SCIENTIFIC LETTER

Recurrent Infective Endocarditis Due to *Klebsiella Pneumoniae*

Endocarditis infecciosa recurrente por Klebsiella pneumoniae

FERNANDO ALBERTO MACHADO GÓMEZ[1], MATEO AGUIRRE FLÓREZ[1], EFRAÍN SANTIAGO GUZMÁN BEDOYA[2], DIEGO ALEJANDRO MEDINA MORALES[2], JAVIER GUSTAVO MARTÍNEZ AROCA[2]

Infective endocarditis (IE) is the inflammation of the heart's lining and valves of infectious origin. (1) It is classified as acute, subacute, and chronic. (2) It is also necessary to differentiate whether a native or prosthetic valve is involved, the number of valves affected, and the form of acquisition (in the community or associated with health care). (3)

In developed countries, IE has an annual incidence of approximately 2.7 to 10 cases per 100 000 persons per year. In Colombia, the incidence is around 0.25 to 0.31 per 100 000 inhabitants, translating into approximately 500 cases annually. Mortality varies among different populations but may range from 15% to 45% of cases, depending mainly on the age and the patient, whether it affects a native or prosthetic valve, and the causal microorganism. (1,2)

In 80 to 90% of cases, gram-positive bacteria such as streptococci, staphylococci, and enterococci are IE most frequent causative agents. In a smaller proportion, HACEK gram-negative bacilli (*Haemophilus spp., Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella spp.*), non-HACEK gram-negative bacilli, and fungi are isolated in this pathology. (2)

Several factors favor this infection, including bicuspid aortic valve, mitral valve prolapse, congenital cardiac malformations, rheumatic fever, valve prostheses (especially those recently implanted), implantation of intracardiac devices, age over 60 years, male sex, immunosuppression, and long-term venous access devices. (3)

We present the case of a 56-year-old male, farmer, without medical history of cardiovascular risk factors or illness. He consulted a first-level hospital for lower abdominal pain, fever, chills, dysuria, pollakiuria, urinary urgency, and urinary retention. The patient presented with a heart rate of 80 bpm, respiratory rate of 20 breaths per minute, blood pressure of 110/80 mm Hg, oxygen saturation of 92% on room air and a temperature of 38.2°C. Physical examination revealed diaphoresis, hypogastric pain, and a ballon-like bladder. Laboratory tests showed leukocytosis (24 700 cells/μL, 95% neutrophils), hemoglobin 11.8 g/dL, platelet count 28 000, sodium 123 mmol/L, potassium 4 mmol/L, and blood urea nitrogen (BUN) 158 mg/dL. Prostate specific antigen (PSA) was elevated at 10.4 ng/mL.

The urinary tract tomography revealed bilateral perirenal inflammatory changes. Blood cultures identified *Klebsiella pneumoniae ESBL ssp* (producing extended-spectrum beta-lactamase), resistant to several antibiotics including ceftazidime, ceftriaxone, and ciprofloxacin, but sensitive to imipenem, meropenem, tigecycline, and amikacin. Meropenem was started. The patient progressed to septic shock and multiorgan dysfunction and was admitted to the Intensive Care Unit (ICU) requiring vasopressor support, transfusion of hemocomponents due to severe thrombocytopenia (8000/μL), and renal replacement therapy. A transthoracic echocardiogram was performed with findings suggestive of vegetations. A transesophageal echocardiogram (TEE) showed multiple vegetations in the aortic valve with valvular stenosis and severe regurgitation . A diagnosis of possible native valve endocarditis was made (according to Duke criteria), (4) and he was referred to a higher complexity institution for aortic valve replacement with a mechanical prosthesis without complications. He completed 42 days of antibiotic coverage and was discharged.

