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Lactobacillus endocarditis: a case report in France and literature review

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ABSTRACT

Lactobacilli are commensal bacteria in the normal flora of the oral cavity, gastrointestinal and genital tract. However, few cases of lactobacilli-induced bacteremia or endocarditis have been reported, particularly in immunocompromised patients. We reported a rare case of a 57-year-old man with a *Lactobacillus rhamnosus* endocarditis without immunodeficiency in his medical history. He received a dental scaling one year before. Clinical presentation included weight loss, heart murmur, ankle arthritis and splinter hemorrhage. Echocardiography showed a mitral prolapse and a 16 mm vegetation associated with a valvular perforation. All blood cultures were positive for *Lactobacillus rhamnosus*. Antibacterial regimen with amoxicillin and gentamicin led to recovery without surgery. We present a literature review of the lactobacillary endocarditis cases published since 1992. Valvulopathy, dental or invasive procedures and probiotics use were the main underlying conditions, in contrary to immunodeficiency. Diagnosis of lactobacillary endocarditis should be more considered and a treatment with penicillin and aminoglycoside should be promptly introduced in life-threatening cases.

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Introduction

Lactobacilli are rod-shaped bacteria, facultatively anaerobic, found in the normal flora of the oral cavity, gastrointestinal and genital tract. The organisms are used as probiotic bacteria or in fermented food product. Previously considered as a contaminant, the evidence was made that *Lactobacillus* is able to induce severe infections like endocarditis in a rat model (1) and in human (2,3). More than one hundred *Lactobacillus* endocarditis (LE) cases have been described in the literature and already collected in different reviews of cases (3–5). We report a rare case of endocarditis caused by *Lactobacillus rhamnosus* in a patient without immunodeficiency. We reviewed all reported cases since the introduction of the Duke's criteria in 1992, reopening and completing the series of Salvana et al. from 1992 to 2005 (5). All the reports were studied, even papers in Spanish after translation. We assessed patients' characteristics, *Lactobacillus* species, treatments and outcome.

Case presentation

A 57-year-old man was admitted in the unit of internal medicine for a persistent inflammatory syndrome, fatigue and a right ankle arthritis. He was machine operator in the steel industry,

retired one year before. His medical history included an interatrial communication surgery in 2003 and a teeth scaling one year before. He has experienced an extreme fatigue for 9 months. 6 months before, a first laboratory investigation demonstrated elevated CRP and ESR. He related only one episode of hyperthermia (38 °C) and no night sweats. 3 months before, he presented a left ankle arthritis with cutaneous eruption described as petechiae. He received amoxicillin during one week and the symptoms disappeared. He went on losing weight without anorexia or intestinal symptoms. CRP and ESR had varied but always above normal levels. A thoracic-abdominal-pelvic CT was performed and any infectious lesion or tumor was found. 3 weeks before hospitalization, he presented a new swelling of his right ankle and large joint arthralgia. He was referred to our unit.

Clinical examination showed no fever, a total weight loss of 4 kg, an isolated swollen ankle, a nail with a splinter hemorrhage (Fig. 1A) and a systolic, 1/6 intensity heart murmur. He had no signs of heart failure or severe sepsis. A transthoracic echocardiography was rapidly performed and revealed a mitral valvular vegetation of 16 mm associated with a valvular perforation and a grade II leak (Fig. 1B). In addition, a mitral prolapse was seen. It was supposed that the prolapse was anterior to the infectious process because the subvalvular tract was not involved. Empiric intravenous antimicrobial treatment was immediately started by amoxicillin 12 g per day and gentamicin 3 mg/kg after three sets of blood cultures drawn at 30 minute intervals. All of them were positive for *Lactobacillus rhamnosus* after 46 hours. *Lactobacillus rhamnosus*

