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Endocarditis caused by anaerobic bacteria☆

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ABSTRACT

Background: Infective endocarditis (IE) caused by anaerobic bacteria is a rare and poorly characterized disease. Most data reported in the literature are from case reports [1–3]. Therefore, we assessed the situation of anaerobic IE (AIE) in Spain using the database of the Spanish Collaboration on Endocarditis (GAMES).
Methods: We performed a prospective study from 2008 to 2016 in 26 Spanish centers. We included 2491 consecutive cases of definite IE (Duke criteria).
Results: Anaerobic bacteria caused 22 cases (0.9%) of definite IE. Median age was 66 years (IQR, 56–73), and 19 (86.4%) patients were men. Most patients (14 [63.6%]) had prosthetic valve IE and all episodes were left-sided: aortic valves, 12 (54.5%); and mitral valves, 8 (36.4%). The most common pathogens were *Propionibacterium acnes* (14 [63.6%]), *Lactobacillus* spp (3 [13.63%]), and *Clostridium* spp. (2 [9.0%]), and the infection was mainly odontogenic. Fifteen of the 22 patients (68.2%) underwent cardiac surgery. Mortality was 18.2% during admission and 5.5% after 1 year of follow-up. When patients with AIE were compared with the rest of the cohort, we found that although those with AIE had a similar age and Charlson comorbidity index, they were more likely to have community-acquired IE (86.4% vs. 60.9%, $p = 0.01$), have undergone cardiac surgery (68.2% vs 48.7% $p = 0.06$), and have had lower mortality rates during admission (18.2% vs. 27.3%).
Conclusion: IE due to anaerobic bacteria is an uncommon disease that affects mainly prosthetic valves and frequently requires surgery. Otherwise, there are no major differences between AIE and IE caused by other microorganisms.

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1. Introduction

Infective endocarditis (IE) caused by anaerobic bacteria is a rare and poorly characterized disease that has accounted for 2–16% of all cases of IE during the past few decades [1]. Most data are from individual case reports [1–3], and techniques for the detection of anaerobes have been far from uniform in clinical microbiology departments. Nowadays, the causative microorganism is identified in roughly 90% of the episodes [4], and the new mass spectrometry method MALDITOF has proven to be a highly reliable tool for the identification of anaerobic isolates in the microbiology laboratory [5].

The incidence of anaerobic bacteremia has been reported to have decreased by some authors [6,7], although not by all [8,9], and there is no recent direct information on the importance and characteristics of anaerobic IE (AIE). García-Granja et al. [10] reported that anaerobes were cultured in almost 20% of cases of polymicrobial endocarditis, whereas in monomicrobioal endocarditis, their prevalence was anecdotal. However, despite relevant microbiologic differences between polymicrobial and monomicrobial endocarditis, short-term outcome was similar [10].

The Spanish Collaboration on Endocarditis (GAMES), which was created in 2008, consists of multidisciplinary groups from 26 centers dedicated to improving management of IE. Since then, a total of 2491 patients with definite IE have been prospectively enrolled. This resource provides us with a unique opportunity to evaluate the epidemiology, characteristics, and outcome of AIE in a large, contemporary, and national cohort of well-characterized endocarditis patients.

2. Methods

2.1. The Spanish Collaboration on Endocarditis (GAMES)

The Spanish Endocarditis Study Group (GAMES) is a multidisciplinary study group dedicated to improving the management of IE. Participating centers have hospital-based endocarditis groups comprising microbiologists, infectious diseases physicians, echocardiographers, heart surgeons, cadiologists, among others. All episodes of IE are prospectively recorded, and data are collected using a pre-established clinical form with common standard definitions [11–13]. At hospital discharge, the forms are sent to the coordinating center or entered directly by the investigators through a secure data entry system. At the coordinating center, specialists and data managers review the data for accuracy and, if necessary, contact the referring centers for clarification. The resultant GAMES database comprised 2491 cases of proven IE, as defined using the Duke criteria [12]. The covariates analyzed included demographic data, etiology, comorbidity, site of acquisition, occurrence of complications, antibiotic treatment, valve replacement, and outcome.

