

Current Profile of Left-Sided Native Valve Endocarditis Caused by Coagulase-Negative *Staphylococcus*

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Coagulase-negative staphylococci are the most frequently isolated microorganisms in early prosthetic valve endocarditis. However, they rarely cause endocarditis in native valves. The profile of patients with left-sided native valve endocarditis by coagulase-negative staphylococci is unknown, because available data are scarce and outdated. We analyzed the epidemiological, clinical, radiographic, microbiological, and echocardiographic features and clinical course in 17 patients with this entity out of a total of 441 consecutive patients diagnosed as having endocarditis. The results show that left-sided native valve endocarditis caused by coagulase-negative staphylococci is more common than previously reported, can cause heart failure due to valvular involvement, often needs surgery, and is associated with high mortality.

Key words: Endocarditis. Echocardiography. Coagulase-negative staphylococcus.

Perfil actual de la endocarditis por estafilococo coagulasa negativo en válvulas nativas izquierdas

Los estafilococos coagulasa negativos (SCN) son los microorganismos aislados con más frecuencia en la endocarditis protésica temprana. En cambio, afectan en pocas ocasiones a las válvulas nativas. Hay escasos y antiguos datos en la bibliografía sobre la endocarditis nativa izquierda por SCN, por lo que su perfil es poco conocido. Hemos analizado las características epidemiológicas, clínicas, radiológicas, microbiológicas, ecocardiográficas y evolutivas de 17 casos de endocarditis izquierda nativa por SCN obtenidas de una serie de 441 episodios consecutivos de endocarditis. Los resultados muestran un aumento en la frecuencia de esta enfermedad respecto de las series previas. Clínicamente provocan en numerosas ocasiones insuficiencia cardíaca por afección valvular, precisan con frecuencia cirugía y tienen una alta mortalidad.

Palabras clave: Endocarditis. Ecocardiografía. Estafilococo coagulasa negativo.

INTRODUCTION

Although any microorganism can theoretically cause endocarditis, 90% of all cases are the result of 3 major groups of bacteria that share a capacity to

adhere to the endocardium: staphylococci, streptococci, and enterococci.¹ The microorganisms isolated most frequently in native valve endocarditis (NVE) are the streptococci² (particularly *S viridans*), although some series report more cases caused by *S aureus*.^{3,4} The coagulase-negative staphylococci (CNS) are the most common cause of early prosthetic valve endocarditis,⁴ but are an infrequent cause of NVE,² with an incidence <1% in earlier series and 5% in more recent studies.^{5,6} The profile of this entity is little known, since the series in the literature are few, old, and retrospective, do not perform an echocardiogram, or include few patients. Our objective was to define the evolution and the clinical, radiological, microbiological, echocardiographic, and prognostic characteristics of left-sided NVE caused by CNS.

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PATIENTS AND METHODS

We analyzed 441 episodes of infective endocarditis diagnosed consecutively at 5 tertiary referral hospitals since 1996, 333 of them left-sided (75%), and 216 affecting native valves (65%). Seventeen of these were caused by CNS (8%) and are the subject of our study, in which we prospectively compiled 83 variables in each case analyzed. An echocardiogram was performed in all suspected cases of endocarditis, and patients were followed up until a definite diagnosis was obtained. All patients underwent at least 1 physical examination, 1 electrocardiogram, 1 chest x-ray, 1 urinalysis, 3 blood cultures, and 1 transthoracic and transesophageal echocardiogram. The echocardiographic definitions of vegetation, abscess, pseudoaneurysm and fistula are described in a previous article.⁷ When blood cultures were negative after 72 h, specific serology tests were also performed.

The indications for surgery include NYHA Class III or IV heart failure, fungal endocarditis, and uncontrolled infection (persistent bacteremia or fever of more than 7 days' duration despite appropriate antibiotic therapy). Echocardiographic evidence of a periannular complication was not necessarily considered an indication for surgery.

RESULTS

The mean age was 62±15 years (range, 29-81) and 11 were men (65%). Ten (59%) of the patients had a known history of heart disease: 4 rheumatic valve disease, 2 degenerative valve disease, 3 congenital heart

TABLE 1. Clinical, Electrocardiographic, and Radiological Manifestations of Native Valve Endocarditis Caused by Coagulase-Negative Staphylococci

Signs and symptoms	
Fever	14 (82%)
Heart failure	11 (65%)
Kidney failure	5 (29%)
Peripheral arterial emboli	2 (12%)
Stroke	4 (24%)
Ischemic	3
Hemorrhagic	1
Septic shock	2 (12%)
Cutaneous manifestations	2 (12%)
Enlarged spleen	2 (12%)
Electrocardiographic manifestations	
Atrial fibrillation	4 (24%)
Supraventricular tachycardia	2 (12%)
Atrioventricular block	1 (6%)
Radiographic manifestations	
Cardiomegaly	12 (71%)
Heart failure	11 (65%)
Pleural effusion	6 (35%)

TABLE 2. Echocardiographic Characteristics of Native Valve Endocarditis Caused by Coagulase-Negative Staphylococci*

Echocardiographic Variables	Native IE Due to CNS
Aortic valve	9 (53%)
Mitral valve	5 (29%)
Multivalve	3 (18%)
Vegetation, observed by TEE	12 (86%)
Diameter of largest vegetation, mm	19.3±9.2
Diameter of smallest vegetation, mm	7.6±2.6
Area of vegetation, cm ²	1.9±1.1
Periannular complications	2 (13%)
Abscess	1
Pseudoaneurysm	1
Fistula	0
Severe valve regurgitation	9 (70%)

*TEE indicates transesophageal echocardiography; CNS, coagulase-negative staphylococci.

diseases, and 1 myxoid heart disease. Four of the 17 episodes were of nosocomial origin (24%). A trigger factor was detected in only 7 cases (41%): presence of intravascular catheter in 3, history of genitourinary procedure in 2, and prior surgery in 2 others. Ten patients (59%) had a predisposing disease: 4 had chronic anemia, 3 chronic renal failure, 1 diabetes mellitus, 1 cancer, and 1 patient was receiving immunosuppressive therapy. The onset of symptoms was acute (<15 days) in 5 patients (31%).