One week later, he was readmitted to our institution due to dyspnea on exertion and lower limb edema that progressed to anasarca. The patient presented

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Correspondence: E-mail: maguirref96@utp.edu.co

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[1] GIMCCI Critical Medicine and Intensive Care Research Group. Technological University of Pereira, Pereira, Risaralda, Colombia
[2] Internal Medicine Research Group. Technological University of Pereira, Pereira, Risaralda, Colombia

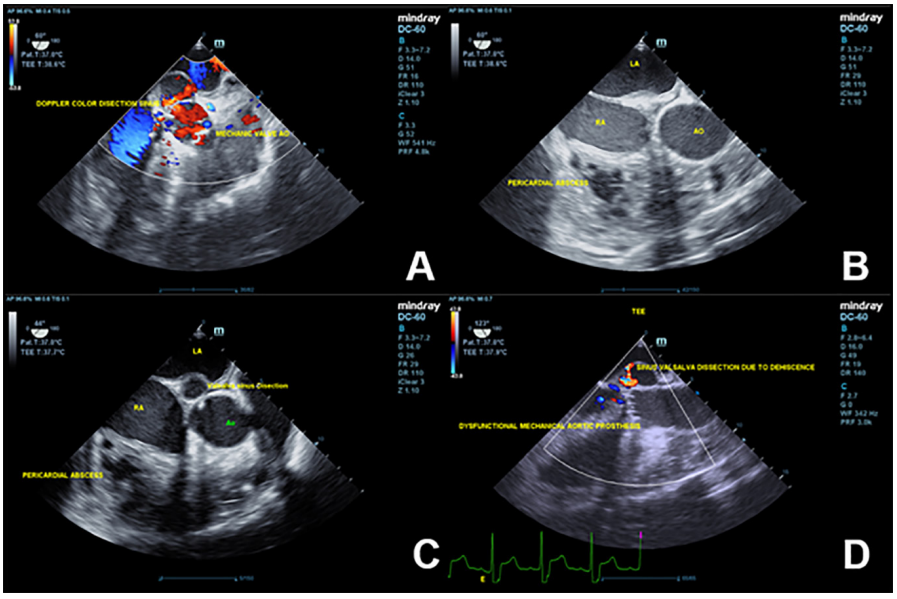

Fig. 1. A. Transesophageal echocardiogram showing a mechanical aortic prosthesis with dissection of the sinus of Valsalva. Note the color Doppler flow of the dissection jet. **B.** Transesophageal echocardiogram with septated pericardial space image compatible with abscess. LA: Left Atrium, RA: Right Atrium, AO: Aorta. **C.** Transesophageal echocardiogram in short axis view for large vessels where the dissected sinus of Valsalva is observed; inferior to the right atrium, a fibrinoid image is observed in the pericardial space. LA: Left Atrium, RA: Right Atrium, AO: Aorta. **D.** Transesophageal echocardiogram showing mechanical aortic prosthesis with dehiscence and aneurysm of the sinus of Valsalva; below the aortic valve, there is rupture of the interventricular septum, with color Doppler flow from the left ventricle to the right ventricle

with a heart rate of 72 bpm, respiratory rate of 20 breaths per minute, blood pressure of 87/52 mmHg, and oxygen saturation of 92% on FiO2 of 28%. The temperature was 36°C. Physical examination revealed a surgical wound without discharge, aortic diastolic murmur, and grade III lower limb edema. Laboratory findings included leukocytes 12 470/μL (88% neutrophils), hemoglobin 11.8 g/dL, platelet count 328 000 / μL , sodium 131 mmol/L, potassium 4 mmol/L, creatinine 3.5 mg/dL, and BUN 50 mg/dL. Blood cultures again identified *Klebsiella pneumoniae ssp* producing ESBL, with similar resistance patterns to previous admission but now also sensitive to ertapenem and cefepime. A new set of blood cultures was positive for *Klebsiella pneumoniae ESBL* growth. Given the recent surgical history, a transesophageal echocardiogram was performed, showing a dysfunctioning mechanical aortic prosthesis, sinus of Valsalva aneurysm, and an image suggestive of vegetation in the anterior mitral chord, and pericardial abscess. (Figure 1) A diagnosis of possible prosthetic valve endocarditis (according to Duke criteria) (4) due to *Klebsiella pneumoniae* was made, and the patient was treated with meropenem for 42 days under the direction of the infectious disease department. Finally, he was again referred to a cardiovascular referral center for further surgery which was successfully performed. The patient recovered and continued with his treatment.

