

# A Double Whammy: *Lactobacillus acidophilus* Bacteremia and Subsequent *Lactobacillus rhamnosus* Prosthetic Valve Infective Endocarditis in an Elderly Diabetic Patient

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## ABSTRACT

The clinical significance of the relatively avirulent organism, *Lactobacillus*, has been debated in the past. At times misdiagnosed as a contaminant, *Lactobacillus* has uncommonly been reported to cause intra-abdominal abscesses, peritonitis, meningitis, bacteremia, pneumonia and endocarditis, especially in the population of patients with underlying comorbid conditions including malignancy, diabetes, recent surgery or organ transplantation. We report a case of a 74-year-old male with *Lactobacillus* bacteremia leading to prosthetic valve infective endocarditis complicated by an aortic root abscess. He was managed with IV antibiotic therapy, ultimately penicillin G, and aortic valve replacement, and completely recovered after a period of rehabilitation. Several factors that predispose to *Lactobacillus* bacteremia were identified in our patient. This case further supports the proposition that *Lactobacillus* is not always a contaminant; when pathogenic, underlying disease conditions should be investigated.

**KEYWORDS:** *Lactobacillus*, Prosthetic Valve endocarditis, Bacteremia

## INTRODUCTION

*Lactobacilli* are facultative anaerobic gram-positive rods and part of the normal flora of the oral, gastrointestinal and genitourinary tracts.<sup>1</sup> There has been controversy regarding the pathogenic potential of *Lactobacilli*.<sup>2,3</sup> While some studies have suggested that the risk of infection due to *Lactobacillus* is extremely rare, leading it to be regarded as a contaminant when identified in human isolates,<sup>4</sup> other case reports have indicated *Lactobacillus* as the causative organism in intra-abdominal abscesses, peritonitis, dental caries, urinary tract infections, chorioamnionitis, endometritis, liver abscess, splenic abscess, septic arthritis, meningitis, bacteremia, pneumonia and endocarditis.<sup>1,2,5,6</sup> It is estimated that *Lactobacillus* represents 0.05–0.4% of cases of infective endocarditis and bacteremia.<sup>6</sup> We report an instance where *Lactobacillus* proved to be more than just an incidental finding.

## CASE PRESENTATION

A 74-year-old male with a history of diabetes mellitus, multi-vessel coronary artery disease status post-coronary artery bypass graft and bio-prosthetic aortic valve replacement (AVR) for severe aortic stenosis a year prior to current presentation, presented to the emergency department (ED) with an acute onset of confusion and disorientation. Notably, his most recent admission was three months prior for acute encephalopathy. During that admission, he was initially treated with IV vancomycin 1250mg every 12 hours, IV ceftriaxone 2g every 12 hours, IV ampicillin 2g every 4 hours and IV acyclovir due to concern for possible meningoencephalitis, with subsequent de-escalation to IV ampicillin 2g every 4 hours to complete the treatment course, when his blood cultures isolated *Lactobacillus acidophilus* in 4 of 4 bottles.

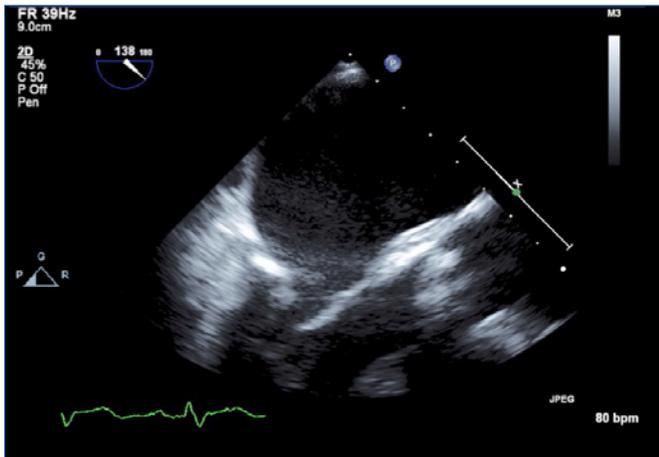
Workup for septic foci during that admission including computed tomography (CT) head, transthoracic echocardiogram (TTE), transesophageal echocardiogram (TEE), and computed tomography angiogram (CTA) of the head was negative, with CSF analysis showing evidence of lymphocytic pleocytosis and CSF cultures isolating no organisms. He was discharged and made a full clinical recovery.

