

# *Aggregatibacter aphrophilus* aortic valve infective endocarditis

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## Abstract

Nowadays, infective endocarditis remains a major cause of morbidity and mortality worldwide and there are concerns related to the increased number of infections associated with virulent agents and medical procedures. We present a case of a homeless man with unknown medical history, admitted for lumbar pain who became confused, hypotensive and tachycardic, evolving to severe sepsis. His initial investigation was also suggestive of acute myocardial infarction but the transthoracic echocardiogram revealed massive aortic valve vegetation with perivalvular abscess leading to severe aortic regurgitation. The patient died with the final diagnosis of infective endocarditis. Later on the blood cultures was identified *Aggregatibacter aphrophilus*, an HACEK group agent. This case confirms that, albeit the general favorable outcomes, there are cases of serious infections, especially if the diagnosis and treatment were late.

**Keywords:** Infective endocarditis; Sepsis; *Aggregatibacter aphrophilus*; HACEK group

## Endocarditis infecciosa en válvula aórtica por *Aggregatibacter aphrophilus*

### Resumen

Hoy día, la endocarditis infecciosa continúa siendo una causa importante de mor-bimortalidad en todo el mundo y es preocupante el aumento del número de infecciones asociadas con agentes virulentos y procedimientos médicos. Presentamos el caso de un indigente con antecedentes médicos desconocidos, ingresado por dolor lumbar, que comenzó a sentirse confuso, hipotenso y taquicárdico. Poco después de su ingreso su estado evolucionó a septicemia grave. Los resultados de las pruebas iniciales también eran indicativos de infarto agudo de miocardio, pero el ecocardiograma transtorácico reveló una vegetación masiva en la válvula aórtica con absceso perivalvular condicionando regurgitación aórtica grave. El paciente murió, con el diagnóstico definitivo de endocarditis infecciosa. Más tarde, en los hemocultivos se identificó *Aggregatibacter aphrophilus*, un microorganismo del grupo HACEK. Este caso confirma que, a pesar de los resultados favorables en general, hay casos de infecciones graves, sobre todo si el diagnóstico y el tratamiento fueron tardíos.

**Palabras clave:** Endocarditis infecciosa; Septicemia; *Aggregatibacter aphrophilus*; Grupo HACEK

## Introduction

Currently, infective endocarditis (IE) is a rare disease with a yearly incidence estimated in 3-10 per 100,000 people,<sup>1</sup> remaining a major cause of morbidity and mortality, apart from improvements both in diagnostic and therapeutic management.<sup>2</sup> Since cardiac valves can be destroyed leading to heart failure and vegetations can embolize, mainly to the brain but also to other organs, if left untreated IE can assume 100% mortality.<sup>3</sup> The epidemiology varies worldwide, and concerning the etiology there have been some changes in the last decades, not only in regard to the microbiological agents, but also to the predisposing factors. While rheumatic heart disease represents the main risk factor and the leading cause of IE in low-income countries, in high-income ones, virulent staphylococci have overwhelmed penicillin-sensitive oral streptococci, especially in relation to health care infections and invasive

procedures.<sup>1</sup> The major traditional risk factors are native valve disease, diabetes, immunosuppression and intravenous drug use. Apart from that, IE is increasingly associated with prosthetic valve and intracardiac devices.<sup>4</sup> Diagnosis relies on clinic aspects, microbiology and echocardiography, either transthoracic or transesophageal echocardiogram, which remains the technique of choice for the diagnosis of IE. Prognosis is determined by patient characteristics, the presence or absence of cardiac and non-cardiac complications, the infecting organism and the echocardiographic findings.<sup>2</sup>

## Clinical case

We present the case of a 50-year-old homeless man, with unknown past medical history, who was admitted at the emergency room after being found lying on the street, complaining of lumbar pain. On examination, he was cachectic

