

## *Lactococcus garvieae* Endocarditis: First Case Report in Latin America

Tatiana Franco Hirakawa<sup>1,2</sup>, Fernando Augusto Alves da Costa<sup>1,2</sup>, Marcos Cairo Vilela<sup>1,2</sup>, Micheli Rigon<sup>1,2</sup>, Henry Abensur<sup>2</sup>, Maria Rita Elmor de Araújo<sup>2</sup>

FGM - Clínica Paulista de Doenças Cardiovasculares<sup>1</sup>; Hospital Beneficência Portuguesa de São Paulo<sup>2</sup>, São Paulo, SP - Brazil

*Lactococcus garvieae*, an emerging zoonotic pathogen, is responsible for mastitis in rodents and sepsis in fish. Although deemed opportunistic and hardly ever causing infections in humans, its incidence is probably underestimated due to the difficulty in diagnosis. There are very few reports of osteomyelitis, liver abscess, and peritonitis, and only nine cases of endocarditis described in worldwide literature. We describe the first case of *Lactococcus garvieae* endocarditis in Latin America, in a female patient with metallic prosthetic heart valve who presented with daily fever, chills, Osler nodes and six positive blood cultures for *Lactococcus garvieae*, which met Duke's criteria for the diagnosis of "definitive infective endocarditis".

### Introduction

*Lactococcus garvieae*, an emerging zoonotic pathogen, was originally isolated in mastitis in rodents and is responsible for sepsis in fish; it is deemed opportunistic and shows low virulence in humans, with very few reports of endocarditis (nine cases in the worldwide literature)<sup>1-7</sup>, osteomyelitis<sup>8</sup>, liver abscess<sup>9</sup>, sepsis, and peritonitis<sup>5</sup>. However, the difficult differential diagnosis with *Enterococcus* may lead to underestimation of its incidence and real importance. In the present study, we report the first case of *Lactococcus garvieae* endocarditis in Latin America, the tenth in the worldwide literature.

### Case report

A 58-year-old female Caucasian patient, a former smoker previously hypertensive, with type-2 diabetes, dyslipidemia, underwent mitral valve replacement by a metallic prosthetic valve six months earlier due to severe mitral stenosis of

rheumatic etiology. Upon arrival at the hospital, the patient had a history of daily fever for six days (38.5° C), chills, diaphoresis, erythematous nodules in hands and legs, myalgia and weakness. As regards her nutritional habits, she often consumed several types of fish and reported having eaten white cheese recently. Despite denying dental treatment in the past few months, the patient had a dental prosthesis and had had a gingival perforation with a "fish bone" five days prior to the onset of symptoms.

On admission, she had fever (38.2° C), Osler nodes on her left hand and legs, and poor dentition. The remainder of her physical examination was unremarkable. Laboratory tests showed alterations in inflammatory tests, with PCR = 81.9 and VHS = 47.1, with no leukocytosis. No focus of infection was identified, despite extensive diagnostic investigation.

In samples for blood cultures drawn from three different sites, Gram-positive cocci were isolated and further identified as *Lactococcus garvieae* by means of biochemical tests and confirmed by genetic studies. The pathogen was isolated again in three other blood cultures samples drawn five days later. The antibiotic susceptibility test showed resistance only to clindamycin, and sensitivity to penicillin, gentamicin, vancomycin and other antibiotics.

Two transesophageal echocardiograms were performed, revealing absence of vegetation and competent mitral valve prosthesis. However, according to Duke's modified criteria, the patient was diagnosed with endocarditis and was treated with vancomycin 1 g every 12 hours for 28 days, due to confirmed penicillin allergy. There was complete remission of signs and symptoms, as well as normalization of laboratory tests; control blood cultures were negative.

In an attempt to identify the source of the infection, the white cheese consumed by the patient was sent for microbiologic testing. In the search for an "entrance door", due to the family history of intestinal polyposis, the patient also underwent barium enema. However, both tests were normal.

The patient was discharged with no symptoms after 30 days of hospitalization, and was referred for cardiology outpatient follow-up.

