CASE REPORT

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# A Rare Agent in Blood: *Rothia kristinae*

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## ABSTRACT

*Rothia kristinae*, a Gram-positive coccus often regarded as a harmless commensal, is emerging as a potential pathogen, especially in immunocompromised patients. We hereby present a case involving *R. kristinae* bacteremia in a 66-year-old female patient with a history of multiple myeloma and end-stage renal disease following a hematopoietic stem cell transplant. Despite initial doubts about its clinical significance, repeated isolation from blood cultures prompted consideration of infection rather than colonization. This case highlights the importance of considering rare pathogens in immunocompromised hosts. Additional investigation is essential to gain a more comprehensive understanding of the clinical features and management of infections caused by *R. kristinae*.

**Keywords:** *Rothia kristinae*, sepsis, multiple myeloma, immunocompromised host

## INTRODUCTION

*Rothia kristinae* is a Gram-positive, non-motile facultative anaerobic coccus, a member of the *Micrococcaceae* family, first described in 1974 by Kloos and colleagues. Nomenclature revisited by Nouioui I. and colleagues in 2018, resulting in its reclassification as *Rothia* spp. (formerly classified as *Kocuria kristinae*) (1, 2). It distinguishes itself from other *Rothia* spp. by its positive catalase, negative oxidase, coagulase reactions, and facultative anaerobic nature (3, 4). This new Gram-positive coccus commonly colonizes in the skin, oropharynx, upper respiratory tract, and occasionally in the gastrointestinal flora and may cause critical infections (3). Despite its recognition as a typical commensal organism, its isolation in culture specimens is routinely dismissed as lacking clinical significance. However, in immunocompromised individuals, its detection through sequential cultures or via polymerase chain reaction (PCR) may warrant consideration as a pathogen. Although its primary clinical manifestations include respiratory tract infections, endocarditis, and bacteremia, the precise clinical import of *R. kristinae* remains an ongoing area of inquiry (4). Here, we present a case of *R. kristinae* bacteremia in an immunocompromised patient, diagnosed as catheter-related bacte-

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remia through multiple blood cultures, including those obtained from an intravascular device, without evidence of organ involvement.

## CASE

A sixty-six-year-old female patient with known diagnoses of IgG-kappa type multiple myeloma, hemodialysis-dependent end-stage renal disease (ESRD) following an episode of acute tubulointerstitial nephritis and primary hypothyroidism had presented with a four-week history of ongoing fever. The patient had received four cycles of chemotherapy (bortezomib, cyclophosphamide, and dexamethasone) along with involved-field radiotherapy for lumbar vertebra and hip, followed by autologous hematopoietic stem cell transplantation. The patient had been evaluated for ongoing persistent fever following bone marrow transplantation, especially after each hemodialysis session via the right internal jugular vein dialysis catheter. The patient received empirical antibiotic therapy with the diagnosis of febrile neutropenia, including the sequential addition of piperacillin-tazobactam, teicoplanin, and micafungin intravenously. Additional work-ups demonstrated histopathologically-proven tissue-invasive cytomegalovirus esophagitis for which she received ganciclovir therapy. A total of four sets of blood cultures from a central catheter and peripheral site were obtained from the first day to the fourth day of fever. Positive flagged blood culture vials were inoculated onto Colombia agar with 5% sheep blood (bioMérieux, France), chocolate agar with PolyViteX (bioMérieux, France), and McConkey's agar (bioMérieux, France) plates, which were then incubated overnight at 5% $CO_2$ atmosphere and ambient air at 37°C. Gram staining of the positive blood culture revealed the presence of Gram-positive cocci, which were mostly arranged in tetrads. Upon examination, colonies of a tiny, pale, non-hemolytic, smooth, and convex nature were observed on blood agar and chocolate agar, whereas no growth was observed on McConkey's agar. The colonies exhibited a similar Gram staining pattern to that observed in the blood culture. The organism was catalase positive, coagulase weakly positive, and non-motile. To identify the isolate, fresh bacterial colonies were examined twice using VITEK® MS MALDI-TOF MS (bioMérieux, France), and the mass spectra obtained were analyzed using the MYLA® software version 3.0 (bioMérieux, France). VITEK® MS system yielded an identification as "*Rothia kristinae*" with a 99.9% confidence score for each run. In consideration of the absence of a specific recommendation for antimicrobial susceptibility testing method and interpretation criteria for *Rothia* spp. in the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (5), it was planned to determine a minimal inhibitory concentration (MIC) value for the antimicrobial agents which are known to have Gram-positive antimicrobial effect (tetracycline, vancomycin, linezolid), based on the recommendations on '*EUCAST guidance on When there are no breakpoints in breakpoint tables? 2023-06-30*'. Since the active substance of the antimicrobial agents for testing was unavailable in the laboratory, MIC values were determined via the gradient diffusion method instead of the broth microdilution method, which is recognized as a reference method for determining MIC values. MIC values of the isolate were determined by the gradient diffusion method using commercially available gradient diffusion strips (ETEST® Vancomycin, ETEST® Linezolid, ETEST® Tetracycline; BioMérieux, France) following the manufacturer's instructions. MIC values were measured as 1 mg/mL for vancomycin, 1 mg/mL for linezolid, and ≤1 for tetracycline. The obtained MIC values were interpreted without categorizing, and were cautiously recommended as a possible choice of therapy, according to "*Antimicrobial agents relevant for the treatment of aerobic bacteria with guidance to exclude resistance in bacteria lacking breakpoints in standard EUCAST breakpoint tables*" on "*EUCAST guidance on When there are no breakpoints in breakpoint tables? 2023-06-30* (6).

