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CASE REPORT

Lactobacillus rhamnosus endocarditis: An unusual culprit in a patient with Barlow's disease

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1. Introduction

Lactobacillus *rhamnosus* (*L. rhamnosus*) is a rare cause of infective endocarditis. To date, a total of 73 cases of lactobacillus endocarditis have been described, and only 18 among them have been attributable to *L. rhamnosus*.[1]

We report a case of *L. rhamnosus* endocarditis, following a minor nasal procedure, in an adult with underlying

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myxomatous degenerative mitral valve disease (Barlow disease). Notably, the patient did not receive preprocedural chemoprophylaxis because, according to the most recent European and American guidelines, mitral valve prolapse is no longer considered a condition that requires chemoprophylaxis.[2,3]

2. Case report

A 74-year-old Caucasian male was referred to our tertiary referral center for further evaluation of suspected mitral valve endocarditis. Apart from a known history of a myxomatous mitral valve with posterior leaflet prolapse and moderate regurgitation, the patient was healthy and in excellent physical condition. Fifty days prior to presentation, he underwent a minor, invasive nasal cavity procedure without preprocedure prophylaxis for endocarditis. In the subsequent weeks, he experienced low-grade fever, fatigue, and progressive weight loss, along with anemia (Hb 11 g/dl) and an elevated white blood count (13.500/mm^3 with 85% neutrophils) as the main findings in the initial laboratory evaluation. Clinical assessment on an outpatient basis performed by his attending physician (including a full-body scan with CT, gastrointestinal tract endoscopy and blood tests) was unremarkable. He received a 10-day empiric trial with cefuroxime without symptom relief or fever remission. In the setting of a fever of unknown origin, transthoracic echocardiography raised suspicion of a vegetation in the anterior mitral leaflet, which was subsequently confirmed by transesophageal examination as well as severe mitral regurgitation (100 ml regurgitant volume).

On admission, the patient had normal vitals and his physical examination was remarkable for a holosystolic murmur (grade 3/6) heard best at the apex. No peripheral signs (both embolic and immunologic) of endocarditis were apparent.

A total of four consecutive blood culture sets were obtained (pairs of both aerobic and anaerobic bottles) and incubated in a BACTEC 9240 automated system (Becton Dickinson and Co, Sparks, MD 21152, USA) for a total of 6 days. All cultures were positive after two to four days of incubation. Gram stain revealed a small Gram-positive coccobacillus that grew on both 5% sheep blood and chocolate agar plates after incubation for 48 h at 5% CO_2. The isolate was catalase-negative and oxidase-negative. The Anaerobe and Corynebacterium (ANC) card of the VITEK 2 system (bioMerieux, Marcy L'Etoile, France) identified the isolate as *Lactobacillus acidophilus*, but it had low discrimination to the species level. Subsequently, two previously described 16S PCR and sequencing protocols[4,5] were used for final genus and species identification, which identified the isolate as *L. rhamnosus* (16S rDNA GenBank accession number KJ939337). Susceptibility testing was performed using the disc-diffusion method. Determination of the Minimum Inhibitory Concentration (MIC) was performed using the gradient strip method and MIC Test Strips (Liofilchem, Roseto Degli Abruzzi, 64026, Italy). Both methods were performed on Mueller-Hinton agar plates that were supplemented with 5% horse blood and incubated at 5% CO_2 for 24 and 48 h. Disk diffusion showed large diameter zones ($\geq$30 mm) in response to ampicillin, penicillin, tetracycline, chloramphenicol, erythromycin, clindamycin, linezolid and levofloxacin, indicating possible susceptibility, and low zones ($\leq$6 mm) to ceftriaxone, vancomycin and meropenem, indicating possible resistance. The MICs obtained (μg/ml) were as follows: penicillin 0.5, ceftriaxone $>$32, linezolid 2, daptomycin 0.5, imipenem $>$32 and meropenem $>$32. Interpretation of the results was not performed because the Clinical and Laboratory Standards Institute (CLSI) M45-A2 guidelines regarding *Lactobacillus* spp. were not available.

