



Case report

Lactobacillus endocarditis in a healthy patient with probiotic use

Swetha Pasala^{a,*}, Lillian Singer^b, Tamooore Arshad^a, Kenneth Roach^a^a Department of Medicine, Inova Fairfax Hospital, 3300 Gallows Road, Falls Church, VA, 20042, USA^b VCU School of Medicine Inova Campus, 3300 Gallows Road, Falls Church, VA, 20042, USA

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ABSTRACT

Lactobacilli are commensal anaerobic gram-positive rod organisms that are normal flora of the oral, genitourinary, and gastrointestinal tracts. *Lactobacillus rhamnosus* is now commonly found in probiotics. They are rarely pathogenic, but occasional cases of bacteremia and associated endocarditis have been noted in patients with pre-disposing factors. We describe a case of Lactobacillus endocarditis in an otherwise healthy patient with probiotic use and gingival laceration and present an accompanying discussion of the potential association of probiotic formulations containing lactobacilli and systemic infection.

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Introduction

Lactobacilli are commensal anaerobic or facultative anaerobic gram-positive rod organisms that are normal flora of the oral, genitourinary, and gastrointestinal tracts. They account for less than 1 % of recovered organisms from blood cultures overall. Lactobacilli are rarely pathogenic, but have been reported to cause dental caries, infective endocarditis, meningitis, splenic abscesses, endometritis, and chorioamnionitis [1].

Case report

A 50-year-old Caucasian male presented to an outside hospital for 6 months of worsening fatigue, night sweats, and 23-pound weight loss. The patient did not have regular primary care and had not been evaluated by a physician in over ten years. He also had a background history of iron deficiency anemia and an unspecified “benign” heart murmur. The patient was otherwise in good health. He was a fitness enthusiast and exercised regularly, denied use of intravenous drugs, alcohol, or tobacco, and was not sexually active. He was not on any prescription medications but regularly took a probiotic supplement and had done so for the past ten years. He did not have any tattoos or body piercings but admits to not getting regular dental care. Although patient denied any dental issues, he did note that he had a gingival cut that bled profusely for 4 days, 3 months prior to admission, for which he did not seek medical care.

At the outside hospital, patient was afebrile with stable vitals, but an examination revealed signs of an unspecified murmur prompting evaluation initially with transthoracic and subsequently a transesophageal echocardiogram. This revealed a 2.2 cm × 1.9 cm mitral valve vegetation and severe mitral regurgitation. Subsequent abdominal CT showed a splenic infarct of the lateral margin. Labs revealed a normocytic anemia, with hemoglobin of 8 g/dL, and normal white blood cell count. Further evaluation with colonoscopy showed melanosis coli, but no evidence of active bleeding, masses, or diverticuli. Blood cultures were obtained as part of the endocarditis evaluation and transferred to our tertiary care hospital for further cardiac surgery evaluation.

At our hospital, the patient was afebrile and hemodynamically stable. Physical exam featured a grade III/VI holosystolic murmur at the cardiac apex, but no other notable findings. Laboratory evaluation showed a CRP of 4.9 mg/dL, and ESR of 91 mm/hr, and again, normal white blood cell count. New blood cultures were drawn. The patient was then started on daily IV ceftriaxone and vancomycin, with the addition of IV gentamicin for coverage of enterococcal species. Cultures from outside hospital indicated growth of gram-positive bacilli in anaerobic and aerobic BACTEC blood culture bottles after 48 h of incubation, initially thought to be suggestive of an atypical enterococcal strain. Vancomycin resistance was noted with 5 microgram vancomycin disc. *Lactobacillus rhamnosus* was identified with MALDI-TOF mass spectrometry and the isolate was determined to be sensitive to penicillin with MIC of 1 per Epsilometer test. Based on these results, patient was continued on gentamicin with the addition of ampicillin. Ceftriaxone and vancomycin were discontinued. Repeat blood cultures obtained after 5 days of therapy showed no bacterial growth.

* Corresponding author at: Department of Internal Medicine, Inova Fairfax Hospital, 3300 Gallows Road, Falls Church, VA, 22042, USA.

E-mail address: swetha.pasala@inova.org (S. Pasala).

Our patient was subsequently found to have *L. rhamnosus* bacteremia, mitral aortic valve infective endocarditis (IE), and splenic infarction thought to be caused by septic emboli. Per the Modified Duke's Criteria for IE, patient met both major criteria: multiple blood cultures positive for endocarditis and signs of endocardial involvement. The latter was evidenced by echocardiographic findings of a vegetative mitral valve lesion, a destructive aortic valve lesion, and a new mitral valve insufficiency.

