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Available online 8 October 2021

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https://doi.org/10.1016/j.rec.2021.09.006

Early biological prosthetic mitral valve endocarditis due to *Tropheryma whipplei:* experience of an antimicrobial treatment approach

Endocarditis precoz sobre válvula biológica mitral por Tropheryma whipplei: *experiencia del tratamiento médico con antibioterapia*

To the Editor,

Tropheryma whipplei endocarditis is a rare disease[1] with little more than 150 cases reported in the literature and less than a dozen with prosthetic valve involvement. However, this microorganism has been isolated in around 5%[2,3] of cases of culture-negative infectious endocarditis, and so its active search is recommended in subacute or chronic endocarditis in which it may be involved.

With the explicit informed consent of the patient, we present the case of a 75-year-old asymptomatic woman with a history of atrial fibrillation, biological mitral valve replacement for severe double mitral lesion, tricuspid annuloplasty, and a single-chamber pacemaker for complete atrioventricular block after surgery 11 months earlier. The patient was transferred to our hospital because a sessile structure was found over the prosthetic valve during routine examination.

Transthoracic and transesophageal echocardiograms showed a hyperechogenic pedunculated structure with free movement

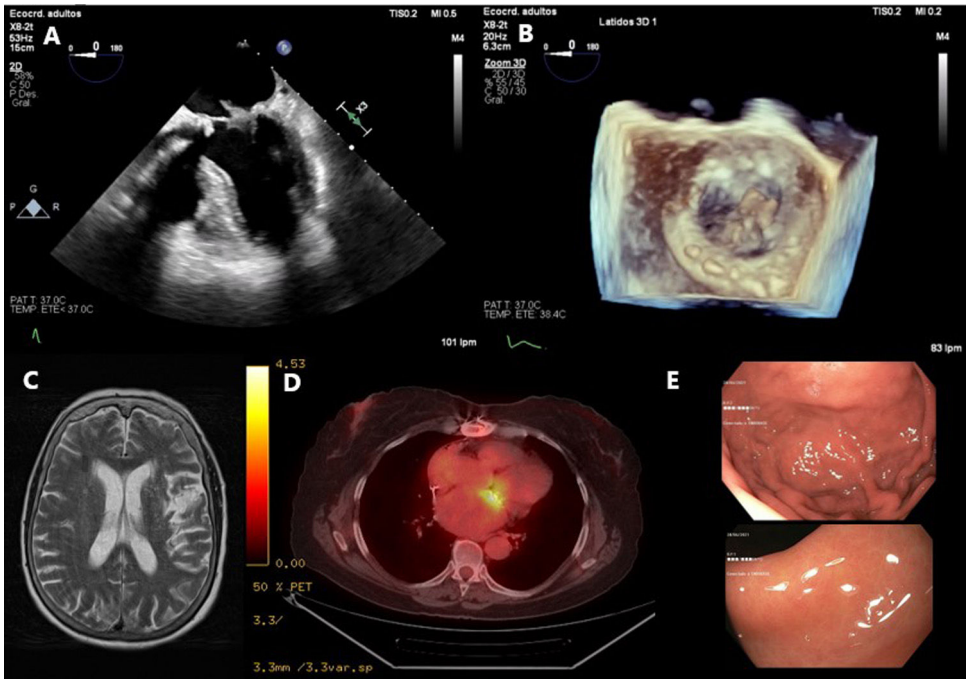

Figure 1. A: transesophageal echocardiogram at 0° showing a pedunculated lesion on the atrial side of the biological mitral valve prosthesis. B: 3-dimensional view of the lesion from the atrial side. C: cranial magnetic resonance imaging with residual left parietal ischemic lesion without septic embolism. D: positron emission tomography showing marked metabolic activity at the level of the prosthetic mitral valve. E: endoscopy with gastric (upper image) and duodenal (lower image) mucosa without erosions.

