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ELIZABETHKINGIA MENINGOSEPTICA BACTEREMIA IN AN OLDER ADULT. A CASE REPORT

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Palabras clave: Farmacorresistencia Microbiana; Bacteriemia; *Elizabethkingia Meningoseptica.*

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ABSTRACT

Introduction: *Elizabethkingia meningoseptica* is a multidrug-resistant gram-negative bacillus that can cause nosocomial infections such as pneumonia, bacteremia, and meningitis. Infection in humans is particularly unusual, as this microorganism is considered an opportunistic pathogen that rarely affects patients with uncompromised immune systems.
Case presentation: A 92-year-old woman presented to the emergency department of a tertiary care institution in Ibagué (Colombia) with symptoms suggestive of acute coronary syndrome. The patient, who had a history of arterial hypertension, type 2 diabetes mellitus, and atrioventricular block, developed unexplained elevation in body temperature on the second day of admission, so a complete blood count was requested, revealing moderate leukocytosis. On the fourth day of hospitalization, her overall clinical condition deteriorated and due to a high suspicion of bacteremia, treatment was initiated with cefepime 1g IV every 8 hours and vancomycin 1g IV every 12 hours for 5 days. Two blood cultures from the upper limbs were requested, confirming the presence of *E. meningoseptica*. Given these findings, treatment was switched to meropenem 2g IV every 8 hours, amikacin 500mg IV every 12 hours, and colistin 150mg IV every 12 hours. However, on the fifth day of the new treatment, the patient experienced further clinical deterioration and ultimately died 14 days after admission.
Conclusions: *E. meningoseptica* is an opportunistic pathogen that is potentially fatal due to treatment challenges. Therefore, it is extremely important to acknowledge its existence in hospital settings and to establish clinical criteria to facilitate its early identification and initiate timely management.

RESUMEN

Introducción. *Elizabethkingia meningoseptica* es un bacilo gramnegativo multirresistente que puede causar infecciones de tipo nosocomial como neumonía, bacteriemia y meningitis. La infección en humanos es especialmente inusual, ya que este microorganismo se considera un patógeno oportunista que rara vez afecta a pacientes con sistemas inmunológicos no comprometidos.
Presentación del caso. Mujer de 92 años que acudió al servicio de urgencias de una institución de tercer nivel de atención en Ibagué (Colombia) por sintomatología sugestiva de síndrome coronario agudo. La paciente, quien tenía hipertensión arterial, diabetes *mellitus* tipo 2 y bloqueo auriculoventricular, presentó aumento de la temperatura corporal (37.4°C) sin causa aparente al segundo día de ingreso, por lo cual se ordenó hemograma completo que evidenció leucocitosis moderada. Al cuarto día del ingreso su estado clínico empeoró, y debido a una alta sospecha de bacteriemia, se inició tratamiento con cefepime 1g intravenoso (IV) cada 8 horas

y vancomicina 1g IV cada 12 horas durante 5 días y se ordenaron 2 hemocultivos de miembros superiores que confirmaron la presencia de *E. meningoseptica*. Dados los hallazgos, se reemplazó el tratamiento con meropenem 2gr IV cada 8 horas, amikacina 500mg IV cada 12 horas y colistina 150mg IV cada 12 horas; sin embargo, al quinto día del nuevo tratamiento la paciente presentó deterioro clínico y finalmente murió a los 14 días de su ingreso.
Conclusiones. *E. meningoseptica* es un patógeno oportunista cuya infección es potencialmente mortal debido a que es difícil de tratar. En este sentido, es de vital importancia que se reconozca su existencia en áreas hospitalarias y que se establezcan criterios clínicos que permitan facilitar su identificación de forma temprana y así iniciar un manejo oportuno.

INTRODUCTION

Elizabethkingia meningoseptica is a gram-negative, rod-shaped bacterium commonly detected in the environment, particularly in soil and water (1). It was originally known as *Flavobacterium meningosepticum* (2), but it was given its current name in honor of the microbiologist Elizabeth O. King, who discovered it in 1959 upon isolating a gram-negative bacillus that caused meningitis in infants (1,2). This bacterium belongs to the family *Flavobacteriaceae*, order *Flavobacteriales*, within the genus *Elizabethkingia* (2-4).

E. meningoseptica is a strictly aerobic, non-spore-forming, non-glucose-fermenting, indole- and catalase-positive bacillus (4). It has a capsule layer (composed mainly of polysaccharides) that makes it hydrophilic (5), as well as hemagglutinin adhesins that allow adequate bacterial attachment and cell accumulation (6).

