Case Report

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Meropenem resistant *Lactobacillus* endocarditis in an immunocompetent patient

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Abstract

Lactobacilli are gram-positive bacteria usually found in the normal flora and are commonly used as probiotic treatments for vaginal candidiasis. *Lactobacilli* are normally considered non-pathogenic; however, certain risk factors can make a patient susceptible to severe infections. This case describes an immunocompetent 61-year-old female with an automated intracardiac defibrillator who presented with a 10-day history of nausea and vomiting. Furthermore, diagnostic tests, including a transesophageal echocardiography, revealed a large vegetation, and blood cultures were consistently positive for *Lactobacillus*. The patient was treated with intravenous penicillin and gentamicin, along with removal of the automated intracardiac defibrillator. In patients with significant underlying conditions, physicians should consider *Lactobacillus* as a causative organism to avoid delays in treatment.

Keywords

Lactobacillus endocarditis, probiotic, endocarditis

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Introduction

Lactobacilli are facultative, anaerobic, and non-spore-forming gram-positive rods that ferment to yield lactic acid.[1] They are part of the normal flora of the oropharynx, gastrointestinal, and genitourinary tracts. *Lactobacillus* strains are commonly sold in supplements and probiotics for a theoretical effect on the stimulation of the immune system and for their ability to prevent colonization of pathogenic organisms in the colon and genitourinary tracts.[2,3] Most of the time, *Lactobacillus* is considered a commensal organism that has limited clinical significance. Risk factors such as diabetes mellitus, implantable heart devices, structural heart disease, and immunosuppression can make a patient susceptible to severe infections.[2,4]

Endocarditis associated with *Lactobacillus* is rare, responsible for less than 0.05% of all endocarditis cases, and is associated with a 30% mortality rate.[5,6] *Lactobacillus* endocarditis is usually associated with immunodeficiency and severe comorbidities.[7] Identifying *Lactobacillus* species and its sensitivity profile is crucial to provide the most effective therapeutic treatment regimen for favorable patient outcomes. However, identifying the species and sensitivity profile can be difficult. In practice, *Lactobacillus* species isolated from blood cultures are not further characterized due to their perceived low virulence.[3]

Here, we describe a case of *Lactobacillus* endocarditis in a patient with no immunodeficiencies and who reported taking a *Lactobacillus* probiotic. The sensitivity profile revealed that the *Lactobacillus* was resistant to meropenem. Given the rising prevalence of diabetes mellitus and the increased use of probiotics, it is expected that there will be a rise in infections due to *Lactobacillus* species. This case emphasizes the importance of early identification and prompt treatment of *Lactobacillus* endocarditis.

Case

A 61-year-old Caucasian immunocompetent female with a past medical history of uncontrolled diabetes mellitus, nonischemic cardiomyopathy (left ventricular ejection fraction 20%–25%), ventricular tachycardia, and ventricular fibrillation status post biventricular automated intracardiac defibrillator (AICD) presented to our hospital with nausea and emesis. She was recently admitted to an outside facility and

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blood cultures from that admission were significant for *Lactobacillus*. Her examination was significant for systolic murmur and extensive bilateral redness around the upper thigh. The rest of the physical examination was within normal limits.

Laboratory data on arrival were significant for a white blood cell count of 20.57 k/μL, total bilirubin of 2.3 mg/dL, alkaline phosphatase of 177 U/L, and lactic acid of 2.20 mmol/L. The patient was afebrile on admission and throughout her hospital stay. A computed tomography (CT) scan of the abdomen showed pericholecystic fluid, but a hepatobiliary iminodiacetic acid scan did not show biliary obstruction. She was initially started on ciprofloxacin 400 mg intravenously (IV) twice daily and metronidazole IV 500 mg every 8 h. Over the next 24 h, she became hypotensive, tachycardic, and tachypneic. Three sets of blood cultures grew *Lactobacillus*, and final speciation showed *Lactobacillus casei, Lactobacillus paracasei, and Lactobacillus zeae*. Ciprofloxacin and metronidazole were discontinued, and meropenem 1 g IV every 8 h was initiated before susceptibility reports were released. Blood cultures were repeated after 2 days and remained positive for *Lactobacillus*. A transesophageal echocardiography (TEE), shown in Figure 1, was performed, revealing 2 × 3 cm vegetations on the tricuspid valve and the right atrial lead, as shown in Figure 2.

The patient was transferred to a tertiary care facility for a cardiothoracic surgery evaluation. As she was considered high risk for open surgical intervention, she underwent catheter-based large-bore aspiration thrombectomy and AICD removal. The removed material was sent for a bacterial culture test, and the presence of *Lactobacilli* was confirmed. Antibiotics were changed to ampicillin 2 g IV every 4 h and gentamicin 80 mg IV daily which she was discharged home on. The patient completed 6 weeks of antibiotic therapy with multiple negative blood cultures, and repeat echocardiogram did not show any vegetations.

