AMK	Full recovery	[19]
AML	*R. mucosa*	n.d.	n.d.	n.d.	CAR	Full recovery	[20]
Meduollobastoma	*R. mucosa*	48hr	AZT, PT, CAZ, CEF	MER, AMK, GEN, CIP, LEVO, TMP/SMX, TOB	MER	Full recovery	[4]
Hemoglobin $S\beta^0$	*R. gilardii*	63hrs	CAZ, PT	MER, AMK, AZT, TMP/SMX, TOB, CEF, LEVO	MER	Full recovery	Current study

Abbreviations: n.d. Not Documented AMK amikacin, AMP ampicillin, AMP-SB ampicillin-sulbactam, AZT aztreonam, CAR carbepenem, CAZ ceftazidime, CEF cefepime, CIP ciprofloxacin, CTM cefotaxime, CTX ceftriaxone, GEN gentamicin, LEVO levofloxacin, MER meropenem, PEN penicillin, PT piperacillin-tazobactam, TET tetracycline, TMP/SMX trimethoprim/sulfamethoxazole, TOB tobramycin, V vancomycin, ALL acute lymphoblastic leukemia, AML acute myeloid leukemia, NB neuroblastoma