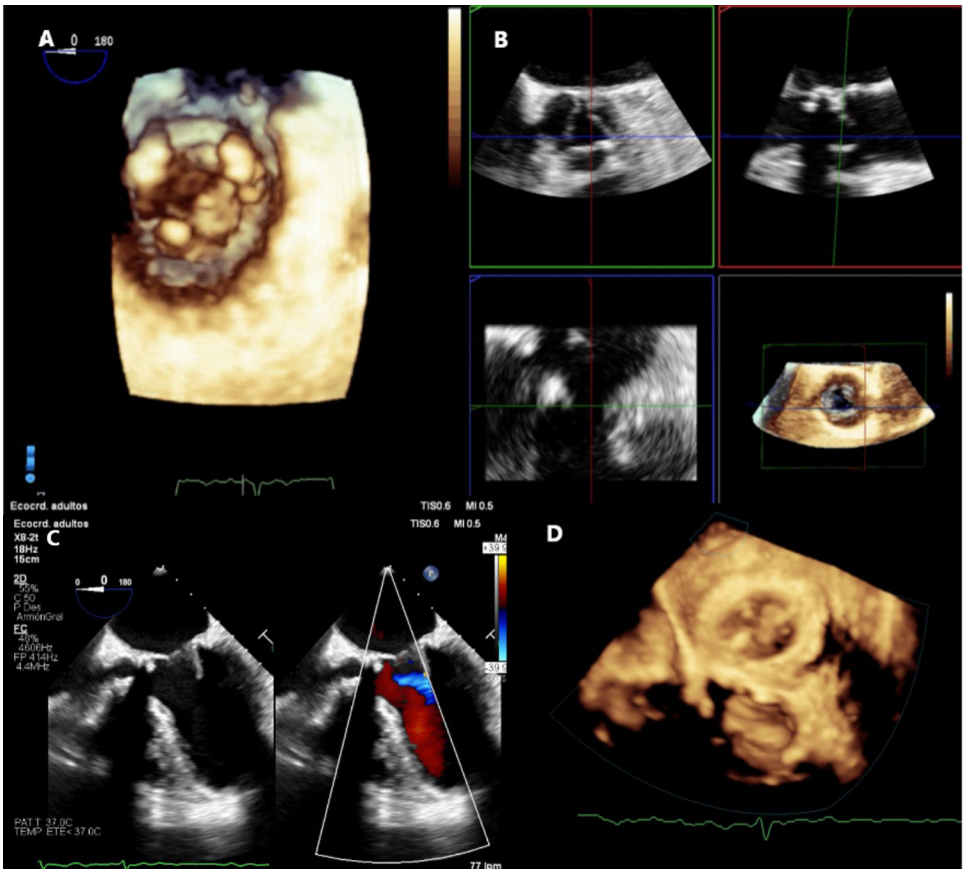

Figure 2. A: 3-dimensional transesophageal echocardiography (ventricular view) showing the lesion with a similar size. B: absence of native aortic valve involvement in orthogonal views. C: decrease in lesion size on transesophageal echocardiography at 0° with and without color. D: 3-dimensional transesophageal echocardiography; size of the lesion is smaller on the atrial side.

through the mitral prosthesis, with a maximum length of more than 1 cm (figure 1A,B), without functional repercussions. Blood analysis showed slightly elevated inflammatory parameters (C-reactive protein, 52 mg/L; leukocytes, 11 590/L; glomerular sedimentation rate, 51 mm). Given the suspicion of early prosthetic endocarditis, blood and urine cultures were obtained and a cranial MRI was performed, which ruled out septic embolism (a residual ischemic lesion was found; figure 1C). Positron emission tomography showed metabolic activity compatible with mitral valve infective endocarditis (figure 1D).

Negative cultures prompted an exhaustive search for etiologic agents implicated in culture-negative endocarditis. Serologic tests for atypical microorganisms were negative and polymerase chain reaction (PCR) test for *T ropheryma whipplei* DNA was positive in stool. Previous studies have described potential asymptomatic colonization by the microorganism, which reduces the specificity of this test in patients without clinical symptoms compatible with Whipple's disease.[4] Therefore, endoscopies were conducted for intestinal involvement, which showed healthy gastrointestinal mucosa (figure 1E) and no evidence characteristic of periodic acid-Schiff-positive granules in the histological specimen from the second duodenal portion. The PCR test was repeated in saliva, stool, blood, and urine, and again the result was positive in stool.

Despite the absence of clinical manifestations compatible with Whipple's disease, empirical antimicrobial treatment for endocarditis that also targeted the microorganism was initiated based on the high probability of infective endocarditis on positron emission tomography, the possibility of isolated valvular involvement as described in the literature,[5] and the detection of *T. whipplei* DNA in 2 separate stool samples.