Minimal inhibitory concentrations (MICs) were determined by use of the agar microdilution method. The cutoffs used for penicillin susceptibility were as follows: less than or equal to 8 μg/mL was considered susceptible and greater than 8 μg/mL was considered resistant. The cutoffs used for meropenem susceptibility were as follows: less than 1 μg/mL was considered susceptible and greater than 2 μg/mL was considered resistant. Susceptibilities of the *Lactobacilli* isolated from the blood cultures and removed material from AICD were listed as penicillin MIC 1 μg/mL (susceptible) and meropenem MIC 4 μg/mL (resistant).

Discussion

Infective endocarditis should be suspected in patients with fever and certain risk factors, with or without bacteremia. Cardiac risk factors include history of infective endocarditis, the presence of a prosthetic valve or cardiac device, or history of valvular or congenital heart disease. Noncardiac risk

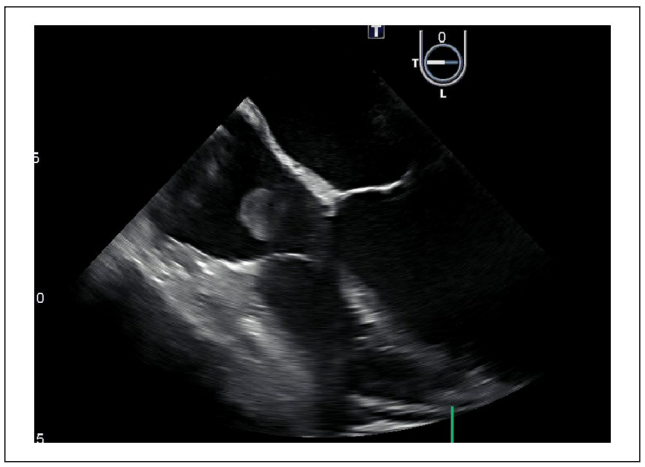

Figure 1. The transesophageal echocardiography showed a 2 × 3 cm vegetation on the anterior leaflet of the tricuspid valve.

factors include intravenous drug use, immunosuppression, or recent surgery. The modified Duke criteria include both major and minor criteria and are used as a guide for diagnosing endocarditis. Diagnosis must be made promptly to ensure the initiation of appropriate empiric antibiotic regimens and identify high-risk patients who may benefit from early surgical intervention. The selection of empiric antibiotic regimens is based on patient factors, prior antimicrobial exposures, and epidemiology. Duration of therapy is to begin on the first day on which blood cultures are negative.[8]

Lactobacilli are part of the normal commensals of the oropharynx, gastrointestinal tract, and the female genital tract.[1] These areas are the most common portals of entry for a *Lactobacillus* bacteremia. *Lactobacilli* have low virulence and rarely cause infection in immunocompetent patients.[9] When *Lactobacilli* grow in a culture, they are usually regarded as contaminants and antibiotic therapy is withheld. Infections with *Lactobacilli* are uncommon and poorly defined. *Lactobacilli* are estimated to cause only 0.05% of all infective endocarditis cases.[10] Careful analysis of the patient's signs, symptoms, and laboratory workup is essential for diagnosis of a clinical infection. In most cases, *Lactobacillus* bacteremia was associated with clear signs of clinical illness, including fever, elevated leukocyte counts, and elevated C-reactive protein values.[10]

Infection with *Lactobacillus* can be a complication in patients who are already chronically ill and debilitated. Risk factors for *Lactobacillus* bacteremia include immunosuppression and underlying comorbidities, including cancer, recent abdominal surgery, implantable heart devices, and diabetes mellitus. Prior prolonged antibiotic therapy ineffective for *Lactobacilli* has also been identified as a risk factor.[11] When *Lactobacillus* bacteremia is identified, it serves as an indicator of serious underlying illness and poor long-term prognosis. Case reports that result in patient death following *Lactobacillus* bacteremia are usually found to be from other