### Keywords

Endocarditis, bacterial; diagnosis; *Lactococcus garvieae*; heart valve prosthesis.

### Discussion

*Lactococcus garvieae* is one of the eight species belonging to the *Lactococcus* genus, originally known as the lactic group of the *Streptococcus* genus, from which it was split in 1985, after genetic analysis<sup>10</sup>.

Mailing address: Fernando Augusto Alves da Costa •

Praça Amadeu Amaral, 47 cj 12A - Bela Vista - 01327-010 - São Paulo, SP - Brasil

E-mail: alvesdacosta@uol.com.br, faacosta@cardiol.br

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Formed by facultatively anaerobic catalase-negative Gram-positive cocci, these bacteria produce lactic acid, which provide them with fermentation ability and bactericidal property; thus, it is used in the food industry for fermentation and preservation of food<sup>10</sup>.

However, it is known that some species may be pathogenic to animals and humans, especially *Lactococcus garvieae* and *Lactococcus lactis*<sup>10</sup>.

Considered an emerging zoonotic pathogen, *Lactococcus garvieae* is responsible for mastitis in rodents, and sepsis in fish. Infected fish which do not develop the disease may contribute to dissemination<sup>5</sup>.

It is considered an uncommon pathogen in humans; it is opportunistic and shows low virulence. Very few cases have been described in the literature with *Lactococcus garvieae* being the causal agent of endocarditis<sup>1-7</sup>, osteomyelitis<sup>8</sup>, liver abscess<sup>9</sup>, sepsis and peritonitis<sup>5</sup>. There are nine cases of endocarditis reported in worldwide literature: in four of them prosthetic valves<sup>1,3</sup> are affected, and in the other five, native heart valves are<sup>2,4,5,7</sup>.

This is the first case report of *Lactococcus garvieae* endocarditis in Latin America in a patient with metallic prosthetic valve in the mitral position who met the modified Duke criteria for the diagnosis of “definitive endocarditis” (Table 1).

**Table 1 - Diagnostic criteria for infective endocarditis**

Major criteria	Minor criteria
Positive blood culture → Typical microorganism for infective endocarditis from two separate blood cultures ( <i>S. viridans</i> , <i>S. bovis</i> , HACEK group, <i>S. aureus</i> , <i>Enterococcus</i> ) in the absence of a primary focus	Predisposition: predisposing heart condition or intravenous drug use  Fever ≥ 38°C
Blood cultures (= 2) drawn more than 12h apart, all of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hr apart	Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions
Single positive blood culture for <i>Coxiella burnetii</i> or antiphase I IgG antibody titer >1:800	Immunological phenomena: glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor.
Evidence of endocardial involvement	Microbiological evidence: positive blood culture, but not meeting major criterion as noted previously or serologic evidence of active infection with organism consistent with infective endocarditis
Positive echocardiogram (TEE advised for PVE or complicated IE). Oscillating intracardiac mass, on valve or supporting structures, or in the path of regurgitant jets, or on implanted material, or abscess, or new partial dehiscence of prosthetic valve, or new valvular regurgitation (increase or preexisting murmur not sufficient)	Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from: previous valve surgery, antibiotic use, injection drug abuse, intravascular catheters, surgeries other than cardiac, and immunocompromised state

Pathogenicity and infectivity of *Lactococcus garvieae* remain inconclusive. It is known that lactococci are not typically a part of the human flora<sup>3</sup>, but the intake of milk or contaminated fish may be sources of infection<sup>5</sup>. They have also been isolated in manufactured food due to their use in food products. However, gastric acidity, pancreatic enzymes, gallbladder and intestinal secretions, peristalsis, and epithelial cell integrity are protective factors against oral and gastrointestinal infections. The existence of gastrointestinal disorders such as ulcers, polyps or diverticula may act as facilitators of bacterial infectivity.

In the case described, the source of infection may have been the fish routinely consumed by the patient; the wound may have been caused by the “fish bone” and her poor dentition which may both been the entrance door. However, no data confirm this hypothesis.