We chose an empirical regimen of gentamicin, daptomycin, and ceftriaxone for 4 weeks and suppressive treatment with cotrimoxazole for 1 year. Although the European guidelines on antimicrobial treatment for Whipple's disease recommend doxycycline and hydroxychloroquine, the relapses described after standard treatment with ceftriaxone and cotrimoxazole appear to be related to resistance to the second compound. A retrospective Spanish national review showed no difference between the 2 regimens[2] and the broader spectrum of ceftriaxone within an empirical regimen led to its selection as the most appropriate treatment for the patient.

Two weeks after initiating treatment, transesophageal echocardiogram showed a stable lesion (figure 2A) without other valvular involvement (figure 2B). We decided to maintain antimicrobial therapy on the basis of these results and the published evidence on *T. whipplei* pulmonary hypertension or endocarditis[6] that had been resolved without surgical treatment. The aminoglycoside was replaced by ciprofloxacin due to nephrotoxicity and daptomycin was replaced by linezolid due to probable pneumonitis. Thus, the combined antimicrobial therapy was prolonged for 6 weeks and then cotrimoxazole was continued as monotherapy until completion of 1 year of treatment. Four months after the start of antimicrobial treatment, there was a clear decrease in the size of the lesion (figure 2C,D). Blood analysis showed the gradual normalization of inflammatory parameters (C-reactive protein, 1.2 mg/L; leukocytes, 7,740/L; glomerular sedimentation rate, 9 mm). To date, this is the first known case of early prosthetic endocarditis due to *T. whipplei* with no evidence of

disease progression and a decrease in the size of the endocardial lesion through antimicrobial treatment alone.

FUNDING

None declared.

AUTHORS' CONTRIBUTIONS

A. García-Olea and G. Ramírez-Escudero were the main authors. N. García, M. de la Peña, and L. Ruiz corrected different versions of the manuscript, provided critical review, and actively contributed to the selection of the audiovisual material.

CONFLICTS OF INTEREST

None declared.

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Available online 19 November 2021

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https://doi.org/10.1016/j.rec.2021.09.012

Incidence and mortality of infective endocarditis caused by oral streptococci in the last three decades at a referral center in Spain

Incidencia y mortalidad de la endocarditis infecciosa causada por estreptococos orales en las últimas tres décadas en un centro de referencia en España

To the Editor,

Until 3 to 4 decades ago, infective endocarditis (IE) was considered to be a subacute disease caused by cardiac lesions infected by oral flora microorganisms (mainly *Streptococcus viridans*). This type of IE has a relatively good prognosis, bearing in mind the severity of this disease.[1] However, the clinical and epidemiological profile and prognosis of IE have changed under the impact of recent social and health care changes, such as aging populations, increased numbers of other causal microorganisms (mainly staphylococci and enterococci), and new risk factors (eg, injectable drug use, prosthetic valves, electrical devices, or health care-related bacteremia).[2–6] The aim of this study was to analyze the characteristics of oral streptococci IE in a Spanish tertiary hospital, as well as changes in its relative incidence, treatment, and prognosis using a large single-center series collected over the last 30 years in this setting.

We analyzed a cohort of consecutive patients diagnosed with IE and followed up in our hospital between 1990 and 2020 (n = 485) to identify cases of IE caused by oral streptococci (*S. viridans* and nutritionally variant streptococci: *Abiotrophia* and *Granulicatella*) and to compare their characteristics during 3 time periods (1990-2000, 2001-2010, and 2011-2020). The study was approved by the ethics committee of our hospital and informed consent was given by all the participants. Of the 485 cases of IE, 346 were native, 59 were early prosthetic, and 80 were late prosthetic. In total,

Table 1
Number of cases and percentage of endocarditis due to oral streptococci in the total series and by the various types of infective endocarditis during the 3 time periods analyzed

	Total 1990-2020	1990-2000	2001-2010	2011-2020	*P**
Total, No.	485	138	167	180	
Oral streptococci	94 (19.4)	30 (21.7)	34 (20.3)	30 (16.7)	.045
Native IE, n	346	94	118	134	
Oral streptococci	73 (20.1)	20 (21.3)	31 (16.7)	22 (16.4)	.160
Early prosthetic IE, n	59	20	21	18	
Oral streptococci	3 (5.1)	1 (5)	0	2 (11.1)	.663
Late prosthetic IE, n	80	24	28	28	
Oral streptococci	18 (22.5)	9 (37.5)	3 (10.7)	6 (21.4)	.089

IE, infective endocarditis.
Unless otherwise indicated, data are expressed as No. (%).
* Chi-square test.