



Case report

Native valve infective endocarditis due to *Micrococcus luteus* in a non-Hodgkin's lymphoma patientNicole M. Ianniello^{a,*}, Diana C. Andrade^{a,c,*}, Stipe Ivancic^b, Paula A. Eckardt^c, Juan C. Lemos Ramirez^c^a Memorial Hospital West, Department of Pharmacy, Pembroke Pines, FL, United States^b Memorial Hospital West, Department of Internal Medicine, Pembroke Pines, FL, United States^c Memorial Hospital West, Department of Infectious Disease, Pembroke Pines, FL, United States

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ABSTRACT

Micrococcus species are typically considered contaminants from skin and mucous membranes. However, especially in severely immunocompromised patients, a blood culture with *Micrococcus* could be the cause of a significant infection. We report a 65-year-old female with non-Hodgkin's lymphoma who developed native valve infective endocarditis due to *Micrococcus luteus*. There is no defined therapeutic regimen for infective endocarditis due to *Micrococcus luteus*; however, our patient was successfully treated for six weeks with vancomycin and rifampin. To our knowledge, there is only one other case report of native valve endocarditis due to *Micrococcus luteus*.

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Introduction

Infective endocarditis (IE) occurs due to bacteria causing vegetations on the heart valves or on the endocardial surface. The typical microorganisms associated with IE are viridans streptococci, *Streptococcus bovis*, *Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella* species, *Staphylococcus aureus*, and community-acquired enterococci [6]. Risk factors for IE include age over 60 years, male sex, injection drug use, poor dentition or dental infection, heart disease, prosthetic heart valve or an intravascular device.

Micrococcus species are gram-positive cocci that are part of the normal flora of the human skin and typically considered nonpathogenic [1]. Although, these microorganisms are known to be contaminants, a subset of particular species, specifically *Micrococcus luteus* have been reported to cause severe infections in immunocompromised populations. Those infections have included peritonitis, brain abscesses, pneumonia, and septic arthritis [1–5]. We present the second case of *Micrococcus luteus* native valve IE.

Case report

A 65-year-old Caucasian female with non-Hodgkin's lymphoma presented to the emergency department (ED) with a chief complaint of fever and productive cough with white phlegm. Her past medical history is significant for hypertension, atrial fibrillation, and chronic obstructive pulmonary disease. She denied any hemoptysis, chest pain, shortness of breath, nausea, vomiting, dysuria, or changes in bowel habits. The patient did note that she took one tablet of acetaminophen prior to admission without relief of symptoms. The preceding week, she had undergone her second cycle of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) for Grade 3b follicular lymphoma in the outpatient setting. She reported feeling well prior to receiving chemotherapy and had no fevers during her first cycle of chemotherapy. Her surgical history was insignificant, other than port placement, and she reported no recent dental procedures. The patient's home medications included, acyclovir 400 mg twice daily, fluconazole 200 mg once daily, bisoprolol 10 mg once daily, levothyroxine 112 mcg once daily, and ondansetron 8 mg every 8 h as needed for nausea.

Upon physical examination, the patient had a fever of 101.4 °F (38.8 °C), mild tachycardia of 108 beats/minute, respiratory rate of 20 breaths/minute and blood pressure of 126/66 mmHg. She appeared cachectic, alert and oriented to person, time and place. Chest auscultation was noted to have clear air entry. The patient had a port-a-cath in place with no signs of infection. Cardiac exam revealed normal S1 and S2 with a grade 3 systolic murmur. There

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were no signs of peripheral stigmata of endocarditis. Neurological exam was otherwise unremarkable.

Laboratory studies showed a serum creatinine of 0.60 mg/dL, white blood cell count of 5,000/uL, platelets of 60,000/uL, and an absolute neutrophil count of 800/uL. Chest X-ray showed no infiltrates or pleural effusions. A respiratory pathogen panel resulted negative for all respiratory viruses, as well as *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. Due to the presentation of neutropenic fever, blood and urine cultures were collected and cefepime 2 g intravenous every 8 h was started.

