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Letter to the Editor

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Streptococcus cristatus, an infrequent cause of bacteremia and infective endocarditis. Case report and literature review

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Sir,

A 72-year-old patient came to the emergency department for 1 week of generalized abdominal pain and stools with hemolytic debris. His medical history included bilateral pulmonary thromboembolism secondary to deep vein thrombosis in the left leg and biological aortic valve replacement 20 years earlier due to severe aortic insufficiency. On examination, the patient only presented generalized pain on palpation of the abdomen. Blood tests showed a C-reactive protein of 72 mg/L (0-5), 16,500 leukocytes (4,500-11,000) with 14,360 neutrophils (2,000-5,000), and the electrocardiogram showed extraventricular and supraventricular extrasystoles.

An abdominal pelvic computed tomography (CT) showed an area at the upper pole of the spleen compatible with splenic infarction, in addition to lesions compatible with ischemic colitis. A blood culture was obtained with suspicion of endocarditis (splenic infarction in a patient with a biological prosthesis) and the patient was admitted with piperacillin-tazobactam (4 g/0.5 g every 8 h IV). All 4 blood culture bottles were positive in the first 12-15 h of incubation and Gram staining showed Gram-positive cocci in chains. Blood culture flasks were inoculated on chocolate agars, TSA with 5% ram blood (Becton Dickinson, New Jersey, USA) and Brucella with hemin and vitamin K1 (BD©), and α-hemolytic colonies identified by MALDI-TOF mass spectrometer (Bruker, Massachusetts, USA) such as *Streptococcus cristatus* with a value >2,00 were observed at 24 h. After 48 h, another blood culture sample was drawn again in which *S. cristatus* was again identified. Antibiotic sensitivity was studied using the SMIC / ID-11 panel (BD©) on the BD Phoenix© AP system and was sensitive to penicillin (MIC = 0.25 mg/L), vancomycin (MIC < 0.5 mg/L) and daptomycin (MIC = 0.5 mg/L), teicoplanin (MIC 1 mg / L) clindamycin (MIC ≤ 0.03 mg/L), and no high-level resistance to gentamicin.

A transthoracic echocardiogram (TTE) showed thickening of the aortic prosthesis leading to mild aortic insufficiency and concentric left ventricular hypertrophy with LVEF 53%. Given the high suspicion of infective endocarditis (one major and two minor criteria), a transesophageal echocardiogram (TEE) was performed, with thickened and calcified leaflets, mild posterior periprosthetic regurgitation, although without stigmata of endocarditis. Although not confirmed by imaging tests, the patient received ceftriaxone (2 g/24 h) for possible infective endocarditis for 6 weeks with two subsequent negative blood cultures.

After treatment, the patient was followed in cardiology consultations with progressive increase in aortic insufficiency over the following months. At 8 months, TTE showed a thickened and calcified biological prosthesis, as well as an increase in periprosthetic aortic regurgitation compared to the subsequent study, and TEE showed images suggestive of endocarditis (Figure 1). It was decided to replace the valve with another biological prosthesis, and during the operation the findings were perforated and sclerosed prosthetic leaflets, sclerosed anterior descending artery, and severely calcified aortic root. The surgical specimen was sent to the microbiology laboratory, but no growth was obtained in the cultures. However, the 16S ribosomal RNA gene was sequenced, obtaining a 638 bp sequence identified as *S. cristatus* with an identification rate of 99.68% in BLASTR and registered in GenBank with the accession number "SUB11912930 HUBStCr".

S. cristatus is described as Gram-positive cocci in 1 µm chain and catalase negative. This microorganism was first isolated in humans from the oral cavity, including teeth and gums, with cariogenic capacity [1,2]. Jensen et al. based on the clustering patterns resulting from phylogenetic analysis of the complete genome of several species of the mitis group concluded that *S. cristatus* is closely related to *Streptococcus oligofermentans* and can be con-

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Table 1 Literature review of previous case reports of *S. cristatus*

Patient [reference]	Source of infection and co-infectants	Clinical picture	Complications	Treatment
3-year-old healthy female [6]	Blood. No	Transient bacteremia	No	Amoxicillin-clavulanic acid
52-year-old healthy male [6]	Aortic valve. *Staphylococcus aureus*	IE	Severe aortic and mitral insufficiency Mitral perforation Left-sided heart failure Intubation	Ceftriaxone + metronidazole failed. Ampicillin, gentamycin, piperacillin/tazobactam and vancomycin.
37-year-old healthy male [6]	Blood. *Streptococcus mitis*	Bacteremia and IE	Cardiac vegetations Severe aortic insufficiency	Ampicillin + gentamycin. Aortic valve replacement
57-year-old male with neurofibromatosis type 1 and mitral valve prolapse [5]	Blood. No	Bacteremia and IE	ANCA-PR3 positive immunocomplex glomerulonephritis	Penicillin. Mitral valve repair with resection
Two patients [7]. No information*	Blood. No	Bacteremia and IE	No information	No information
14-year-old female with 22q11 deletion syndrome and Tetralogy of Fallot [9]	Pulmonary valve	Bacteremia and IE	Pulmonary valve replacement	Cefepime + vancomycin + gentamicin replaced after with ceftriaxone + daptomycin
15-day-old immunocompetent male [8]	Wrist articulation. No	Septic arthritis	No	Vancomycin. Aspiration followed by arthrotomy

IE: Infectious endocarditis; *No information about age, sex and comorbidities of the patients, as well as complications and treatment of the cases.