It can cause nosocomial infections in humans, mainly meningitis, and intravascular device-related bacteremia, wound sepsis, and ventilator-associated pneumonia (5,7), as it is mainly found in invasive medical devices (incubators, ventilator tubing, intravenous fluid containers and catheters) and humid environments (3,5,7-9). However, it has also been identified in objects, devices, and surfaces in hospital environments such as locks, keyboards, telephones, medical records, milk formulas (8), sinks, and faucets (2,7). This species is resistant to chlorine disinfectants as it has the ability to exist as a biofilm structure due to its hydrophilic cell surface and multiple surrounding adhesins (2,7).

E. meningoseptica has six unique genes involved in adherence, which encode the curli nucleator protein (*csgB*), the curli assembly proteins (*curEm1, curEm2, curEm3, curEm4*), and a curli production assembly protein (*csgG*) (10). Curli are extracellular fibers that facilitate cell-cell and cell-surface interactions and, therefore, the formation of biofilms that are essential for bacterial adherence (11).

It is worth keeping in mind that a better understanding of *E. meningoseptica* along with more precise diagnostic procedures, better accessibility to treatment options, and improvements in the prevention of transmission and infection may lead to greater control of this extremely pathogenic and highly resistant bacteria (10). The following is the case of a 92-year-old female patient who developed primary bacteremia due to *E. meningoseptica* infection.

CASE PRESENTATION

A 92-year-old female patient was admitted to the emergency department of a tertiary care hospital in Ibagué (Colombia) showing symptoms that suggested an acute coronary syndrome. The patient, who had not undergone any surgery recently, suffered from high blood pressure, non-insulin-dependent type 2 diabetes mellitus, and second-degree atrioventricular block Mobitz type II, for which she underwent a pacemaker implantation in 2018.

On admission physical examination, the following findings were reported: mean arterial pressure: 93.3mmHg; heart rate: 74 bpm; respiratory rate: 18 rpm; temperature: 36.5°C; and blood glucose: 180mg/dL. Results indicated that the patient was hemodynamically stable and showed no signs of respiratory distress, although she presented with persistent retrosternal chest pain radiating to the dorsum and epigastrium, as well as nausea and episodes of vertigo. Pulmonary auscultation did not reveal abnormal breath sounds but decreased normal breath sounds were noted.

Laboratory tests performed on admission showed increased troponin levels, while an electrocardiogram showed no dynamic changes in the ST segment, leading to a diagnosis of acute myocardial infarction without ST-segment elevation. Invasive cardiovascular risk stratification was not performed owing to the risk-benefit ratio.

Table 1. Laboratory tests on admission.

Test	Result	Reference values
Creatinine	0.96mg/dL	0.7-1.3mg/dL
Troponin I (high sensitivity)	1.069ng/mL	0.0-0.06ng/mL
Follow-up Troponin I (high sensitivity) (6 hours after the initial test)	1.267ng/mL	
Prothrombin time (PT)	10.4 seconds	11-13 seconds
Partial thromboplastin time (PTT)	23.1 seconds	25-35 seconds
International normalized ratio	0.99	≤1.1
Hemoglobin	14.6g/dL	12.0-16.0 g/dL
Hematocrit	42%	37.0-47.0 %

Test	Result	Reference values
Red blood cell count	4.92x10^6/µL	4.2-6.1x10^6/µl
Mean corpuscular volume	86.4fL	80.0-99.0fL
Mean corpuscular hemoglobin (MCH)	29.8pg	27.0-31.0pg
Mean corpuscular hemoglobin concentration (MCH)	34.4g/dL	33.0-37.0g/dL
Red cell distribution width	12.6%	11.5-14.5%
Leukocyte count	9.25x10^3/µL	4.5-10.6x10^3/µL
% neutrophils	82%	40.0-74.0%
Absolute neutrophil count	7.58x10^3/µL	1.9-8.0x10^3/µL
% lymphocytes	9.9%	19.0-48.0%
Absolute lymphocyte count	0.92x10^3/µL	0.9-5.2x10^3/µL
% eosinophils	1%	0.0-7.0%
Absolute eosinophil count	0.09x10^3/µL	0.0-0.8x10^3/µL
% monocytes	5.1%	3.4-9.0%
Absolute monocyte count	0.48x10^3/µL	0.1-1.0x10^3/µL
% basophils	0.8%	0.0-1.5%
Absolute basophil count	0.08x10^3/µL	0.0-0.2x10^3/µL
Platelet count	239x10^3/µL	130.0-400.0x10^3/µL
Mean platelet volume (MPV)	7.1fL	7.2-11.1fL

Source: Own elaboration.