On the second day of admission, blood culture resulted with gram positive cocci in clusters in 1 of 2 bottles. Infectious Disease was consulted and vancomycin 750 mg every 12 h was started. On day three, the blood cultures were identified as *Micrococcus luteus*. Susceptibilities were not reported by the microbiology lab after *Micrococcus* identification, as this is considered a commensal organism. Upon the request of the infectious disease physician, sensitivities were reported (Table 1). Repeat blood cultures and an echocardiogram were then ordered. Transthoracic echocardiography (TTE) showed moderate aortic valve regurgitation and vegetation present in the non-coronary cusp. The patient met one major (echocardiogram positive for IE) and two minor (fever and positive blood culture of a microorganism that does not typically cause endocarditis) Duke Criteria, confirming the diagnosis of native valve IE [6]. Cefepime was discontinued. Vancomycin 750 mg IV every 12 h was continued, amikacin 15 mg/kg IV every 24 h and rifampin 300 mg by mouth twice daily were added for a 6 week duration of treatment. Although the port-a-cath had no signs of infection, it was removed and replaced due to the predilection with *Micrococcus* species in the formation of biofilms with prosthetic material. Cardiology was consulted to assess valve functionality and agreed with infectious disease recommendations for medical management. A vancomycin trough was drawn 30 min prior to the fourth dose, on day 4, and was 9.4 mcg/mL, which was not in the desired range of 15–20 mcg/mL. Vancomycin was re-dosed at 500 mg IV every 8 h. A random level of amikacin was drawn 11 h from the start of the infusion and resulted as 1.6 mcg/mL, which was in the desired dosing interval parameters per the Hartford nomogram. Amikacin was discontinued after two doses due to increased risk of renal impairment.

Six days following primary admission, the patient was discharged on vancomycin 750 mg IV every 8 h and rifampin 300 mg by mouth twice daily. Prior to discharge, a subsequent vancomycin level resulted as 14.9 mcg/mL. Drug interactions due to rifampin were also monitored during the treatment course. Infectious disease considered the patient to be stable to receive her next cycle of chemotherapy of R-CHOP. The patient successfully finished her endocarditis treatment regimen after 6 weeks of antimicrobial therapy. A repeat TTE was scheduled a week after completion of antimicrobials which showed stable aortic valve vegetation.

Discussion

The majority of patients infected with IE present with fever, with or without cardiac abnormalities. Since there is such

Table 1
Susceptibility Testing for Final *Micrococcus luteus* Isolate.

Antibiotic	MIC, ug/mL	Interpretive Result
Penicillin	0.125 ug/mL	No interpretation
Vancomycin	0.250 ug/mL	Sensitive

Note: Isolates were tested and verified based on Clinical and Laboratory Standards Institute (CLSI) Performance Standards for Antimicrobial Susceptibility Testing guidelines [10]. MIC, minimum inhibitory concentration.

variability in clinical presentation of IE, early diagnosis is critical. The Duke Criteria is the gold standard for diagnosis of IE based on the American Heart Association (AHA) and Infectious Diseases Society of America (IDSA) guidelines for IE [6]. The guidelines recommend that blood cultures be drawn and an echocardiogram be performed immediately if there is a suspicion of IE. Empiric treatment is based on the suspected microorganism, native or prosthetic valve infection, and susceptibility patterns. Treatment involves monotherapy or combination of intravenous antimicrobials for a duration of up to 6 weeks.

Although *Micrococcus* species are not typically associated with chronic infections, our patient was immunosuppressed due to active chemotherapy treatments. A potential source of infection from the port-a-cath was excluded due to negative cultures. It is possible that the *Micrococcus luteus*, which is considered normal oral flora, translocated into the blood during the neutropenic episode and seeded the valve. *Micrococcus* species are not mentioned to be a typical microorganism associated with IE according to AHA and IDSA guidelines [6]. Thus, there is no guidance on the treatment of IE due to *Micrococcus luteus*.

To the best of our knowledge, there is only one other documented case of native valve endocarditis due to *Micrococcus luteus* to date [7]. Other infective endocarditis cases are documented due to *Micrococcus*, but of prosthetic valve infections. *Micrococcus* species have the ability to form biofilms with prosthetic material, which is why most cases of endocarditis are with prosthetic valves [8]. There is no defined therapeutic regimen for infective endocarditis due to *Micrococcus luteus*; however, based on previous reported cases and antimicrobial susceptibilities to *Micrococcus* species, the treatment of choice is vancomycin and rifampin [9]. This regimen was selected based on the treatment of choice for prosthetic valve endocarditis due to coagulase-negative staphylococci. Rifampin has shown to be the most active against *Micrococcus* species to avoid relapse of the infection, supported by in vitro susceptibility data [9]. The patient did successfully complete therapy for IE with vancomycin and rifampin with no evidence of embolic events, persistent bacteremia, or progressive valve destruction.

This case is significant to note that patients that are severely immunocompromised are susceptible to life threatening infections from microorganisms that are normally considered harmless or contaminants. Clinicians should be aware for early recognition for treatment of a true infection caused by these microorganisms that could be crucial for this patient population. This case represents the challenge of managing IE in those who are immunosuppressed, as these infections can be dangerously undiagnosed. Although this patient was successfully treated with vancomycin and rifampin, further objective evidence is needed for the optimal treatment of IE caused by *Micrococcus luteus*.

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Declaration of Competing Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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