

REFERENCES

1. Fulcher J, O'Connell R, Voysey M, et al. Efficacy and safety of LDL-lowering therapy among men and women: Meta-analysis of individual data from 174 000 participants in 27 randomised trials. *Lancet*. 2015;385:1397–1405.
2. Cannon CP, Blazing MA, Giugliano RP, et al. Protocol - Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. *N Engl J Med*. 2015;372:2387–2397372.
3. Nicholls SJ, Puri R, Anderson T, et al. Effect of Evolocumab on Progression of Coronary Disease in Statin-Treated Patients The GLAGOV Randomized Clinical Trial. *JAMA*. 2016;316:2373–2384.
4. Godzien J, Ciborowski M, Armitage EG, et al. A single in-vial dual extraction strategy for the simultaneous lipidomics and proteomics analysis of HDL and LDL fractions. *J Proteome Res*. 2016;15:1762–1775.
5. Walley KR. Role of lipoproteins and proprotein convertase subtilisin/kexin type 9 in endotoxin clearance in sepsis. *Curr Opin Crit Care*. 2016;22:464–469.
6. Sánchez-Hernández RM, Civeira F, Stef M, et al. Homozygous Familial Hypercholesterolemia in Spain: Prevalence and Phenotype-Genotype Relationship. *Circ Cardiovasc Genet*. 2016;9:504–510.

<http://dx.doi.org/10.1016/j.rec.2017.04.009>
1885-5857/

© 2017 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.

Infective Endocarditis Due to *Leuconostoc* Species



Endocarditis infecciosa por *Leuconostoc* species

To the Editor,

We present a case of infective endocarditis due to *Leuconostoc* species and *Staphylococcus hominis* in a patient with no underlying disease and complaining of gastrointestinal symptoms. A systematic review of the literature identified only 2 other cases of infective endocarditis due to *Leuconostoc* species,^{1,2} neither of them occurring in combination with coagulase-negative *Staphylococci*, which is quite common in other clinical scenarios.³ The main findings of the 3 episodes are summarized in the Table.

Our patient was an 80 year-old man, with a personal history of colon cancer surgery in 2001. He was admitted because of

unspecified abdominal pain, nausea, vomiting, constitutional syndrome, and episodic fever (39 °C) for the last 2 months, despite antacid treatment and with negative gastric and colorectal endoscopic studies. Hematologic analysis showed leukocytosis (12 300/μL), neutrophilia (82%), and C-reactive protein 169 mg/L. Acute cholecystitis was initially suspected but, despite the presence of lithiasis in an enlarged gall bladder, there were no signs of inflammation, and this diagnosis was ruled out by general surgeons. Blood cultures were obtained and empirical antibiotic therapy was initiated. However, the presence of a systolic and diastolic aortic murmur required an echocardiographic evaluation, which was performed 72 hours after admission. A vegetation (17 x 14 mm) above the aortic native valve with severe regurgitation and a pseudoaneurysm (19 x 15 mm) in the anterior leaflet of the mitral valve were detected (Figure). *Leuconostoc* species and *Staphylococcus hominis* grew in 2 out of 2 blood cultures. Antibiotic treatment was adapted to the antibiogram with amoxicillin-clavulanic acid and gentamicin. There were no signs of heart

Table
Main Findings of Patient With *Leuconostoc* Species Infective Endocarditis

	Episode 1 ¹	Episode 2 ²	Episode 3
Age, y	72	55	80
Sex	Female	Male	Male
Comorbidities	Aortic and mitral prostheses Mitral prosthesis IE due to <i>Streptococcus sanguis</i>	Not significant	Past colon cancer
Risk factors	Oral endoscopy Colonoscopy	No	No
Fever	Yes	No	Yes
Heart failure	No	No	No
Septic shock	No	No	No
Abdominal symptoms	No	No	Yes
Septic emboli	No	Central nervous system	Central nervous system
Empirical antibiotic treatment	Unknown	Ceftriaxone Vancomycin	Levofloxacin
Blood cultures	Positive	Positive	Positive
Microorganism	<i>Leuconostoc mesenteroides</i>	<i>Leuconostoc</i> species	<i>Leuconostoc</i> species <i>Staphylococcus hominis</i>
Vancomycin sensitivity	Resistant	Sensitive	Resistant
Echocardiogram			
Vegetation, mm	11	> 10	17 x 14
Periannular complication	No	No	Mitral pseudoaneurysm
Location	Mitral prosthesis	Native aortic valve	Native aortic and mitral valves
Valvular insufficiency	No	Not specified	Severe
Treatment	Penicillin G 6 weeks Gentamicin 10 d	Penicillin G 6 wk Gentamicin 2 wk	Amoxicillin-clavulanic acid 4 wk Gentamicin 2 wk
Cardiac surgery	No	Elective	Elective
In-hospital mortality	No	No	No
Long-term follow-up	Died (possible reinfection) (3 mo)	Asymptomatic (6 wk)	Asymptomatic (6 mo)