During the present admission, he denied a history of probiotic use. His diabetes was well controlled with oral medications. His physical exam was notable for fever (38.6°C). His heart rate was 84 beats per minute, BP 115/88 mmHg, respiratory rate 16 cycles/minute, oxygen saturation 94% on ambient air. Dentition was fair. He had a grade 3/6 ejection systolic murmur heard best at the right upper sternal border. His lungs were clear to auscultation, mental status had returned to baseline at the time of evaluation in the ED, and he had no motor or sensory neurological deficits. He did not have stigmata of endocarditis or skin rash.

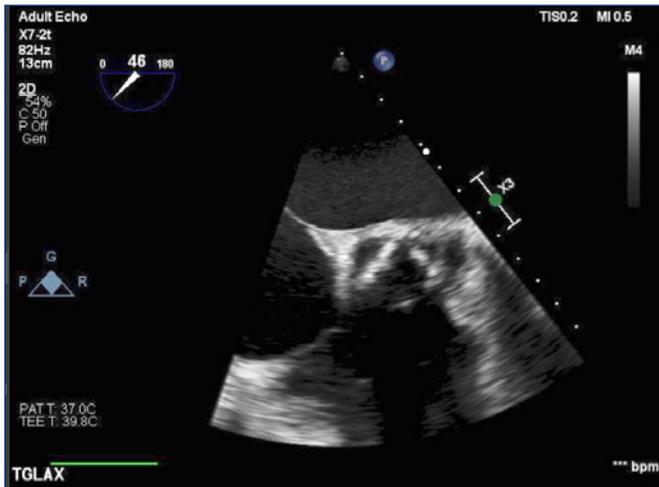
Initial laboratory investigations showed leukocytosis 20,300 cells/ $\mu$ L. CT Head, lumbar puncture, urinalysis, chest x-ray showed no abnormal findings. Lactate was 0.8 mmol/L, renal and liver function tests were within normal limits.

TTE on admission showed a thickened aortic valve leaflet, ejection fraction (EF) 40-45% which was reduced compared to a prior study two months earlier. Blood cultures isolated gram-positive coccobacilli; patient was started empirically on ampicillin-sulbactam 1.5g every 6 hours and vancomycin 1500 mg every 12 hours after blood cultures were drawn. He

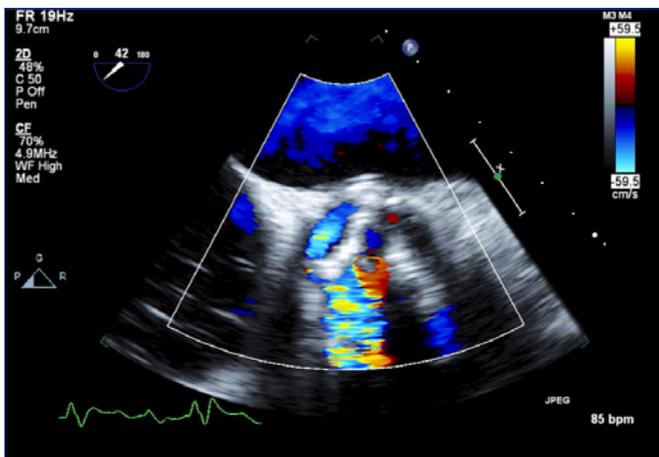
**Figure 1.** Demonstration of aortic valve vegetation on early transthoracic echocardiogram



**Figure 2.** Short axis view of the aortic valve on transesophageal echo showing aortic cusp root abscess



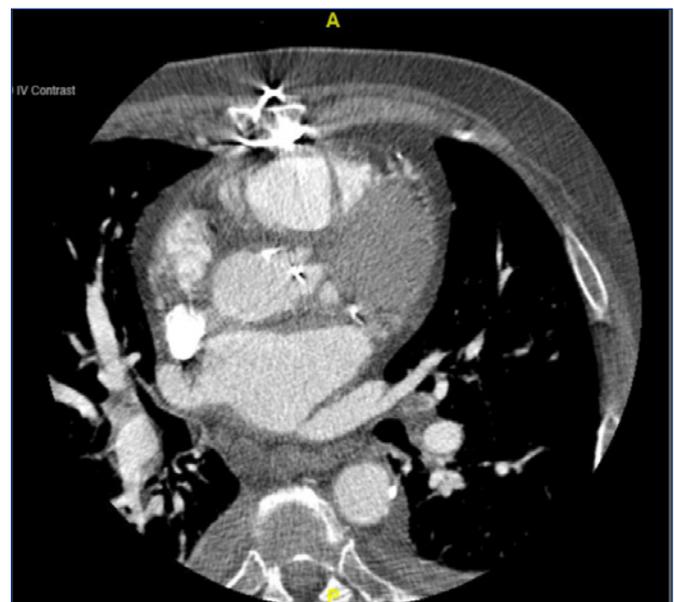
**Figure 3.** Short axis view of the aortic valve on transesophageal echo showing a regurgitant jet around the aortic valve suggestive of aortic valve dehiscence



