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BRIEF REPORT

Lactobacillus rhamnosus Endocarditis After Upper Endoscopy

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Lactobacillus rhamnosus is commonly found in gastrointestinal flora and used in probiotics but is a rare human pathogen. We report a case of *L. rhamnosus* endocarditis following upper endoscopy in a frequent consumer of yogurt containing the organism, who required aortic and mitral valve replacement for cure.

Keywords. *Lactobacillus*; *Lactobacillus rhamnosus*; endocarditis; endoscopy; yogurt.

Lactobacillus species are facultatively anaerobic, Gram-positive rods that are part of the normal human gastrointestinal and genitourinary flora [1]. They are used in the production of fermented foods and found in numerous probiotics [2]. *Lactobacillus* spp. are rare human pathogens but have been implicated in a variety of infections, including bacteremia and endocarditis, with *Lactobacillus casei* and *Lactobacillus rhamnosus* among the most frequently isolated species [3, 4]. Immunosuppression, structural heart disease, recent dental work, and other invasive procedures have been associated with *Lactobacillus* endocarditis [3, 5, 6].

Both upper endoscopy and colonoscopy have been associated with the development of transient bacteremia with gastrointestinal flora, including *Lactobacillus* [2, 7]. Despite this potential risk, reports of endocarditis following upper endoscopy are rare [8]. Although cases of *Lactobacillus* endocarditis have been described following colonoscopy [9, 10], to our knowledge there are no prior cases of *Lactobacillus* endocarditis following upper endoscopy reported in the literature.

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CASE PRESENTATION

An 80-year-old male presented with 1 month of malaise and dyspnea on exertion. He had a past medical history of paroxysmal atrial fibrillation on warfarin and mitral regurgitation of unknown severity from which he had never been symptomatic. Approximately 1 week before the onset of symptoms, the patient underwent an upper endoscopy to investigate chronic anemia that revealed mild gastritis and duodenitis on biopsy. Several days after his endoscopy, he developed increasing fatigue and worsening dyspnea on exertion. Two weeks after the procedure, he noted swelling and erythema of his right ankle and was seen in the emergency department of another institution where he was diagnosed with cellulitis and treated with 10 days of oral trimethoprim-sulfamethoxazole. The erythema resolved, but his malaise and dyspnea persisted. One week later, he was seen by his primary physician, who noted bilateral lower extremity edema and started furosemide. His symptoms failed to improve, his exercise tolerance declined to less than half a block, and a cough productive of white phlegm developed. He remained afebrile.

The patient presented to a cardiologist for evaluation after 2 more weeks of symptoms. A transthoracic echocardiogram revealed a large (1.4 × 0.7 cm) mobile echodensity on the ventricular side of the aortic valve with moderate aortic insufficiency, a large (1.0 × 0.6 cm) mobile echodensity on the atrial side of the anterior mitral valve leaflet, and a small echodensity on the posterior leaflet with moderate to severe mitral regurgitation (Figure 1). He was admitted for suspected subacute infective endocarditis.

On admission, the patient was afebrile with temperature of 36.8°C, blood pressure of 92/64 mm Hg, pulse of 73 beats per minute, and pulse oximetry of 89% on room air. The cardiac examination revealed a regular rate and rhythm with a grade 2 of 6 holosystolic murmur and a grade 2 of 4 early diastolic murmur loudest at the right upper sternal border. Lung examination revealed bibasilar crackles. There was 1+ pitting lower extremity edema bilaterally with no erythema and no peripheral stigmata of endocarditis. Laboratory results demonstrated a hemoglobin of 9.0 g/dL and a white blood cell count of 12 000 per microliter. A chest x-ray showed interstitial thickening suggestive of edema and small bilateral pleural effusions with adjacent hazy bibasilar opacities. Four sets of peripheral blood cultures were obtained before the initiation of empiric vancomycin and oxacillin.

After 48 hours, all 4 sets of blood cultures were growing small, Gram-positive rods. Records from the prior emergency department visit 3 weeks before admission revealed a positive blood culture for a *Lactobacillus* species that had been presumed a contaminant. Antibiotics were then changed to ampicillin.

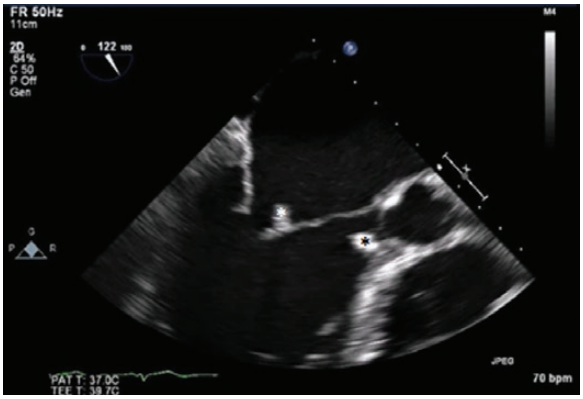

Figure 1. Transesophageal echocardiogram image depicting vegetation on mitral valve (white asterisk) and aortic valve (black asterisk).