By applying the Dukes criteria, given the presence of 2 major criteria (i.e., blood cultures positive for a microorganism consistent with infective endocarditis and mitral valve vegetation illustrated by TEE – Fig. 1A), the diagnosis of community-acquired infective endocarditis was established. Based on the susceptibility testing results, and according to the infectious disease specialist recommendations, treatment with IV penicillin (24 MU daily) plus gentamycin (80 mg tid) was started. After completion of 8 weeks of antibiotics treatment, due to severe mitral regurgitation accompanied by exertion dyspnea, the patient underwent successful valve replacement with a metallic prosthesis. It should be noted that, although the Gram stain of the excised native valve (Fig. 1B) revealed small Gram-positive coccobacilli, the culture was negative, which was possibly due to the prolonged antimicrobial treatment.

Postoperatively, the course was complicated by persistent complete atrioventricular block that required permanent pacemaker implantation and left pleural effusion (postpericardiectomy syndrome), which was managed with pleural drainage. Three subsequent blood cultures were negative, and, at patient follow up, there was a evidence of infection relapse after approximately 8 months.

3. Discussion

This is an unusual report of endocarditis with *L. rhamnosus* as the culprit bacterium. This case illustrates the diagnostic difficulties regarding strain isolation and the usefulness of molecular technique implementation. Moreover, the clinician should always consider individualized treatment as well as apply current practice guidelines tailored to each specific patient.

Lactobacillus, a gram-positive, rod-shaped bacterium is a common inhabitant of the oral, gastrointestinal and female genital tract flora.[6] *Lactobacillus* species are linked to various serious infections, most frequently endocarditis and bacteremia. The species *L. casei* and *L. rhamnosus* are the most common virulent strains.[1] In a series investigating over 200 cases of lactobacilli bacteremia, factors predisposing to *L. rhamnosus* bacteremia are prior dental procedures, periodontitis, immunosuppression, intravenous drug use and indwelling catheters.[7] As depicted in Table 1, which summarizes all reported cases of *L. rhamnosus*-associated endocarditis, pre-existing heart valve disease is the major predisposing factor for infective endocarditis development, even in patients who have not undergone immunosuppression or central line insertion.[13]

The virulence of Lactobacilli has been tested in animal models of endocarditis.[8] The results of these studies suggest that lactobacilli strains can be virulent, and infective

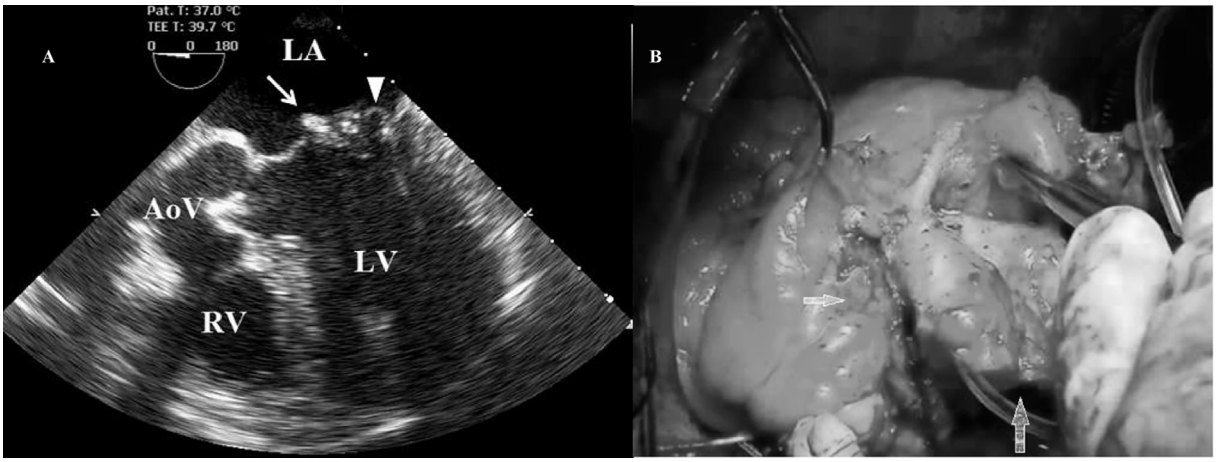

Figure 1 (**A**) Transesophageal echocardiography, illustrating a long axis image at the level of upper esophagus at 0°. A 0.7 × 0.5 cm mass is attached at the atrial side of the anterior mitral valve leaflet (arrow), which is compatible with a vegetation. Note also the prolapse of the posterior leaflet (arrowhead). LV = left ventricle, RV = right ventricle, LA = left atrium, and AoV = aortic valve. **(B)** Intraoperative view of the mitral valve. Note the abundant tissue of the leaflets and presence of vegetations attached to the anterior leaflet (arrows).