It is difficult to distinguish *L. garvieae* from *Enterococcus*, because their phenotypes are similar. It is also challenging to distinguish *Lactococcus garvieae* from *L. lactis*. Some studies suggest the use of antibiotic susceptibility tests, because *L. garvieae* is resistant to clindamycin, whereas *L. lactis* is always sensitive to this antibiotic: this proved true in the present case.

In relation to the echocardiogram, few reports are found in the literature of patients presenting with vegetations in the native valve<sup>2</sup>, and cases without abnormalities both in the transthoracic and transesophageal test of patients with endocarditis in prosthetic valves<sup>8</sup>, as in the present case report.

The gold-standard test for the identification of *Lactococcus garvieae*, despite its high cost, is the genetic study with confirmation of its DNA sequence<sup>10</sup>.

## Conclusion

*Lactococcus garvieae* endocarditis is extremely uncommon, this being the tenth case described in worldwide literature, and its pathogenesis remains inconclusive. Possible sources of infection are contaminated milk and fish, with reports of growth of these bacteria in manufactured food. Gastrointestinal comorbidities and poor oral conditions may facilitate infectivity of this pathogen. Prosthetic heart valves are also predisposing factors, and this implies the need to advise patients on the importance of oral hygiene and dental treatment in the prevention of endocarditis. Gastrointestinal disorders should also be investigated whenever necessary.

Phenotypic similarities between *Lactococcus* and *Enterococcus* make it difficult to establish a microbiological diagnosis, so that genetic studies are still necessary for the definite identification of *Lactococcus garvieae*. The fact that these tests are unavailable in most of the medical centers worldwide probably cause *Lactococcus garvieae* to be underdiagnosed, so its clinical significance may be far greater than is thought.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

## Case Report

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### Study Association

This study is not associated with any post-graduation program.

## References

1. Furutan NP, Breiman RF, Fischer MA, Facklam RR. *Lactococcus garvieae* infections in humans: a cause of prosthetic valve endocarditis. In: 91st General Meeting American Society for Microbiology. Washington, DC; 1991. p. 109, C-297 [Abstract].
2. Fefer JJ, Ratzan KR, Sharp SE, Saiz E. *Lactococcus garvieae* endocarditis: report of a case and review of the literature. *Diagn Microbiol Infect Dis*. 1998;32(2):127-30.
3. Fihman V, Raskine L, Barrou Z, Kiffel C, Riahi J, Berçot B, et al. *Lactococcus garvieae* endocarditis: identification by 16S rRNA and sodA sequence analysis. *J Infect*. 2005;52(1):e3-6.
4. Vinh DC, Nichol KA, Rand F, Embil JM. Native-valve bacterial endocarditis caused by *Lactococcus garvieae*. *Diagn Microbiol Infect Dis*. 2006;56(1):91-4.
5. Wang CY, Shie HS, Chen SC, Huang JP, Hsieh IC, Wen MS, et al. *Lactococcus garvieae* infections in humans: possible association with aquaculture outbreaks. *Int J Clin Pract*. 2007;61(1):68-73.
6. Yiu KH, Siu CW, To KK, Jim MH, Lee KL, Lau CP, et al. A rare cause of infective endocarditis; *Lactococcus garvieae*. *Int J Cardiol*. 2007;114(2):286-7.
7. Li WK, Chen YS, Wann SR, Liu YC, Tsai HC. *Lactococcus garvieae* endocarditis with initial presentation of acute cerebral infarction in a healthy immunocompetent man. *Intern Med*. 2008;47(12):1143-6.
8. James PR, Hardman SM, Patterson DL. Osteomyelitis and possible endocarditis secondary to *Lactococcus garvieae*: a first case report. *Postgrad Med J*. 2000;76(895):301-3.
9. Mofredj A, Baraka D, Kloeti G, Dumont JL. *Lactococcus garvieae* septicemia with liver abscess in an immunosuppressed patient. *Am J Med*. 2000;109:513-4.
10. Facklam R, Elliott JA. Identification, classification, and clinical relevance of catalase-negative, Gram-positive cocci, excluding the streptococci and enterococci. *Clin Microbiol Rev*. 1995;8(4):479-95.