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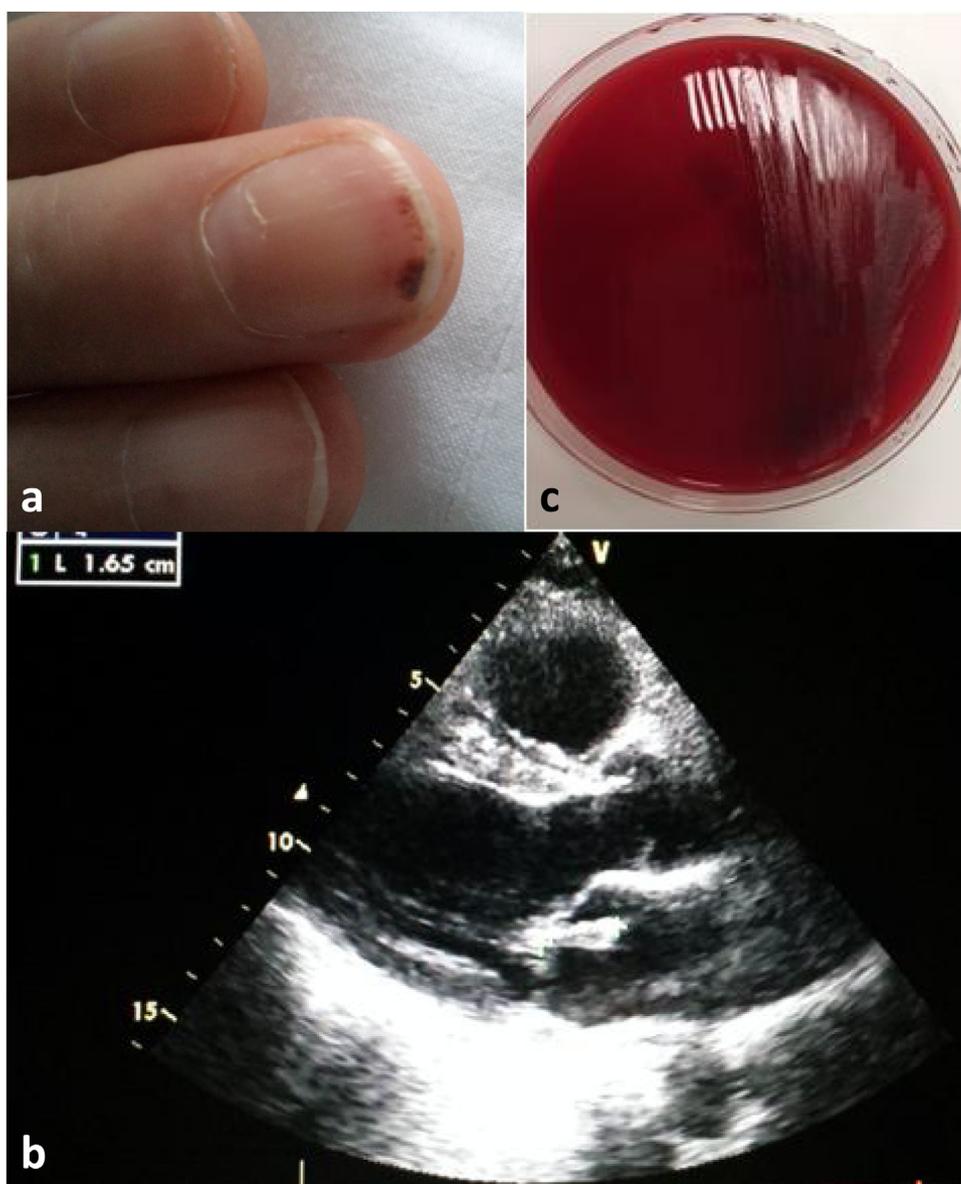


Fig. 1. Splinter hemorrhage (a). Transthoracic echocardiography: mitral valvular vegetation (b). Bacterial growth on Columbia blood agar with sheep blood (c).

was identified by Matrix-Assisted Laser Desorption Ionization - Time of Flight (MALDI-TOF) Mass Spectrometry with the MALDI Biotyper[®] from Bruker Corporation[©] (Fig. 1C). The sensitivity profile allowed us to continue the same antibacterial regimen. The ankle swelling disappeared after two days, the blood inflammation markers rapidly decreased and the blood cultures were negative after one week. The embolic risk was high and a surgery was planned 15 days later. But two days before the surgery, a transoesophageal echocardiography showed that the mitral vegetation almost completely disappeared, thus the surgery was cancelled. Gentamicin was stopped after 2 weeks, switched by orally rifampin. Amoxicillin and rifampin were continued 4 more weeks. During this period, he consulted a dentist and several teeth extractions were decided.

Discussion

Since 1992, 50 cases of LE were reported (6–25,5,26–50). Their characteristics were summarized in the Table 1. The mean age of patients was 52.4 years [16–85]. 68% of them were male.

Concerning underlying conditions, a valvulopathy was reported in 64% of patients and 14% of endocarditis occurred on a prosthetic valve. A dental procedure or an invasive procedure were found in 34% and 22% of cases, respectively. 22% of patient used probiotics. Immunosuppression involved only 16% of them. After fever or chills, experienced by 72% of patients, the most common symptoms were a new murmur (30%), respiratory signs (30%), such as dyspnea or crackles) and weight loss (28%). LE affected aortic and mitral valve in the same proportion (22%). Tricuspid valve was involved in only 2 cases (4%) and any cases with pulmonary valve endocarditis has been reported. *Lactobacillus rhamnosus* was the most isolated species (24%) following by *L. acidophilus* (18%), *L. paracasei* (12%) and *L. casei* (12%). Surgery was needed in half of the cases (54%). Mortality rate remained high (10%). Antimicrobial susceptibility was available in 26 studies (5,9,10,17,18,20–25,28–31,34–37,39,41,44,46–48), including ours (Table 2). Lactobacilli are highly sensitive to penicillin G (86%), aminopenicillins (amoxicillin 86%, ampicillin 83%), clindamycin (100%), rifampin (90%), aminoglycosides such as gentamicin (79%) but most of time resistant to vancomycin and cefotaxime

Table 1
Summary of patients' characteristics.