Also on admission, a transthoracic echocardiogram was requested, revealing failure of contractility in the anterior descending artery supply territory, mild aortic and mitral insufficiency, well-positioned pacemaker, and no thrombus in situ. In addition, it was established that the patient exhibited an intermediate risk of pulmonary hypertension. Given the findings, anti-ischemic therapy was started with clopidogrel 300mg orally (PO) as a loading dose, with maintenance of 75mg PO daily, and acetylsalicylic acid 300mg PO, with maintenance of 100mg daily. Moreover as recommended by the internal medicine service, the patient received prophylactic treatment with subcutaneous low molecular weight heparin at a dose of 40mg daily.

On the second day of hospital stay, the patient presented an increase in body temperature (37.4°C) and an episode of diarrhea that resolved on its own, so a complete blood count was requested to establish the infectious focus. The results of this test showed moderate leukocytosis, mainly neutrophils (Table 2); thrombocytopenia was not observed.

Table 2. Blood count 48 hours after admission.

Test	Value	Reference values
Hemoglobin	13.30g/dL	12.0-16.0g/dL
Hematocrit	39%	37.0-47.0%
Red blood cell count	4.49x10^6/µL	4.2-6.1x10^6/µl
Mean corpuscular volume	86.9fL	80.0-99.0fL
Mean corpuscular hemoglobin (MCH)	29.7pg	27.0-31.0pg
Mean corpuscular hemoglobin concentration (MCH)	34.2g/dL	33.0-37.0g/dL
Red cell distribution width	12.8%	11.5-14.5%
Leukocyte count	17.56x10^3/µL	4.5-10.6x10^3/µL
% neutrophils	89.1%	40.0-74.0%
Absolute neutrophil count	15.64x10^3/µL	1.9-8.0x10^3/µL
% lymphocytes	5.9%	19.0-48.0 %
Absolute lymphocyte count	1.03x10^3/µL	0.9-5.2x10^3/µL
% eosinophils	1.30%	0.0-7.0 %
Absolute eosinophil count	0.22x10^3/µL	0.0-0.8x10^3/µL
% monocytes	3.00%	3.4-9.0%
Absolute monocyte count	0.53x10^3/µL	0.1-1.0x10^3/µL
% basophils	0.3%	0.0-1.5%
Absolute basophil count	0.04x10^3/µL	0.0-0.2x10^3/µL
Platelet count	219x10^3/µL	130.0-400.0x10^3/µL
Mean platelet volume (MPV)	7.3fL	7.2-11.1fL

Source: Own elaboration.

In view of the patient's clinical deterioration, a physical examination was performed four days after admission, finding dyspnea, heart rate at the upper limit (98bpm), mucosal dryness, and desaturation. It was therefore decided to initiate low-flow oxygen therapy and an arterial blood gas test was requested, which indicated metabolic acidosis with a slight elevation of lactate levels (Table 3). Considering the results, 4 hours after their administration, blood cultures were taken from both upper limbs, and treatment was started with intravenous (IV) cefepime 1g every 8 hours and vancomycin 1g IV every 12 hours for 5 days due to a high suspicion of bacteremia of unknown origin. Until that moment, a venous catheter in the right upper limb was the only invasive device that the patient had.

Table 3. Arterial blood gas test.

Measurement	Result	Reference values
Fraction of inspired oxygen (FiO_2)	0.32 (with oxygen at 3L/min)	0.21 (at room air)
Partial pressure of carbon dioxide ($PaCO_2$)	19.3mmHg	35-45mmHg
Oxygen saturation (SaO_2)	95.6%	94-98%
Hemoglobin (Hb)	13g/dL	12.0-16.0g/dL
Partial pressure of oxygen (PaO_2)	71.3mmHg	75-100mmHg
Alveolar–arterial oxygen gradient	73.56mmHg	-
Lactate (serum lactate)	2.5mmol/L	0.6-1.40
Bicarbonate (HCO_3^-)	12.8mEq/L	22-26mEq/L
Blood pH (pH)	7.43	7.35-7.45
Base excess (BE)	-9.0mmol/L	±2
Capillary oxygen content (CcO_2)	17.87ml/dL	-
PaO_2/FiO_2 ratio (PaO_2/FiO_2)	222.81	≥300

Source: Own elaboration.

