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CES MEDICINA

CASE REPORT

A Rare Case of HACEK Endocarditis in the Context of a Permanent Pacemaker

Un caso raro de endocarditis HACEK en el contexto de un marcapasos permanente

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How to cite: Echavarría-Cross A, Escobar-Gil T, Roncancio-Villamil G, Durango-Gutiérrez L. A Rare Case of HACEK Endocarditis in the Context of a Permanent Pacemaker. *Rev CES Med*. 2023;37(2). pp. 90-95. https://dx.doi.org/10.21615/cesder.7273

Abstract

Introduction: Infective endocarditis (IE) is a serious medical condition that can lead to high morbidity and mortality rates. The prevalence of healthcare-associated IE is increasing due to the use of therapeutic devices, such as intravascular catheters and cardiac devices. The HACEK group of bacteria, are commonly found in human respiratory and genitourinary tracts, are low virulence and fastidious organisms that are associated with blood culture-negative endocarditis. Proper diagnosis requires a combination of clinical, microbiological, and imaging results. The following study presents a case of atypical device-associated IE caused by Haemophilus influenzae in a 56-year-old man with a permanent pacemaker. **Methodology:** description of a clinical problem, its diagnosis, management, and outcome, accompanied with a literature review. **Conclusion:** This study highlights the importance of considering the HACEK group of bacteria in culture-negative IE cases and the use of advanced imaging techniques in diagnosis to prevent further complications and improve patient outcomes.

Keywords: bacterial endocarditis; HACEK group; Haemophilus influenzae; artificial pacemaker; cardiac imaging techniques.

Resumen

Introducción: La endocarditis infecciosa (EI) es una condición médica grave que puede llevar a altas tasas de morbilidad y mortalidad. La prevalencia de la EI asociada a la atención médica está aumentando debido al uso de dispositivos terapéuticos, como catéteres intravasculares y dispositivos cardiacos. El grupo de bacterias HACEK, se encuentra comúnmente en las vías respiratorias y genitourinarias humanas, son organismos de baja virulencia y de crecimiento fastidioso, los cuales están asociados con la endocarditis de hemocultivos negativos. El diagnóstico adecuado requiere una combinación de resultados clínicos, microbiológicos y de imágenes. El siguiente estudio presenta un caso de una EI atípica asociada a un dispositivo cardiaco causada por Haemophilus influenzae en un hombre de 56 años con un marcapasos permanente. **Metodología**: descripción de un problema clínico, su diagnóstico, manejo y resultado, acompañado de una revisión de la literatura. **Conclusión**: Este estudio destaca la importancia de considerar el grupo de bacterias HACEK en casos de EI negativos para cultivos y el uso de técnicas avanzadas de imágenes en el diagnóstico para prevenir complicaciones adicionales y mejorar los resultados del paciente.

Palabras clave: endocarditis bacteriana, grupo HACEK, Haemophilus influenzae, marcapaso artificial, técnicas de imagen cardíaca.

Date of correspondence:
Received: March 27, 2023.
Revised: March 30, 2023.
Accepted: June 20, 2023.

DOI: 10.21615/cesmedicina.7273
ISSNe: 2215-9177
ISSN: 0120-8705
https://revistas.ces.edu.co/index.php/medicina

Introduction

Infective endocarditis (IE) is a relatively rare but life-threatening disease [1]. It is associated with considerable morbidity and mortality, resulting from local damage to cardiac structures, metastatic infection, embolic phenomenon, or immune-mediated damage [2]. The incidence of IE is estimated to be around 1.5 to 11.6 cases per 100,000 person-years, and its mortality close to 25 % [1,3].

Healthcare-associated IE, which is an even more infrequent entity, arises secondary to the introduction of new therapeutic modalities, such as intravascular catheters, cardiac devices, and dialysis shunts [1].

The main microorganisms implicated in device associated IE are *Staphylococcus, Streptococcus,* and *Enterococcus,* followed by Gram-negative bacteria [1,4]. However, in up to 20 % of cases of IE, cultures come back negative, and no causal agent can be identified [1]. One important group of bacteria to consider in these cases is the HACEK group [5]. HACEK is an acronym comprising the first letters of the generic names of the following group of bacteria: *Haemophilus, Aggregatibacter, Cardiobacterium., Eikenella* and *Kingella*. These organisms are fastidious Gram-negative bacteria found in the human upper respiratory and genitourinary tracts. It accounts for only 3 % of cases of IE [1,3,6], and only 1.4 % of prosthetic valve endocarditis (PVE) [5,7].