IE, infective endocarditis.

failure or of persistent infection but a cerebral computed tomography scan due to confusional symptoms showed frontal embolisms. Elective double valvular replacement with biological prostheses was performed and antibiotic treatment lasted 4 weeks. Valve culture was negative, reflecting the effectiveness of the antibiotic treatment. Despite postoperative renal failure, the clinical course was favorable and the patient was discharged successfully. Six months later, he remains asymptomatic.

Left-sided infective endocarditis is a peculiar disease, with in-hospital mortality around 30%, which remains unchanged despite major advances in diagnostic and therapeutic procedures.⁴ The possibility of polymicrobial involvement is not uncommon but does not mean a worse prognosis.⁵ To the best of our knowledge, there are only 2 reports of *Leuconostoc* species,^{1,2} and ours is the first report of this microorganism in combination with coagulase-negative *Staphylococcus*.

Until 1985, *Leuconostoc* were known as “nonpathogenic to plants and animals”. However, due to continued reports of different infections, they are currently recognized as opportunistic pathogens affecting patients with a wide spectrum of underlying diseases.^{3,6} However, the portal of entry remains uncertain. One possibility is their introduction into the blood stream during catheter implantation, which could explain the frequent association with indwelling catheters and the codetection of *Staphylococcal* species (nearly 50% in some reports). Another is the gastrointestinal tract due to the natural habitat of *Leuconostoc* in foodstuff, which would explain the association with underlying gastrointestinal disease and frequent gastrointestinal symptoms, as in the case presented. Blood culture contamination was ruled out due to the positivity of 2 out of 2 blood cultures, and the frequent coinfection by *Leuconostoc* and *Staphylococcal* species.³

Leuconostoc species are nonsporulated, microaerophile, catalase- and oxidase-negative, Gram-positive coccobacilli, with high nutritional requirements and intrinsic resistance to vancomycin.³ In fact, *Leuconostoc* is not easy to distinguish from some other microorganisms in the clinical laboratory, unless vancomycin resistance is identified. *Streptococcus viridans* have similar morphology, hemolysis and fermentation reactions but do not produce gas from glucose and rarely show vancomycin resistance.⁶ Although cases of vancomycin-resistant streptococci have been reported, the organisms were identified by conventional means and some of these isolates may have been *Leuconostoc* species.⁶ *Leuconostoc* must also be distinguished from *Enterococcus*,⁶ another *Streptococcaceae* family member, and the best way is by using the pyrrolidonyl arylamidase (PYRase) test, which is negative in *Leuconostoc*s and positive in *Enterococci*.

High-level resistance to vancomycin is nearly a constant in *Leuconostoc* species. Reports suggest the involvement of a chromosomal factor, which leads to a change in the end of a pentapeptide in the cell wall. This vancomycin binding site usually ends in alanine-alanine, but in *Leuconostoc* species it ends in alanine-lactate. Another possibility, as in *Enterococci*, is the production of a new membrane protein codified by plasmids.⁶ Until microbiology laboratories routinely test for *Leuconostoc* species, the true prevalence of vancomycin resistance may remain unknown. In fact, the *Leuconostoc* infective endocarditis episode 2 showed vancomycin sensibility.

Treatment alternatives are beta-lactams. Penicillin and first-generation cephalosporins are generally effective, but second- and third-generation cephalosporins show moderate to high-level resistance. Macrolides, aminoglycosides and lincosamides are options in patients with penicillin allergies.³ Apart from antibiotics, appropriate therapy includes the removal of infected foci.