The positive blood cultures from admission were identified as *Lactobacillus rhamnosus* by 16S rRNA amplification and sequencing. Minimum inhibitory concentrations were obtained by E-test. The isolate was found to be sensitive to ampicillin, penicillin G, gentamicin, erythromycin, and clindamycin and resistant to vancomycin. Blood cultures remained negative after the initiation of ampicillin. A computerized tomography scan of the chest revealed a lingular consolidation consistent with pneumonia and bilateral pleural effusions, but a scan of the abdomen and pelvis was unremarkable. The patient was also started on levofloxacin after a nasopharyngeal respiratory pathogen polymerase chain reaction was positive for *Mycoplasma pneumoniae*. On further history, the patient denied any recent dental work or procedures other than his recent endoscopy. He had an inpatient dental evaluation that was unrevealing. He denied taking probiotic supplements but did report regularly eating a yogurt brand labeled as containing *Lactobacillus bulgaricus*, *Lactobacillus acidophilus*, and *L. casei*.

The patient underwent mitral and aortic valve replacements on hospital day 9. Intraoperative findings included a large vegetation on the right coronary cusp of the aortic valve with a destroyed left leaflet and a large vegetation on the anterior mitral leaflet. Histopathologic examination of the excised valves showed acute and organizing endocarditis with necrosis and vegetation. A Gram stain showed clusters of Gram-positive bacilli. His aortic valve tissue culture remained negative, but the mitral valve culture grew *L. rhamnosus*. Following the positive culture, intravenous gentamicin was added to ampicillin at a low dose for synergy. Blood cultures remained negative after surgery. The patient had an uneventful postoperative course until discharge. Ampicillin was switched to penicillin G on discharge, and he completed a total of 2 weeks of gentamicin and remained on intravenous penicillin G until 8 weeks after surgery. He also completed a 10-day course of levofloxacin for pneumonia. A repeat transthoracic echocardiogram showed aortic and mitral valve bioprostheses without evidence of vegetations. Two sets of repeat blood cultures after completion of antibiotics were negative.

A sample of the patient's regular brand of yogurt was cultured, and *Lactobacillus paracasei* and *L. rhamnosus* were isolated and identified by 16S rRNA amplification and sequencing (1200 base pairs). The valve and yogurt *L. rhamnosus* strains were both 99.6% identical to the type strain with a single base-pair difference between the two. The yogurt and blood *L. rhamnosus* isolates had identical bands on pulsed-field gel electrophoresis, but a 2-band difference was seen when compared with the valve isolate. The *L. paracasei* isolate was not included in the gel.

DISCUSSION

Lactobacillus species are a rare cause of infective endocarditis, comprising <0.5% of cases [4, 11, 12]. Despite their low virulence, certain species of the genus can adhere to endovascular surfaces and cause infection [1]. Manipulation of the gastrointestinal mucosa during upper endoscopy has been linked to transient *Lactobacillus* bacteremia [7] and rare reports of infective endocarditis with other more common pathogens, most frequently Streptococci [8]. This patient's underlying valve disease may have further increased his risk for endocarditis following instrumentation.

Many *Lactobacillus* spp. are sensitive to ampicillin and penicillin and resistant to vancomycin, but empiric therapy decisions can be complicated by variability in antibiotic susceptibilities between species and isolates [13]. Cases of endocarditis described in the literature are most frequently treated with a combination of a penicillin and an aminoglycoside; decisions regarding therapy should be tailored to susceptibilities of the isolate [3]. In the case described, the degree of valvular dysfunction and vegetation size were indications for surgery. Twenty percent to 39% of cases of *Lactobacillus* endocarditis described in the literature have required valve replacement [3, 5, 14]. Historically, the mortality associated with *Lactobacillus* endocarditis was reported as high as 27% [14], but more recent reviews of the literature have described 100% survival [5]. This increase has been attributed to publication bias, but advances in microbiologic diagnostic techniques may also identify positive blood cultures earlier, allowing for more targeted antibiotic therapy.

Lactobacillus spp. isolated from blood cultures are often not further characterized due to their perceived low virulence. Depending on available laboratory resources, species identification can be challenging, and incorrect genus identifications have been described [4, 15]. Cannon et al [3] found *L. casei* to be the most commonly reported species to cause endocarditis, but given the difficulty distinguishing it from *L. rhamnosus* phenotypically or by 16S rRNA sequencing, newer diagnostic technologies may alter the described distribution of *Lactobacillus* infections [16].