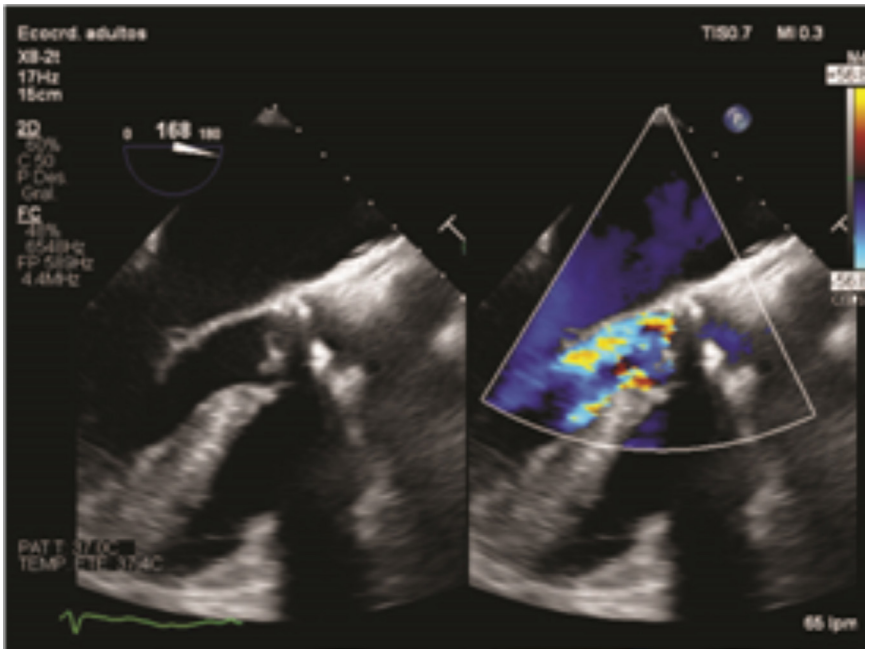

Figure 1 Biological aortic prosthesis with suggestive sings of endocarditis, with severe periprosthetic aortic insufficiency.

sidered practically the same species [3]. In fact, phylogenetic studies performed by Teng JL et al. in 2014 have shown that *S. oligofermentans* is closely related to *Streptococcus sinensis* and a new phylogenetic clade, the "sinensis group", has been proposed to include *Streptococcus sinensis*, *S. oligofermentans* and *S. cristatus* [4].

Currently, only eight clinical cases of infections caused by this microorganism have been described: one case of bacteremia, six cases of infectious endocarditis, and another of septic arthritis (Table 1) [5-9]. This is the sixth confirmed case of endocarditis after the microorganism by sequencing the 16S ribosomal RNA gene when processing the surgical specimen of a replaced heart valve. The use of molecular techniques such as whole genome sequencing or 16S rRNA gene sequencing have been used in some of the described cases of endocarditis, being useful, for example, when the bacterial inoculum is low due to previous treatment.

The relationship of infections such as bacteremia or endocarditis with dental extraction processes has been proven, so prophylaxis is recommended in patients with associated risk factors, such as valve carriers. In addition, poor dental hygiene (dental plaque or bleeding after brushing) also seems to be associated with a risk factor for the development of these infections [10]. However, only in one of the cases described so far was the patient's history of previous dental procedures.

Regarding the treatment of prosthetic valve endocarditis caused by the viridans group streptococci, current guidelines recommend a 6-week regimen of penicillin (24 million U/24 h IV in continuous perfusion or in 4-6 doses) or ceftriaxone (2 g/24 h IV or IM) with a class IIa recommendation strength and level of evidence B, which could be combined with a 2- or 6-week regimen of gentamicin (3 mg/kg every 24 h IV or IM, depending on whether the penicillin MIC is ≤0.12 mg/L or >0.12 mg/L). Although in highly susceptible strains (penicillin MIC ≤ 0.12 mg/L) the combination of penicillin or ceftriaxone with gentamicin has not shown better cure rates compared to monotherapy, in those with MICs > 0.12 mg / L, the combination with gentamicin is recommended for 2 weeks, as it is reasonable to prolong it to 6 weeks [11]. In our case, the patient received ceftriaxone for 6 weeks in monotherapy because the patient was taking an angiotensin II receptor antagonist and a diuretic.

Viridans group streptococci are a frequent cause of subacute or chronic endocarditis, both in native and prosthetic valves. Molecular techniques can be of great help, especially in cases where cultures are negative. This case adds more scientific evidence on the capacity of *S. cristatus* to produce serious infections such as bacteremia or endocarditis, although further studies are needed to investigate its virulence factors.

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None to declare.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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