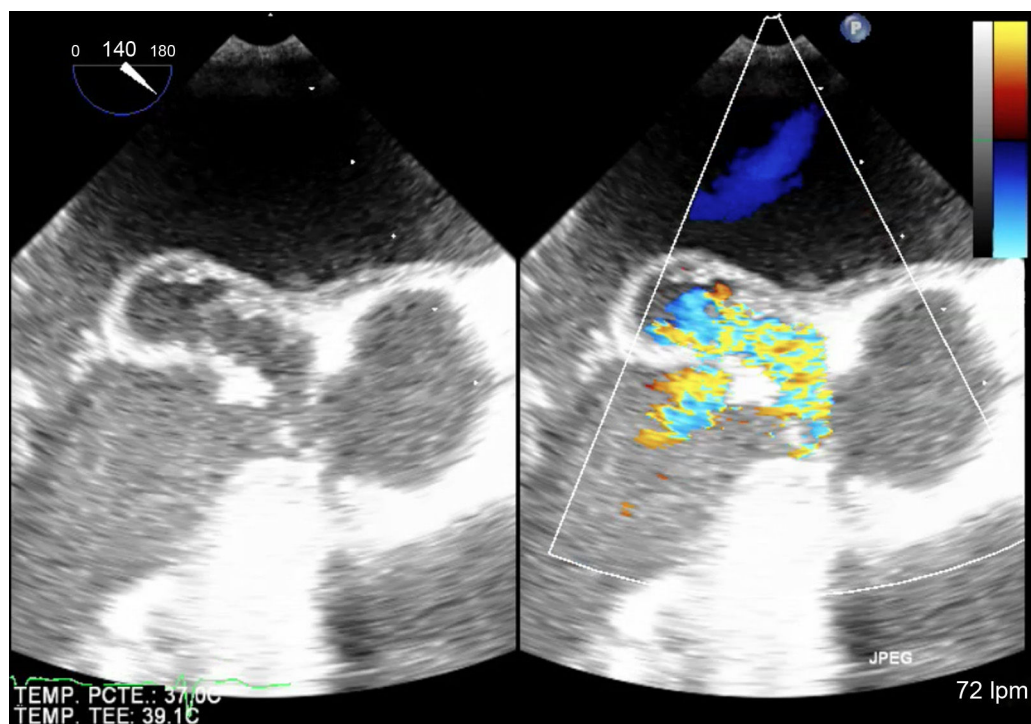


Figure. Transesophageal echocardiogram. Long-axis aortic view at 140°. There is a pseudoaneurysm of the anterior leaflet of the mitral valve. TEMP PCTE, temperature patient; TEMP TEE, temperature transesophageal echocardiography.

In conclusion, *Leuconostoc* species does not need the presence of important comorbidities or indwelling catheters to cause infective endocarditis. The clinical course is favorable with standard management. Because of vancomycin resistance, beta-lactams in combination with gentamicin seem to be a good antibiotic option.

Pablo Elpidio García-Granja,* Javier López, Raquel Ladrón,
and J. Alberto San Román

*Instituto de Ciencias del Corazón (ICICOR), Hospital Clínico
Universitario, Valladolid, Spain*

* Corresponding author:

E-mail address: pabloelpidio88@gmail.com (P.E. García-Granja).

Available online 15 May 2017

REFERENCES

1. Vázquez E, Carazo I, Martín A, Lozano C, Cuesta I, Pagola C. Infectious endocarditis caused by *Leuconostoc mesenteroides*. *Enferm Infecc Microbiol Clin*. 1998;16:237–238.
2. Starr JA. *Leuconostoc* Species Associated Endocarditis. *Pharmacotherapy*. 2007;27:766–770.
3. Ballesteros Sanz MA, Ruiz De Alegría-Puig C, Fernández-Mazarrasa C, Gutiérrez-Cuadra M. Bacteremia and sepsis due to *Leuconostoc mesenteroides*. *Med Clin (Barc)*. 2010;134:87–92.
4. Moreillon P, Que YA. Infective endocarditis. *Lancet*. 2004;363:139–149.
5. García-Granja PE, López J, Vilacosta I, et al. Polymicrobial Infective Endocarditis: Clinical Features and Prognosis. *Medicine (Baltimore)*. 2015;94:e2000.
6. Horowitz HW, Handwerker S, van Horn KG, Wormser GP. *Leuconostoc*, an emerging vancomycin-resistant pathogen. *Lancet*. 1987;2:1329–1330.

<http://dx.doi.org/10.1016/j.rec.2017.04.013>
1885-5857/

© 2017 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.