Gram-positive bacteria mainly cause IE; gram-negative organisms (GN) are relatively rare causative agents associated with significant morbidity and mortality. Among the GN organisms causing IE, the HACEK group stands out; other GN organisms are less frequent and have attracted attention because of their propensity to develop and spread resistance, their high attributable mortality, and their association with increased healthcare costs. (5) Among the latter, *Klebsiella pneumoniae* accounts for an incidence of approximately 1.5% of cases of IE but with a mortality rate of up to 20%. (3-5)

A systematic review of the literature on Klebsiella endocarditis was published in 2021 by Petros Ioannou et al. Up to February 2021, 67 cases were reported, 45 due to *Klebsiella pneumoniae*; the aortic valve was the most frequently involved and in 16% of patients it affected the prosthetic valve. The main clinical features were fever in 98% of cases, sepsis in 78%, shock in 31%, paravalvular abscess in 15%, and heart failure in 21% of cases. (5) These findings are consistent with those found in our patient who initially presented with native aortic valve involvement and later with prosthetic aortic valve involvement, in addition to the fact that he presented with clinical characteristics similar to those reported in that study, plus the finding of paravalvular abscess. A case report of *Klebsiella pneumoniae* IE associated with emphysematous cystitis described a patient with urinary tract infection that progressed to septic shock. (5,6) Transesophageal echocardiography showed vegetation and perforation of the mitral valve, and also renal dysfunction (creati-

nine 2.7 mg/dl), leukocytosis (27 000 /μL), thrombocytopenia (17 000/μL), and hypoalbuminemia (2.3 mg/dL). Compared with our case and except for valvular involvement, both patients share similar characteristics, highlighting the presence of thrombocytopenia, renal injury, and hypoalbuminemia. (5)

This case of IE relapse, initially of the native valve and later of the prosthetic valve due to Klebsiella pneumoniae, highlights several essential aspects in the clinical management of this entity. While infective endocarditis is an uncommon complication of valvular prostheses, *Klebsiella pneumoniae* as the etiologic agent is even more unusual and deserves special attention due to its potential virulence and antimicrobial resistance.

Worldwide, most prosthetic valve-associated IE cases are caused by organisms such as *Staphylococcus aureus, Streptococcus viridans*, and *Enterococcus spp*. However, a greater diversity of pathogens is observed in Latin America and other developing regions, including gram-negative bacteria such as *Klebsiella pneumoniae*. (5,6) This may pose additional challenges in diagnosis and treatment, especially in settings with limited microbiology and laboratory resources. In addition, the lack of epidemiological data reporting the causative agents and their distribution by population, coupled to the clinical features with which patients debut, that differ from one patient to another, means that clinical suspicion and treatment may only sometimes be timely. (5)

Diagnosing infective prosthetic valve endocarditis is challenging due to variability in clinical presentation and laboratory findings. Early identification of *Klebsiella pneumoniae* as the causative agent was crucial to guide appropriate antimicrobial treatment in the present case. (5) However, in areas with limited microbiology resources, diagnosis may be delayed or missed, with severe consequences for the patient. This can lead to heart failure of valvular origin, sepsis, embolic stroke, and even death. (6)

Treatment of infective prosthetic valve endocarditis also presents unique challenges, especially in cases caused by gram-negative bacteria such as *Klebsiella pneumoniae*. Selection of appropriate antibiotics is crucial, but increasingly common antimicrobial resistance can complicate this process. In addition, surgical management may sometimes be necessary to remove infected tissue and restore valve function. (1,6)

This case report presents an uncommon manifestation of infective aortic prosthetic endocarditis caused by *Klebsiella pneumoniae*, which adds value to medical knowledge by providing a detailed description of the clinical presentation and an accurate diagnosis of the etiologic agent. In addition, follow-up during treatment offers valuable information on the therapeutic response and the need for surgical intervention. However, the limited availability of advanced microbiological tests may have affected the speed of diagnosis. Also, the generalization of findings from a single case may be limited, highlighting the need for additional studies for better understanding. Furthermore, more than the duration and completeness of follow-up may be required to assess full long-term prognosis. At the same time, the lack of comparative data with other similar cases makes it difficult to interpret and contextualize the results.

In conclusion, Non-HACEK GN organisms are rarely responsible for IE, and are mainly related to IE associated with intravenous drug use or IE associated with health care in patients with complex comorbidities (end-stage renal disease, neoplasia). It is essential to follow up on this disease since knowing this type of case allows to determine the multidisciplinary team's diagnostic and therapeutic strategies.

Ethical considerations

This report was written following Helsinki's declaration. The institutional bioethics committee endorsed this work and recognized this research as safe. Informed written consent was obtained from the patient when he moved to the general ward.

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Conflicts of interest

None declared.

(See conflicts of interest forms on the website).

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