Characteristic	All cases n = 50	Characteristic	All cases n = 50
Age (years)		Valve, n (%)	
Mean	52.4	Aortic	22 (44)
Median	56.5	Mitral	22 (44)
Range	16-85	Pulmonary	2 (4)
		Tricuspid	0
Sex, n (%)		Embolus, n (%)	
Female	19 (38)	Yes	15 (30)
Male	31 (62)	No	23 (46)
		Unknown	12 (24)
Medical history, n (%)		Species, n (%)	
Valvulopathy	32 (64)	<i>L. rhamnosus</i>	12 (24)
Valve prosthesis	7 (14)	<i>L. acidophilus</i>	9 (18)
Dental procedure	17 (34)	<i>L. spp</i>	7 (14)
Invasive procedure	11 (22)	<i>L. paracasei</i>	6 (12)
Probiotics use	11 (22)	<i>L. casei</i>	6 (12)
Immunosuppression	8 (16)	<i>L. jensenii</i>	5 (10)
		<i>L. garvieae</i>	1 (2)
Symptoms, n (%)		<i>L. gasseri</i>	1 (2)
Weight loss	14 (28)	<i>L. zeae</i>	1 (2)
Malaise	5 (10)	<i>L. curvatus</i>	1 (2)
Fever/chills	36 (72)	<i>L. fermentum</i>	1 (2)
New murmur	15 (30)		
Respiratory signs	15 (30)	Surgery, n (%)	
Edema	4 (8)	Yes	27 (54)
Arthritis	8 (16)	No	20 (40)
Myalgia	8 (16)	Unknown	3 (6)
Cutaneous signs	10 (20)		
Abdominal pain	3 (6)	Death, n (%)	5 (10)
Hepato/splenomegaly	6 (12)		
Splinter hemorrhage	3 (6)		
Chest pain	3 (6)		
Neurological signs	7 (14)		
Unusual sweats	5 (10)		

Table 2
Antimicrobial susceptibility

Antibiotic agents	Percent sensitive, % (n)
penicillin G	86% (n=21)
ampicillin	86% (n=7)
amoxicillin	83% (n=6)
erythromycin	100% (n=11)
clindamycin	100% (n=18)
rifampicin	90% (n=10)
vancomycin	21% (n=19)
cefotaxime	43% (n=7)
gentamicin	79% (n=14)
imipenem	73% (n=11)
ciprofloxacin	57% (n=7)

(sensitivity in 21% and 43% of cases, respectively). In cases reported here, a large number of different antibacterials were used, often in combination, showing that no consensual treatment exists (Table 3). Penicillin G, ampicillin and gentamicin were the most given drugs in first line (36%, 18% and 42%, respectively). Double antimicrobial therapy was proposed in first line in 58% of cases. 40% of patients were treated with only one line of antimicrobial, meaning that first line was continued after results of antibacterial susceptibility. Changes were needed in 36% of cases. Mean of duration was 44.7 days, and median was 42 days. In conclusion, lactobacilli were proved to be responsible for severe infection like endocarditis, with a common use of surgery and a substantial mortality rate. Valvulopathy appeared as the main predisposing factor. Dental or invasive procedures but also probiotics intake could be associated with LE. As patients were mostly immunocompetent, LE diagnosis should be considered more often. High-dose penicillin, combined with an aminoglycoside should be

Table 3
Antimicrobial use in *Lactobacillus* endocarditis (type, associations, number of lines and duration).

azithromycin	1 (2)	–
clindamycin	3 (6)	4 (8)
Other		
vancomycin	8 (16)	4 (8)
teicoplanin	2 (4)	2 (4)
linezolid	–	1 (2)
rifampicin	2 (4)	4 (8)
cotrimoxazole	1 (2)	–
daptomicin	1 (2)	1 (2)
doxycyclin	1 (2)	–
chloramphenicol	1 (2)	1 (2)
probenicid	–	1 (2)
Monotherapy	6 (12)	13 (26)
Bithery	29 (58)	27 (54)
Tritherapy	7 (14)	4 (8)
Number of lines		
1	20 (40)	
2	18 (36)	
3	7 (14)	
4	1 (2)	
Antibiotic duration (d)		
Mean	44.7	
Median	42	
Range	5-93	

recommended in first line and clindamycin should be preferred to vancomycin in penicillin-allergic patients. Antimicrobial duration should be at least 6 weeks. Guidelines for the management of LE are needed.

Patient's consent statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRediT authorship contribution statement

J. Campagne: Writing - original draft. **J.F. Guichard:** Writing - review & editing. **M.C. Moulhade:** Writing - reviewing & editing. **H. Kawski:** Writing - review & editing. **F. Maurier:** Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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