developed Mobitz type 2 second degree AV block on day 5 of admission, requiring transvenous pacing. TEE on hospital day 7 showed an EF 30–35%, severe aortic valve leaflet thickening, a vegetation on the aortic bioprosthetic leaflet (Figure 1) and an aortic cusp root abscess (Figure 2). A regurgitant jet was noted around the aortic valve suggestive of valve dehiscence (Figure 3). A CT coronary angiogram also suggested the presence of an aortic root abscess (Figure 4). Gentamicin was added to vancomycin, but had to be discontinued a few days after initiating therapy due to concern for drug-induced liver injury (DILI).

Blood cultures subsequently revealed *Lactobacillus rhamnosus* in 4 of 4 bottles. The patient’s antibiotics were de-escalated to ampicillin-sulbactam based on susceptibilities showing susceptibility to penicillin. Patient thereafter underwent a redo AVR with patch closure of aortic root abscess. The intra-operative specimen of this patient’s prosthetic valve vegetation isolated *Lactobacillus rhamnosus*, also sensitive to penicillin. Workup for infection foci and underlying conditions included dental imaging (showing periodontal disease but no focal abscesses), CT chest, abdomen and pelvis with contrast (negative for occult abscess), abdominal ultrasound (showing no cholelithiasis or nephrolithiasis), colonoscopy (no pathology), and esophagogastroduodenoscopy (EGD) which showed white plaques concerning for esophageal candidiasis. The patient was treated with fluconazole 100 mg once daily for 2 weeks with good results. He cleared his blood cultures on hospital day 14 on IV ampicillin-sulbactam, and was discharged to a skilled nursing facility on post-operative day 17 in stable condition, afebrile with resolved leukocytosis and improved mentation.

**Figure 4.** Coronary CTA showing aortic pseudo-aneurysms consistent with aortic root abscess



He subsequently finished a 6-week course of IV penicillin G 18 million units per day, selected per sensitivities from intraoperative cultures; repeat blood cultures in one month were negative. He was thereafter seen in follow-up at the Infectious Diseases clinic after a prolonged period of rehabilitation and was noted to be in satisfactory health.

## DISCUSSION

*Lactobacillus* species are normal flora of the mouth, gastrointestinal tract, and female genital tract, where they produce lactic acid and competitively inhibit more typically pathogenic organisms.<sup>7</sup>

A review of the epidemiology of the few pathogenic cases reported in the literature reveals a higher incidence in the elderly population, with a mean age of greater than 60 years,<sup>1</sup> most likely related to its association with immunosuppression and several comorbidities such as malignancies or serious gastrointestinal disorders like hepatic cirrhosis and chronic pancreatitis,<sup>6</sup> chronic renal failure, pulmonary fibrosis, colon cancer, chronic obstructive lung disease, diabetes mellitus,<sup>1</sup> and the well documented high prevalence of lactobacilli as intestinal microflora in this population.<sup>8</sup>

Lactobacilli aggregate platelets, bind both fibronectin and fibrinogen, and adhere to collagen types I and V, which compose the extracellular matrix of endothelial cells and have been shown to be present at sites of endothelial damage.<sup>5</sup> This represents a potential mechanism for endocarditis and valve disease associated with this bacteria.