Despite its recognition as a typical commensal organism, in immunocompromised individuals, its detection through sequential cultures or via polymerase chain reaction (PCR) may warrant consideration as a pathogen (7). This was also supported by the isolation of the same organism from the central tunneled catheter in two consecutive sets of blood cultures, and one in peripheral blood culture obtained during febrile episodes. Transthoracic echocardiography was performed on day three to exclude the possibility of infective endocarditis

and did not reveal any sign of vegetation or newly diagnosed valvular insufficiency. With the classification of the isolated organism as infectious, the central hemodialysis catheter was removed within 48 hours to reduce the risk of persistent infection and further complications. Neutrophile engraftment occurred on post-transplant day 10. The fourteen-day course of intravenous teicoplanin therapy, along with tunneled hemodialysis catheter removal, resulted in clinical and laboratory improvement. Informed consent of the patient was obtained.

## DISCUSSION

*R. kristinae* is a member of human flora that is rarely described as a pathogen, especially in immunocompromised patients, with a limited number of studies regarding the prevalence, prognosis, and clinical course. A systemic review study evaluating the global characteristics of *Rothia* spp. infections has identified *Rothia* spp. as a rare cause of infections in humans, especially affecting immunocompromised individuals, including hematological and solid organ malignancies, dialysis-dependent ESRD or patients with indwelling long-term devices. *R. kristinae* is the most common species identified among *Rothia* spp.; bacteremia (36.3%), infective endocarditis (13.7%), skin and soft tissue infections (18.6%), endophthalmitis (15.7%) and upper respiratory tract infections (5.9%) are the most common presentations (4). Similarly, we described an immunocompromised patient with a tunneled hemodialysis catheter presenting with *R. kristinae* bacteremia, who also had ESRD, hematological malignancies, and neutropenia. The knowledge of therapeutic algorithms for *Rothia* spp. infections is limited, as is the data on clinical features. A systematic review study including a total of 25 patients from 22 case reports and three case series has demonstrated high rates of susceptibility against vancomycin with only one case of vancomycin-resistance, teicoplanin, tigecycline, linezolid, and daptomycin with no reported case of resistance (8, 9). As the isolate obtained in our case showed susceptibility against glycopeptides, we completed a fourteen-day teicoplanin therapy course with clinical and laboratory improvement. Vancomycin therapy is avoided in HD patients to avoid ototoxicity and challenges in dose titration. Control blood cultures obtained on the fifth and sixth days showed no growth, suggesting a favorable clinical course.

*Rothia* spp. growth on sterile material may not always indicate an infectious state, though such rare pathogens should be evaluated with caution, especially in immunocompromised hosts. Our case is significant by demonstrating a rare case of *R. kristinae* bacteremia in an autologous hematopoietic stem cell transplant recipient responding to a course of glycopeptide therapy. Nonetheless, there is a clear need for future large-scale clinical studies to evaluate better and determine the clinical course, risk factors, and diagnostic and therapeutic algorithms.

**Ethical Approval:** N.A.

**Informed Consent:** Informed consent was obtained from the patient.

**Peer-review:** Externally peer-reviewed

**Author Contributions:** Concept – O.U., S.Ç.; Design – S.Ç.; Supervision – Ö.E.; Materials – O.U.; Data Collection and/or Processing – O.U., S.Ç.; Analysis and/or Interpretation – Ö.E., Y.B.; Literature Review – S.Ç., Y.B.; Writer – O.U., S.Ç., Y.B.; Critical Reviews – Ö.E.

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