On hospital day 8, given his severe mitral regurgitation, he had a mitral valve replacement using a bioprosthetic valve. During the procedure, the anterior leaflet of his aortic valve was found to have a 3 mm perforation likely due to concomitant aortic valve endocarditis. The aortic valve was also replaced during this procedure with a bioprosthetic valve. Microbiology cultures of the mitral valve vegetation showed growth of gram positive bacilli under gram stain which did not grow under aerobic conditions, as patient had been receiving antimicrobial regimen. Repeat blood cultures shortly before the time of discharge showed no growth at 4 days. The patient recovered well and was discharged home on hospital day 14 with a peripherally inserted central catheter in place to continue antimicrobial treatment outpatient for a total duration of 6 weeks days of dual treatment with ampicillin and gentamicin. Patient was seen in our outpatient clinic and completed his antimicrobial regimen without complications. He had just started cardiac rehabilitation and was doing well.

Discussion

Lactobacilli are estimated to cause 0.05 to 0.4% of all infectious endocarditis cases [2], but appear to be more prevalent in the setting of structural heart disease, invasive procedures, and dental infection/procedures [3]. Per molecular studies, lactobacillus species could enable the breakdown of human glycoproteins and the synthesis and lysis of human fibrin clots, which may aid in the colonization of a valve and survival of bacteria [4].

Aside from an established history of iron deficiency anemia, prior to this episode of fatigue the patient had been fairly healthy. The patient did not have any high risk practices predisposing him to this infection. The patient had what was thought to be a benign flow murmur, which raises the question of underlying undiagnosed structural heart disease though the patient did not exhibit any signs of valvular heart previously. In most case patients, *L. rhamnosus* bacteremia have been reported to feature fever, leukocytosis, and elevated CRP. Our patient only exhibited a mild elevation of CRP.

The patient did endorse a ten-year daily intake of a commercially-available probiotic formulation (containing "25 billion probiota per serving" including two forms of *L. rhamnosus*, totaling 5 billion CFU per company) [8]. There has been an increasing trend of probiotic use containing lactobacillus species for the prevention of *Clostridioides difficile* infection (CDI) and general health, as in the case of our patient. Ultimately, the patient's strain was confirmed to be *L. rhamnosus* per MALDI TOF spectrometry, which was cited in the formulation of his probiotic. A previous literature search of endocarditis associated with probiotic use showed that all cases were linked to various species of lactobacillus [9]. Strains of *L. rhamnosus* isolated in patients with endocarditis are indistinguishable from strains isolated from probiotics per pulsed-field gel electrophoresis [10], suggesting that probiotic strains of *L. rhamnosus* may give rise to bacteremia and endocarditis.

Many strains of Lactobacillus including *L. rhamnosus* are resistant to vancomycin, with some reports of resistance to ciprofloxacin, tetracycline, meropenem, metronidazole, and sulfonamides and intermediate resistance to linezolid [5]. Previous time-kill assays have demonstrated that synergistic therapy with penicillin and an

aminoglycoside was shown to be effective clinically and provided optimal medical treatment [6]. In cases of infective endocarditis, in addition to medical therapy, valvular surgery is indicated if there is significant valvular regurgitation or destruction [7].

While probiotics are often discouraged for patients with underlying structural heart disease and immunocompromised patients, it is rare for an otherwise healthy patient to develop infection. About three months prior to this current admission, our patient noted a deep gingival cut that went untreated and bled for many days. Given recent history of gingival laceration and continued daily probiotic consumption, there is a question of possible dental infection leading to bacteremia or probiotic access to the bloodstream. Furthermore, since *L. rhamnosus* is also a commensal gastrointestinal bacterium, the possibility of translocation was considered. Though cases of *Lactobacillus* bacteremia have been previously shown to be associated with upper endoscopy and colonoscopy [11,12] our patient had not undergone either prior to presentation. After admission, he did undergo both procedures as part of initial anemia workup, though both were unrevealing.

The etiology of our patient's *L. rhamnosus* bacteremia is not clear. Given his significant bacteremia and infective endocarditis in the setting of probiotic use, we are led to conclude that presence of lactobacillus in a blood culture should not always be considered a contaminant, as is often assumed. A careful history, clinical status, sources of infection, and possible relationship to diet, trauma, surgical history, and probiotic use should be elicited. When determined to be true bacteremia, it should be treated promptly and aggressively. Moreover, this case highlights the need to thoroughly evaluate for any evidence of structural heart disease, dental infections, and outpatient follow-up before starting a patient on probiotics.

Disclosures

None.

CRediT authorship contribution statement

Swetha Pasala: Conceptualization, Methodology, Writing - original draft, Writing - review & editing. **Lillian Singer:** Writing - original draft. **Tamoore Arshad:** Supervision, Writing - review & editing, Validation. **Kenneth Roach:** Supervision, Writing - review & editing.

Declaration of Competing Interest

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