The most important clinical, electrocardiographic, and radiographic characteristics are shown in Table 1. In all cases, the blood cultures were positive for coagulase-negative staphylococci (16 *S epidermidis*, 1 *S haemolyticus*). In 4 cases, the microorganisms isolated were methicillin-resistant (2 nosocomial and 2 community). One case presented intermediate resistance to vancomycin.

The most important data from transesophageal echocardiography are shown in Table 2.

During the course of the disease, 8 patients required surgery (47%), 4 of them urgently for heart failure and another 4, elective surgery for severe residual valve regurgitation. Eight of the patients died (47%), 5 in the medical treatment group (2 from septic shock, 2 from stroke, and 1 from cardiac tamponade) and 3 during the postoperative period.

DISCUSSION

Coagulase-negative staphylococci are the most common microorganisms in positive blood cultures.^{6,8} Except in patients who have implants of foreign materials, such as prostheses or intravascular stents, isolation of these microorganisms is usually attributed to contamination of the sample.^{6,9} This view could lead to

an underestimation of the importance of CNS as a cause of endocarditis in patients with no known heart disease or any of the above factors, and could cause a delay in the diagnosis and start of treatment with the resulting increase of morbidity and mortality. Endocarditis due to CNS is usually caused by bacteremia from a skin source (wounds, abscesses, catheters), although in many cases these foci are silent and go unnoticed. This was also observed in our series, as the origin of infection could not be determined in most patients. In cases where it was known, intravascular stents and prior surgery accounted for a high percentage.

We found a higher percentage of nosocomial-related cases (24%) than has been reported by other authors.⁸ Although NVE due to CNS has traditionally been considered an infection almost exclusively of community origin,⁸ an increase in nosocomial cases has already been reported.^{6,10} This has been exacerbated by pharmacological immunosuppression and aggressive, prolonged hospital procedures and treatments, such as intravenous lines and catheters for administering drugs, parenteral nutrition, or dialysis,^{6,10} that facilitate the development of bacteremia by microbiotic microorganisms on the skin that enter when the skin's defense barrier is compromised. The repeated use of vascular access techniques for dialysis could explain the high percentage of patients with chronic renal failure observed in our series. All these factors may explain the decrease we observed in patients with a history of heart disease as compared to other studies that report up to 74% of patients with such a condition^{8,10} and probably explain the increased incidence with respect to the earliest articles (8% vs 1%-5%).^{9,10-12}

Infection is generally subacute,^{8,9} although in our study there were a number of acute cases (31%), which confirmed the aggressiveness of the disease. Clinically, our patients presented the usual signs and symptoms of endocarditis.⁸ The percentage of patients with heart failure (65%) was higher than previous series,⁸ because valvular and subvalvular involvement was frequent, making cardiac surgery necessary in many cases. These results are similar to those reported in a retrospective series with 11 patients.⁹ However, the authors reported lower mortality than in our patients (27% vs 48%), potentially associated with the more aggressive approach taken in the study (surgery in 72% of patients, compared to 47% in our series).

Prosthetic valve endocarditis due to CNS is generally caused by methicillin-resistant microorganisms acquired in the hospital setting.¹³ In contrast, most cases of NVE caused by CNS are methicillin-sensitive (76% in our series). The antibiotic resistance of CNS probably depends, however, on the origin of the infection rather than the type of valve affected. In our group, 50% of nosocomial endocarditis cases were resistant to these antibiotics, compared to only 15%

TABLE 3. Mortality of Left-sided Endocarditis Caused by Different Microorganisms in Our Series

	Mortality
Native valve endocarditis due to CNS	47%
Early prosthetic valve endocarditis due to CNS	23%
Late prosthetic valve endocarditis due to CNS	57%
Native valve endocarditis due to SA	46%
Native valve endocarditis due to SV	13%

*SA indicates *Staphylococcus aureus*; CNS, coagulase-negative staphylococci; SV, *Streptococcus viridans*.

among community-acquired infections.

Although the vegetations were not large, 29% of the patients had an embolism (2 peripheral, 3 cerebral). This incidence is toward the higher end of the range reported by earlier series (8% and 24%)^{8,10} and suggests that vegetation size is not the only factor influencing the onset of stroke in endocarditis, as reported in previous studies.¹⁴

Although previous series indicate that the course of the disease was favorable with medical treatment in most cases and left no sequelae,⁸ our results suggest that NVE caused by CNS has a poor prognosis more similar to that of endocarditis due to *S aureus* rather than *S viridans*, as indicated by the mortality for the various groups in our series (Table 3).

CONCLUSIONS

Native valve endocarditis due to CNS is more frequent than has been reported in earlier series. The clinical course of this disease is difficult and the prognosis is poor, often making combined medical-surgical treatment necessary.

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