Lactobacillus bacteremia is considered an important marker of an underlying serious or fatal disease and poor long-term prognosis for hospitalized patients.<sup>3</sup> This evidence reiterates findings of Husni et al in 1999, in their study which reviewed 45 cases of *Lactobacillus* bacteremia and endocarditis over a 15-year period at Cleveland Clinic: 48% were in the intensive care unit at the time of onset of *Lactobacillus* bacteremia, 40% had an underlying malignancy. Also, 38% had recently undergone surgery, 27% had diabetes mellitus, 22% were receiving corticosteroids, and 14% were receiving other immunosuppressive therapy, 7% had valvular heart disease.<sup>1</sup> Similar findings were also reproduced in the study by Salminen et al in 2004, who found that 82% of cases reviewed had an association with fatal or severe co-morbidities.<sup>6</sup>

*Lactobacillus* endocarditis is typically associated with pre-existing structural heart disease, recent dental infection or manipulation.<sup>9</sup> Some reports implicate recent upper endoscopy, colonoscopy and otological procedures as the only cause for *Lactobacillus* bacteremia, plausibly due to a breach in the mucosal barriers.<sup>10-12</sup> The incidence of bacteremia following TEE was reported to be 1.4% in a prospective study by Mentec et al;<sup>13</sup> however, the American Heart Association considers this a low-risk procedure in the absence of infection and does not recommend routine antibiotic prophylaxis (class III).<sup>14</sup>

In the case of our patient, predisposing factors for

*Lactobacillus* bacteremia or endocarditis included: a history of cardiac surgery, recent endoscopy (TEE), presence of a prosthetic valve and history of diabetes mellitus. Workup for underlying disease conditions was only significant for esophageal candidiasis revealed on EGD. Colonoscopy and CT abdomen and pelvis showed no evidence of underlying malignancy or abscess respectively. On the basis of his EGD findings, bacterial translocation from the gastrointestinal tract was considered the most likely mechanism of infection.

In a review by Cannon et al. analyzing the characteristics of over 200 cases of pathogenic *Lactobacillus* infections associated with bacteremia, endocarditis, and localized infection, the species *L. casei* and *L. rhamnosus* were the most common.<sup>2</sup> We reason that our patient's recurrent infection with two different *Lactobacillus* species originated from the gastrointestinal tract where lactobacilli dwell as normal flora, via a breached esophageal mucosal barrier. An automated phenotypic microbial identification and antimicrobial susceptibility testing system, the VITEK anaerobe and *Corynebacterium* (ANC) identification card, was used to identify both *Lactobacillus* species. Epidemiologic evidence has shown that the VITEK ANC card achieves 98.5% identification accuracy of clinical anaerobic isolates at the genus level, and 86.5% identification accuracy at the species level.<sup>15</sup>

Probiotic use was also considered in our patient, as *Lactobacillus acidophilus* and *Lactobacillus rhamnosus* are commercially significant bacterial probiotics,<sup>16</sup> with reported cases of bacteremia and endocarditis related to probiotic use.<sup>17,18</sup> The FDA, in a 2010 draft guidance, has recognized immunosuppression, structural heart disease, pregnancy, neutropenia, radiation and active intestinal disease as risks for adverse events in probiotic clinical trials. In 2011, a report released by the Agency for Healthcare Research and Quality concluded that the current literature is not well-equipped to answer with confidence questions on the safety of probiotics based on existing interventional studies.<sup>19</sup>

Our patient also presented with acute disorientation and confusion, which has not been reported as the prominent presenting symptom in other cases published. He also had fever and leukocytosis, present in 69% and 22% of patients respectively, per Husni et al's review.<sup>1</sup> Work-up for other possible causes of encephalopathy was negative.

Our patient was appropriately managed with antimicrobial therapy, which was deescalated to IV penicillin G, when susceptibilities became available, and aortic valve replacement, with satisfactory clinical recovery. Therapy with penicillin and an aminoglycoside has been reported to be successful in other cases of *Lactobacillus* bacteremia, and can be considered as empiric therapy until susceptibilities are available to help guide decision making.<sup>20</sup> In this case, gentamicin had to be discontinued due to the development of DILI.

Prompt recognition and appropriate treatment of our patient's *Lactobacillus* prosthetic valve infective endocarditis were major contributory factors to his overall survival and recovery.

## CONCLUSION

This case highlights the importance of recognizing *Lactobacillus* sp. as a potential pathogenic isolate, especially in the presence of predisposing immune factors and medical comorbidities like advanced age, diabetes, or preexisting structural heart disease. A diagnosis of *Lactobacillus* bacteremia should always prompt workup for the underlying disease conditions noted above, as this is an uncommon pathogen, but is not always a contaminant. Prompt recognition of *Lactobacillus* bacteremia or infective endocarditis is essential to preventing morbidity and mortality related to this disease process.

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