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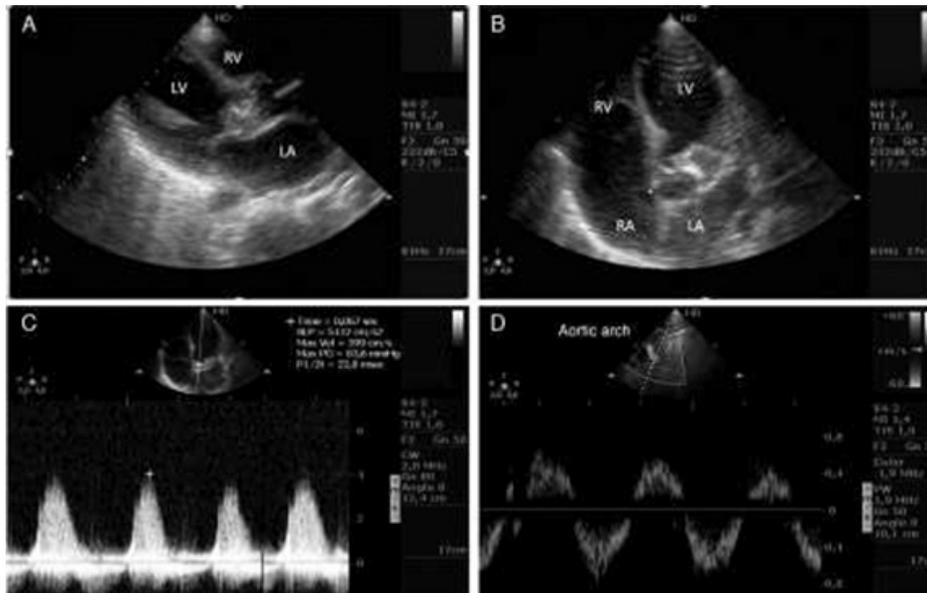
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with evident poor hygiene. Initially conscious, he became confused, showing signs of shortness of breath (respiratory rate 30 breaths/min), hypotensive (blood pressure of 79/33 mmHg) and tachycardic (pulse rate of 130 bpm). His cardiac sounds were arrhythmic, presenting grade II diastolic murmur and pulmonary examination was significant for crackles on the posterior basal region, bilaterally. He had no visible puncture wounds and the remaining observation was unremarkable. Assessment of arterial gases was compatible with severe metabolic acidemia (pH: 7.096; pCO<sub>2</sub>: 12.4 mmHg; HCO<sub>3</sub>: 3.7 mEq/L) with raised lactates (19.1 mg/dL) and laboratory tests revealed leucocytosis (white blood count of 49.2 × 10<sup>9</sup>/L with 96.3% neutrophils), thrombocytopenia (platelets of 14 × 10<sup>9</sup>/L), azotaemia (urea nitrogen: 231 mg/dL and cre-atinine 2 mg/dL), elevated myocardial necrosis markers (myoglobin: 1314.8 ng/mL; creatine kinase: 732 UI/L and troponin T hs: 672 ng/L with reference normal less than 13 ng/L) as well as C-reactive protein (10.2 mg/dL). The electrocardiogram showed atrial fibrillation with rapid ventricular response, ST-segment depression on inferior derivations and Q waves on the precordial ones. According to this, initially, severe sepsis and type 2 acute myocardial infarction were assumed. However, transthoracic echocardiogram showed diffuse left ventricle hypokinesia with depressed ventricular ejection and massive aortic valve vegetation with perivalvular abscess leading to severe aortic regurgitation (Fig. 1). The patient died 12 h after admission with the final diagnosis of native valve infective endocarditis. Meanwhile, the 3 blood cultures collected on admission were incubated in BACTEC® (Becton and Dickinson) automated blood culture monitoring

system, and since growth index of blood was positive in all samples were cultured on blood agar plate and incubated at 37 ° C in 5% CO<sub>2</sub>. After 48 h, colonies were finally identified as *Aggregatibacter aphrophilus*, using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) sequencing method.

### Discussion

*Aggregatibacter aphrophilus*, which includes both species *Haemophilus aphrophilus* and *H. paraphrophilus*, is a Gram-negative bacteria member of the normal flora of the human oral cavity and pharynx.<sup>5</sup> It was described, in 1940, as an atypical cause of IE and currently is an agent of the HACEK group (*Haemophilus parainfluenzae*, *Aggregatibacter actinomycetemcomitans*, *Aggregatibacter aphrophilus*, *Aggregatibacter paraphrophilus*, *Cardiobacterium* spp., *Eikenella corrodens* and *Kingella* spp.), responsible for 1.4-3% of cases of IE.<sup>6</sup> *A. aphrophilus* may also cause brain abscess and has been isolated in different sites, including peritoneum, pleura, wound and bone.<sup>5</sup> These organisms are fastidious and antimicrobial susceptibility testing is difficult and impractical in many laboratories, which can be problematic especially in those without automated identification methods. Since ampicillin-resistant strains were recognized, the recommended empirical treatment of IE due to these organisms is therefore a broad-spectrum cephalosporin or a fluoroquinolone.<sup>7</sup> Although outcomes are generally successful, the IE HACEK infections can be extremely serious, especially if the organism is not early identified.<sup>8</sup>



**Figure 1.** Transthoracic echocardiogram: parasternal long-axis view in panel A showing a voluminous mass attached to aortic valve (red arrow) compatible with a vegetation obstructing the left ventricle outflow tract (LVOT); apical five chambers view in panel B showing an echo lucent area in the aortic root area suggesting the presence of a paravalvular abscess (red arrow); continuous Wave Doppler through the LVOT showing a dense aortic regurgitant flow with a very short pressure-half time (panel C); panel D - Pulsed Wave Doppler on descending part of aortic arch showing holodiastolic flow reversal in favor of severe aortic regurgitation. LA: left atrium; RA: right atrium; LV: left ventricle; RV: right ventricle.

This case presents special relevance, not only for its presentation with sepsis and severe aortic regurgitation, but also highlights the serious complications that infections related to fastidious growth bacteria can assume, demanding a prompt diagnosis and treatment. Moreover, since *A. aphrophilus* is a member of the normal oral human flora, dental programs campaigns and health community surveillance are needed in order to prevent these kinds of infections.

### Ethical disclosures

Protection data of people and animals. The authors state that for this investigation have not been performed experiments on humans or animals.

Confidentiality of data. The authors declare that this article does not appear names or data of the patient.

Right to privacy and informed consent. The authors declare that this article does not appear patient data.

### Conflict of interest

The authors declare no conflict of interest.

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