As the use of *L. rhamnosus*–containing probiotics and dairy products has increased, questions about the safety of these agents have arisen. There have been multiple cases of *Lactobacillus* bacteremia and endocarditis reported in probiotic users and individuals with high dairy intake [6, 10]. Our patient did report frequent consumption of a brand of yogurt found to contain *L. rhamnosus*, which could have been misidentified as *L. casei* on commercial labeling [16]. Based on our pulsed-field gel electrophoresis analysis, although the pathogenic organism may be related to the strain found in the yogurt, we cannot conclusively link the organism causing infection to his diet. This potential relationship remains difficult to prove given the frequent presence of this species as part of normal human flora. Molecular methods have been used to investigate probiotics as potential sources of *Lactobacillus* bacteremia, but prior reports have failed to demonstrate a clear association [17, 18]. Larger population studies in Finland also failed to show an increase in *Lactobacillus* spp. bacteremia rates despite increasing consumption of probiotic and dairy products containing the organism [2].

In conclusion, we describe a case of *L. rhamnosus* endocarditis following upper endoscopy. Although it remains a rare pathogen, the detection of *Lactobacillus* bacteremia should always prompt further investigation of its source and to ensure clearance because it remains a potential cause of severe infection, including endocarditis.

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References

1. Aguirre M, Collins MD. Lactic acid bacteria and human clinical infection. J Appl Bacteriol. **1993**;75:95–107.
2. Salminen MK, Rautelin H, Tynkkynen S, et al. *Lactobacillus* bacteremia, clinical significance, and patient outcome, with special focus on probiotic *L. rhamnosus* GG. Clin Infect Dis. **2004**;38:62–9.
3. Cannon JP, Lee TA, Bolanos JT, Danziger LH. Pathogenic relevance of *Lactobacillus*: a retrospective review of over 200 cases. Eur J Clin Microbiol Infect Dis. **2005**;24:31–40.
4. Gouriet F, Million M, Henri M, et al. *Lactobacillus rhamnosus* bacteremia: an emerging clinical entity. Eur J Clin Microbiol Infect Dis. **2012**;31:2469–80.
5. Salvana EM, Frank M. *Lactobacillus* endocarditis: case report and review of cases reported since 1992. J Infect. **2006**;53:e5–e10.
6. Kato K, Funabashi N, Takaoka H, et al. *Lactobacillus paracasei* endocarditis in a consumer of probiotics with advanced and severe bicuspid aortic valve stenosis complicated with diffuse left ventricular mid-layer fibrosis. Int J Cardiol. **2016**;224:157–61.
7. Baltch AL, Buhac I, Agrawal A, et al. Bacteremia after upper gastrointestinal endoscopy. Arch Intern Med. **1977**;137:594–7.
8. Breuer GS, Yinnon AM, Halevy J. Infective endocarditis associated with upper endoscopy: case report and review. J Infect. **1998**;36:342–4.
9. Avlami A, Kordossis T, Vrizidis N, Sipsas NV. *Lactobacillus rhamnosus* endocarditis complicating colonoscopy. J Infect. **2001**;42:283–5.
10. Franko B, Vaillant M, Recule C, et al. *Lactobacillus paracasei* endocarditis in a consumer of probiotics. Med Mal Infect. **2013**;43:171–3.
11. Encarnacion CO, Loranger AM, Bharatkumar AG, Almassi GI. Bacterial endocarditis caused by *Lactobacillus acidophilus*. Tex Heart Inst J. **2016**;43:161–4.
12. Patnaik S, Davila CD, Chennupati A, Rubin A. Endocarditis of the native aortic valve caused by *Lactobacillus jensenii*. BMJ Case Rep. **2015**; doi:10.1136/bcr-2014-206288.
13. Salminen MK, Rautelin H, Tynkkynen S, et al. *Lactobacillus* bacteremia, species identification, and antimicrobial susceptibility of 85 blood isolates. Clin Infect Dis. **2006**;42:e35–44.
14. Griffiths JK, Daly JS, Dodge RA. Two cases of endocarditis due to *Lactobacillus* species: antimicrobial susceptibility, review, and discussion of therapy. Clin Infect Dis. **1992**;15:250–5.
15. Tommasi C, Equitani F, Masala M, et al. Diagnostic difficulties of *Lactobacillus* casei bacteraemia in immunocompetent patients: a case report. J Med Case Rep. **2008**;2:315.
16. Martinez RM, Hulten KG, Bui U, Clarridge JE 3rd. Molecular analysis and clinical significance of *Lactobacillus* spp. recovered from clinical specimens presumptively associated with disease. J Clin Microbiol. **2014**;52:30–6.
17. Presterl E, Kneifel W, Mayer HK, et al. Endocarditis by *Lactobacillus rhamnosus* due to yogurt ingestion? Scand J Infect Dis. **2001**;33:710–4.
18. Aroutcheva A, Auclair J, Frappier M, et al. Importance of molecular methods to determine whether a probiotic is the source of *Lactobacillus* bacteremia. Probiotics Antimicrob Proteins. **2016**;8:31–40.