2.2. Definitions

IE was defined according to the modified Duke criteria [12].

Anaerobic bacteria were defined as bacteria that derive energy only from metabolic processes in the absence of oxygen [14].

Site of IE acquisition was defined following the recommendations of the International Collaboration on Endocarditis (ICE) [11]. In brief, community-acquired IE was defined as IE diagnosed within the first 48 h of admission in a patient who did not fulfill the criteria for nosocomial or health care–associated infection. Nosocomial IE was defined as IE that developed in a patient who was hospitalized for more than 48 h before the onset of signs or symptoms consistent with IE or who was hospitalized for prosthetic valve infections, when onset was within 12 months of valve implantation. Health care–associated IE was IE diagnosed within 48 h of admission in an outpatient with any of the following criteria: (1) intravenous therapy, wound care, or specialized nursing care at home within the 30 days before the onset of IE; (2) attendance at a hospital or hemodialysis clinic or receipt of intravenous therapy within the 30 days before the onset of IE; (3) hospitalization in an acute care center for 2 or more days during the 90 days before the onset of IE; or (4) residence in a nursing home or long-term care facility [11].

The origin of the infection was established when there was a clinically evident focus (eg, oral/dental, cutaneous). If no focus could be demonstrated, the episode was classified as primary. Whenever possible, the colon was examined using colonoscopy or PET-CT.

A cardiac device was defined as a permanent pacemaker and/or cardioverter-defibrillator.

Perivalvular extension was considered to be substantial when abscesses were present or other echocardiography findings suggested the infection was invasive (communication between chambers, wall dissection, or large valvular dehiscence). Prosthetic valve IE was defined as infection occurring on any type of nonnative tissue or mechanical device. The EuroSCORE20 was used to assess operative risk [15,16].

The age-adjusted Charlson comorbidity index was used to categorize comorbidities [17].

A central nervous system event was defined as an acute neurological deficit of vascular etiology lasting more than 24 h [18]. Systemic embolization was defined as an embolic event outside the central nervous system. Congestive heart failure was defined according to the New York Heart Association classification system [19].

Persistent bloodstream infection was defined as the isolation of the same microorganism in blood cultures obtained >72 h after the initial cultures despite adequate antimicrobial therapy [20].

Intra-cardiac complications were based on echocardiography or intraoperative findings (communication between chambers, wall dissection, abscess, or dehiscence).

Since 2011, anaerobes cultured from blood cultures have been identified using MALDITOF. In the case of inconclusive results, identification is with 16S PCR and sequencing. Identification was further confirmed with 16S PCR of the valve tissue, when available. In the 3 episodes of endocarditis diagnosed before 2011, the isolates were identified using conventional biochemical tests.

2.3. Statistical analysis

Quantitative variables were expressed as mean ± SD or as medians with IQR as appropriate. Qualitative variables were expressed as frequency and percentage. Continuous variables were compared using the *t*-test, and categorical variables were compared using the chi-square test or Fisher exact test when the chi-square test was not appropriate. All statistical analyses were performed using SPSS software version 18 (IBM PASW Statistics 18.0, Armonk, NY, USA).

3. Results

Among the 2491 patients with definite IE, 22 cases (0.9%) were caused by anaerobic bacteria. The remaining cases of non-anaerobic IE were distributed as follows: aerobes, 2469 (90.1%); unknown etiology, 82 (5.0%); fungi, 32 (1.9%); and polymicrobial, 34 (2.1%).

The most common pathogens were *Propionibacterium acnes* (14 [63.6%]), *Lactobacillus* spp (3 [13.63%]), and *Clostridium* spp. (2 [9.0%]), followed by *Peptostreptococcus* spp. (2 [9.0%]), and *Bacteroides fragilis* (1 [7%]).