The diagnosis of IE typically requires a combination of clinical, microbiological, and imaging results [1]. Furthermore, the diagnosis of device-associated IE or PVE, is even more challenging, since classical and modified Duke criteria lack sensitivity[5,8]. Transesophageal echocardiography (TEE) becomes a valuable tool in all cases of suspected device-associated IE, as detection of vegetations may be difficult due to artifacts, and therefore a negative transthoracic echocardiography (TTE) cannot be considered a rule out. Other alternatives like F-fluodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) scan, have been used supplementally in these cases with success [2,8–10].

Case description

We present the case of a 56-year-old male, with a past medical history of well controlled type 2 diabetes mellitus, chronic pulmonary thromboembolism (anticoagulated with warfarin), and a carrier of a bicameral pacemaker due to sinus dysfunction implanted 13 years ago. He consulted his primary care physician for 25 days of dyspnea on medium exertion and fever. Plain X rays and bloodwork were done in a local hospital (with unknown results) and during follow-up clarithromycin was prescribed for a short term.

The patient felt no improvement and decided to go to the emergency department at our institution in which normal vital signs and an unremarkable physical exam were noted, later on the patient kept. On admission, the patient had no fever, however, daily fever was documented during hospitalization. An electrocardiogram (EKG) was done, and it evidenced correct pacemaker functioning, therefore complete blood count, blood cultures, and a transthoracic echocardiogram (TTE) was requested. The TTE described normal sized cavities, a left ventricular ejection fraction of 60-65 % with preserved systo-dyastolic function, right cavities with an hyperechogenic image corresponding to a pacemaker electrode and normal valvular structures (except for having mild valve regurgitation), without vegetations.

During the initial approach to the disease, thorax and abdomen contrasted CT scans were also done, without relevant findings; blood cultures were negative; HIV, Hepatitis B and C virus infection were excluded as well as tuberculosis; blood count documented 12,500 white blood cells, with neutrophilia; and CRP was 19 mg/dL, indicating significant inflammation. At this point, fever of unknown origin was considered and a few days later the patient developed polyarthritis of his shoulders, elbows, and wrists as well as lower back pain. ANA, ANCA, ENAS were all negative, and PET/CT scan was warranted in search of infectious/neoplastic foci.

The PET/CT scan revealed increased metabolism around the pacemaker electrodes in a moderate and diffuse manner, mainly at the level of the coronary venous sinus and right atrium (Figure 1A and 1B).