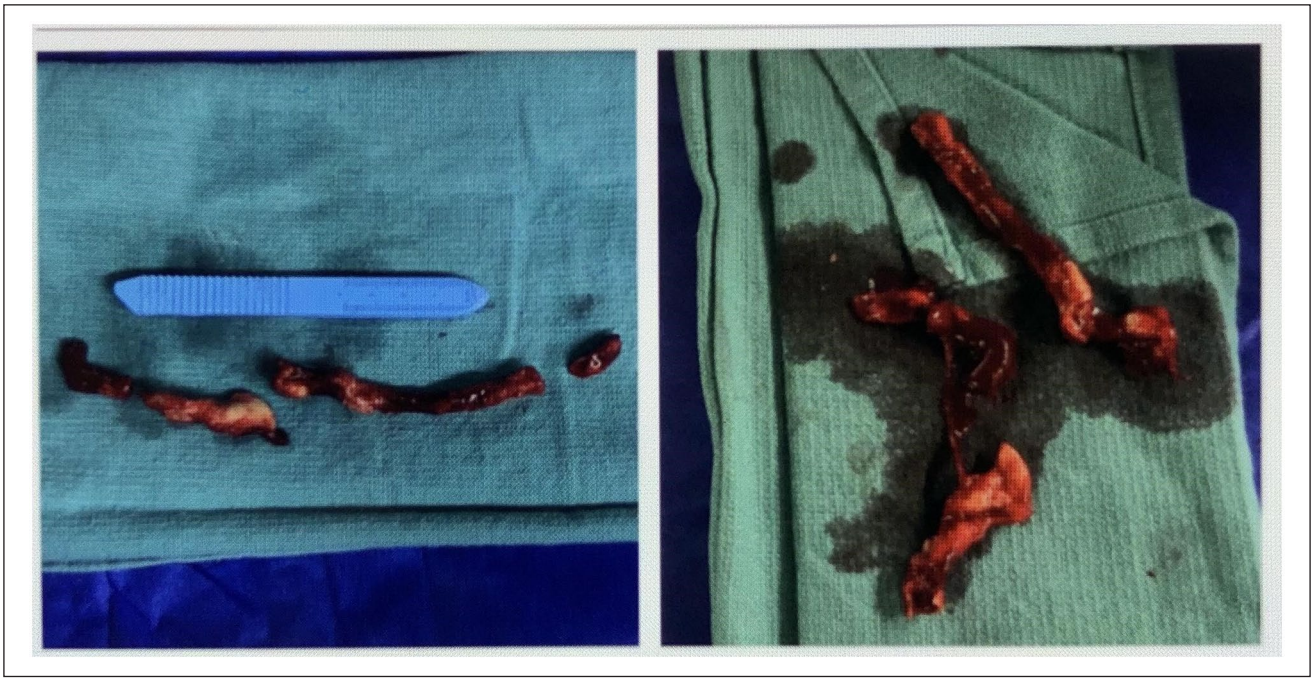

Figure 2. Post-surgical vegetations.

underlying conditions and not the infection itself.[4] Our patient has a past medical history of uncontrolled diabetes mellitus and an AICD, but does not have any other immunosuppressive-related comorbidities that would put her at risk for *Lactobacillus* bacteremia.

Lactobacillus bacteremia may be polymicrobial. Polymicrobial isolates were identified in between 39% and 60% of cases of *Lactobacillus* bacteremia. Concomitant bloodstream isolates usually include streptococci, Candida species, and/or enteric gram-negative bacilli.[4] In our patient, *Lactobacillus* was the only organism isolated from the total of five positive blood cultures.

In a review of 45 cases of *Lactobacillus* bacteremia, 44% of patients died during hospitalization, and mortality 1 year following the bacteremia was 60%.[4] This emphasizes the importance of prompt recognition, organism isolation, and treatment for *Lactobacillus* bacteremia. An immunocompetent patient is described in a published case study of a bioprosthetic aortic valve *Lactobacillus* endocarditis, presenting with severe aortic regurgitation, which responded to conventional medical and surgical treatment.[12] This may suggest *Lactobacilli* could target intracardiac devices more than native valves.

Molecular studies suggest that *Lactobacillus* species may facilitate the breakdown of glycoproteins and the synthesis and lysis of fibrin clots, which may aid in the colonization of a valve and survival of bacteria.[13] Antibiotic susceptibility of *Lactobacilli* is variable. In a retrospective study of 200 cases of *Lactobacillus* infections, the most commonly used regimens included penicillin monotherapy (n=35), penicillin therapy combined with aminoglycoside (n=20), and cephalosporins in monotherapy (n=16).[14] *Lactobacillus* is typically susceptible to β-lactam antibiotics, yet resistant strains have been reported.[9] Clindamycin and penicillin are the most active agents in vitro, and vancomycin resistance is common, dependent on the strain of *Lactobacillus*.[4] Previous data demonstrate generally low MICs to imipenem, piperacillin-tazobactam, erythromycin, and clindamycin.[15] Although no prospective trials have been conducted, combination therapy with a penicillin and an aminoglycoside has been successful in treatment for *Lactobacillus* bacteremia and is the recommended regimen for this type of infection.[16]

Conclusion

This case report demonstrates the need to use caution and clinical judgment in patients who have positive blood cultures for *Lactobacillus* and risk factors such as implantable heart devices, especially with the rising incidence of diabetes mellitus and overall use of probiotics. Our patient, who reports taking probiotics, had a positive culture with *Lactobacillus* at an outside facility which was left untreated. The patient required multiple surgical interventions and a prolonged antibiotic course as a result. We believe that more data are required to guide assessment and treatment in patients with infective endocarditis secondary to *Lactobacillus*.

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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