endocarditis is the most frequent infection.[8] This is true even for the probiotic strains that are currently used in dairy products, although they have lower infectivity rates.[9,10]

It is emphasized that lactobacillus can be difficult to recognize in clinical laboratories because its growth can be extremely demanding. Molecular techniques, including PCR with 16S rRNA gene sequencing (as applied in our patient), have been reported as an effective method for identifying *L. rhamnosus*.[11]

L. rhamnosus is reported to be susceptible to penicillin and aminoglycosides, with susceptibility rates up to 70%.[12] Daptomycin could be utilized as an alternative to penicillin. However, some strains are resistant to standard antibiotic regimens; therefore, the MIC and minimum bactericidal concentration (MBC) should be reported, and synergy tests should be performed.[12] The duration of therapy should be determined according to standard guidelines for treating infective endocarditis, although there is no hard evidence defining the most appropriate duration.

Nevertheless, *Lactobacillus endocarditis* is considered difficult to eradicate; in 30% of reported cases, the administered therapy was inadequate and relapses have been reported.[7] Both the lack of proper microbial susceptibility studies and lack of standardized therapy seem to be predisposing factors for relapses and even death. It has been speculated that the production of lactic acid by

Table 1 Reported cases *Lactobacillus rhamnosus*-associated endocarditis.

Authors	Age (years)/sex	Medical history	Outcome
Knight *et al.*	57/Female	Porcine aortic valve	Cure
Naude *et al.*	66/Male	Dental procedure	Death
Holiman *et al.*	71/Female	Prosthetic aortic valve	Death
Avlami *et al.*	65/Male	Colonoscopy — native aortic valve	Cure
Presterl *et al.*	23/Male	Diabetes-daily yogurt ingestion	Cure
Wallet *et al.*	73/Male	Prosthetic aortic valve	Cure
Monterisi et al.	29/Male	Mitral valve prolapse	Cure
Land *et al.*	6-week-old/Male	Double outlet right ventricle and pulmonary stenosis	Cure
Kochan *et al.*	24/Female	Previous aortic mechanical valve endocarditis — probiotic ingestion	Cure
McKay *et al.*	67/Male	Mitral regurgitation, probiotic consumption	Cure
Griffiths *et al.*	45/Male	Dental procedure	n/a
Tornos *et al.*	7/Female	Tricuspid atresia carious teeth	n/a
Fritsche *et al.*	6/Female	Dental procedure	Cure
Sharpe *et al.*	31/Male	Rheumatic valve disease	Cure
Sharpe *et al.*	17/Female	Marfan syndrome	Cure
Sharpe *et al.*	36/Female	Aortic coarctation	Cure

n/a = not available.

lactobacilli strains, and the subsequent lowering of the pH, could lead decrease the effective concentrations of antibiotics, lessening their effect.[13] In addition, in most of the reported cases, valve replacement was deemed necessary. The reported mortality rates can be as high as 23%, especially in people with multi-microbial infections.[7]

4. Conclusion

This case illustrates an uncommon case of infective endocarditis in a patient with Barlow's disease. According to the most recent European Heart Association (ESC) and American Heart Association (AHA) guidelines for infective endocarditis, mitral valve prolapse is no longer considered to be a condition that requires prophylactic chemotherapy prior to interventions.[2,3] Moreover, upper airway interventions are consistent with Class III indications for chemoprophylaxis.[2] This case highlights the compelling need for individualized therapeutic approaches with respect to chemoprophylaxis recommendations. In fact, accumulating experience in everyday clinical practice could eventually modify our policy on the conditions that require prophylactic antibiotic administration.

Conflicts of interest

The authors declare that there are no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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