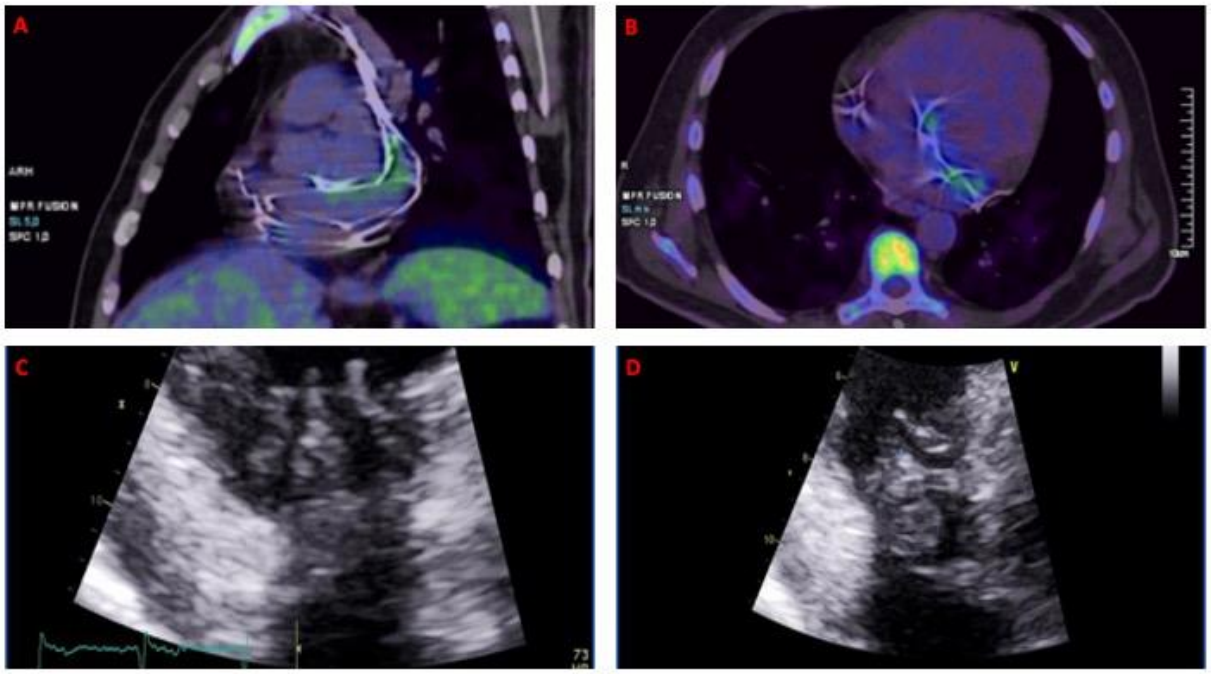

Figure 1: A and B: Abnormal increase of metabolism is observed in a positron emission tomography (PET) around the pacing electrodes in a moderate and diffuse manner, mainly at the level of the coronary venous sinus and the right atrium, without tomographic representation; **C and D:** Vegetations in the anterior and septal leaflets of the tricuspid valve are seen on echocardiography, measuring 1.2x1.7 cm and 1.1x1.7 cm, and adhered to pacemaker leads.

Thereafter electrophysiology and infectious diseases were consulted, and the patient was scheduled for device instrumented extraction; a second blood culture set (both blood culture sets were monitored for up to 5 days, without special growth media for HACEK bacteria), was also taken with a final negative result and due to the patient's clinical stability and lack of identification of the causal agent, antibiotic treatment was deferred. An intraprocedural ultrasound documented a mass on the septal and posterior leaflets of the tricuspid valve. After the procedure, deep tissue, the pacemaker capsule, electrodes, and cables were sent to be cultured for bacterial and fungal agents; vancomycin and ceftriaxone were started, and a temporary electrode was inserted to be connected to an externalized device.

Transesophageal echocardiogram (TEE) was obtained confirming the presence of vegetations in the anterior and septal leaflets of the tricuspid valve, measuring 1.2x1.7 cm and 1.1x1.7 cm, respectively, with mild valve regurgitation (Figure 1C and 1D). In addition, another mass of 3.6 cm extended through the coronary sinus, and no other complications were noted. Infectious diseases considered that there was no surgical indication at this time, and while culture results arrived, empiric antibiotics were continued. Five days later, *Haemophilus influenzae* was isolated from the atrial and ventricular electrodes. The sensitivity report indicated that the specimen tested negative for betalactamase and consequently treatment was suspended, ampicillin/sulbactam was started.

After a week of antibiotic course, a second TEE was performed, documenting persistence of the vegetations previously described, and consequently antibiotics were continued for one more week. Afterwards, a new TTE was obtained, documenting vegetations on the anterior leaflet (2.1 x 1.2 cm) and septal leaflet (1.1 x 1.6 cm) of the tricuspid valve, with mild valvular regurgitation, and the previously documented vegetation protruding through the coronary sinus (0.9 x 1.4 cm) (Figure 2).

Figure 2: Echocardiography showing vegetations on the anterior leaflet and septal leaflet of the tricuspid valve, and the previously documented vegetation protruding through the coronary sinus.

Finally, due to persistence of the lesions despite targeted antibiotic therapy, it was decided in conjunction with cardiology and cardiovascular surgery to perform minimally invasive cardiac surgery.

Valvuloplasty was performed and a 2 cm “mushroom-shaped” lesion was found implanted between the posterior annulus and the atrial side of the tricuspid leaflet, with rupture of a tendinous cord of the anterior leaflet. Intraoperative TEE was performed documenting no complications and a good biventricular function. After almost a month of hospitalization, the patient was discharged with follow-up and targeted treatment for 3 more weeks from the time of surgery. Due to the patient's low pacing percentage and the high risk of infection associated with implanting a new cardiac pacing device, he was discharged without receiving a new device.

Discussion

Prosthetic valves and cardiac devices (such as permanent pacemakers and cardioverter defibrillators) are significant risk factors for IE and difficult diagnosis [1,4,8,11,12]. Since rates of cardiac device implantation have increased in the last years, rates of associated infectious endocarditis are also increasing. In a recent worldwide cohort of 2,781 adults in 20 % had a prosthetic valve and 7 % had a cardiac device. Right-side endocarditis account for up to 5-10 % of cases, and 90 % of them affect the tricuspid valve, as in our case [1].

The decision to perform TTE or TEE does not exclude one from the other, they are complementary. TTE is a more sensitive method for right structures (pulmonary and tricuspid valves). On the other hand, TEE is in general more sensitive and specific, it performs better for left structures, especially in the presence of prosthetic valves and to detect mechanical complications [1,9,10,13,14]. In the context of cardiac device-related disease both are recommended but TEE results in better performance compared to TTE. Neither modality is useful for evaluating pocket/generator infections, or extravascular electrodes [10,11]. The use of PET/CT becomes useful in the context of prosthetic valve infection or presence of cardiac devices. This method provides adequate visualization of anatomical structures, pocket/generator, and extracardiac/extravascular lead involvement. On the counterpart, sensitivity is low for small vegetations and electrode-related lesions if the documented hypermetabolism is low and mild, however if the tracer is well visualized (and interpreted under the appropriate clinical setting) can result highly specific for infectious lesions associated with device leads and motivate removal [10,14].

In our case, the patient had previously received antibiotics for suspected pulmonary infection. As a result, he did not have fever upon admission, and the initial cultures were negative. An alternative diagnosis was considered and in light of having a cardiac device a TTE was ordered to explore the possibility of IE. Despite negative TTE and other imaging modalities mentioned, inflammation was evident through elevated acute phase reactants and daily fever. A high suspicion of infective endocarditis remained, and a PET/CT was performed to investigate possible inflammatory/infectious sources, taking into account the development of rheumatological symptoms mentioned. It was thought that this diagnostic tool could provide valuable information regarding these two differential diagnoses. PET/CT ruled out inflammatory bone involvement and described a hypermetabolic activity in right sided leads, which motivated device removal and a 14-day antibiotic course was warranted to consider device reimplantation provided blood cultures were negative. Intraoperative tissue, cable and lead material was cultured because of the difficulty in documenting an infectious etiology [11,14]. Finally, *Haemophilus influenzae* grew in the cultured material. The initial cultures were probably grown for a very short period, so no positive results were obtained. The HACEK group bacteria are considered low virulence fastidious organisms, relevant in blood culture negative endocarditis, mostly affecting structurally damaged or prosthetic cardiac valves and accounting for less than 10 % of the cases of IE [1,5,6].

In the first instance, this patient did not meet the indications for cardiac surgery due to right-sided endocarditis (vegetations >20mm in persistent tricuspid valve after recurrent pulmonary embolism with or without right heart failure or severe tricuspid insufficiency), despite directed antibiotic treatment, there was persistence of the lesions so that surgery was needed [9,13]. Notably when he was discharged, he did not require implantation of a new device, consistent with literature reports in up to 30 % of cases (possibly due a diagnosis of sinus dysfunction that was not well supported at the time) [4,6,11,12,14,15].

Conclusions

After a thorough English and Spanish language literature search, this is one of the few cases, to our knowledge, of *Haemophilus influenzae* endocarditis in a patient with a permanent pacemaker. Our patient had a cardiac pacing device and diabetes as risk factors, and despite initial imaging and negative blood cultures, he was taken to advanced imaging techniques that led to device removal, culture, and etiologic diagnosis. The importance of recognizing this type of organism is that, although it is an infrequent etiology of endocarditis, it should be considered in the context of culture-negative cases.

Financing disclosure

No funding was received for the elaboration or publication of this article.

Conflict of interest

The authors of this research declare that there are no conflicts of interest that may affect the content, results, or conclusions of the article.

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