Five days after starting the antibiotic scheme with cefepime and vancomycin, carba NP tests performed on blood cultures confirmed the presence of carbapenemase-producing multidrug-resistant *E. meningoseptica*. The antibiogram reported susceptibility to amikacin and trimethoprim-sulfatomexazole (determined using the VITEK automated system) (Table 4). It should be noted that the antibiogram did not include information on susceptibility to vancomycin. The patient continued in the observation area and 9 days after her admission she was transferred to the general ward.

Table 4. Isolation of blood cultures 1 and 2.

Gram stain	Gram-negative bacilli		
Comments	Gram stain Gram-negative bacilli Possible serine carbapenemase producer. Presumptive test for carbapenemase (carba NP): positive. Ethylenediaminetetraacetic acid disk synergy test: negative.		
Characterization	*Elizabethkingia meningoseptica*		
Antibiogram for *Elizabethkingia meningoseptica*			
Antibiotic	**Value (µg/mL)**	**Interpretation**	**Method**
Amikacin	16	Susceptible	VITEK
Aztreonam	≥64	Resistant	VITEK
Cefazoline	≥64	Resistant	VITEK
Cefepime	32	Resistant	VITEK
Ceftazidime	≥64	Resistant	VITEK

Antibiotic	Value (µg/mL)	Interpretation	Method
Ceftriaxone	≥64	Resistant	VITEK
Ciprofloxacin	≥4	Resistant	VITEK
Gentamicin	≥16	Resistant	VITEK
Meropenem	≥16	Resistant	VITEK
Piperacillin Tazobactam	≥64	Intermediate	VITEK
Tigecycline	4	Intermediate	VITEK
Trimethoprim sulfamethoxazole	40	Susceptible	VITEK

Source: Own elaboration.

Since *E. meningoseptica* was isolated in blood cultures, it was decided to replace the treatment with meropenem 2g every 8 hours, amikacin 500mg every 12 hours, and colistin 150mg every 12 hours (all intravenous). However, five days after initiation of the new treatment, the patient's clinical condition further deteriorated due to dyspnea on little exertion and lack of response to stimuli, which led to a cardiac arrest. Monitoring showed an isoelectric line and absence of pulse, so cardiopulmonary resuscitation maneuvers were started; however, the patient died 14 days after being admitted to the institution.

DISCUSSION

E. meningoseptica infection has become increasingly common, resulting in high mortality since sepsis and meningitis caused by this bacteria are resistant to empirical antibiotic therapy (8). Risk factors for poor prognosis include use of indwelling venous catheters, mechanical ventilation, neoplasms, diabetes mellitus, chronic kidney disease, liver disease, among others (9).

Reports on the isolation of this bacterium in Latin America are scarce (8). However, there are some reports in Colombia, such as Echeverry & Ospina (3), who published in 2010 the case of a patient treated in a hospital in Medellín that was diagnosed with acute lymphoblastic leukemia; after being exposed to therapeutic medical equipment (central venous catheter and Ommaya reservoir), the patient presented a fever that resolved after starting a course of antibiotics based on the results of a blood culture that isolated *E. meningoseptica* and its corresponding antibiogram. Similarly, Perez *et al.* (8) conducted a case series study in 2016 in which they found that *E. meningoseptica* was isolated in 9 of 673 patients admitted to the neonatal intensive care unit of a clinic in Sucre (12 blood culture and cerebrospinal fluid samples). Pérez *et al.* (8) also reported that the most relevant medical history factors was prematurity; low birth weight; congenital gastrointestinal, cardiac, and neurological malformations; and necrotizing

enterocolitis. They also noted that the blood culture reports and their corresponding antibiograms are extremely useful for determining the most effective antibiotic therapy against this pathogen, as was the case in the present study.

Given that the patient in the present case had an increase in body temperature without any apparent cause, bacteremia was suspected and treatment was started with broad-spectrum antibiotics focused on eliminating gram-negative bacteria, which are common in the hospital setting, considering that bacteremias are usually caused by these microorganisms (9).

According to Ma *et al.* (12), mortality rates associated with *E. meningoseptica* infection are considerably high, with reports ranging from 11.0% to 66.6%. Inappropriate antibacterial therapy is an independent risk factor for mortality and infection, so prompt and appropriate treatment can significantly help improve survival rates.

E. meningoseptica is an opportunistic pathogen that mainly affects immunocompromised patients such as the elderly and newborns; individuals who have had recent prolonged hospitalizations; persons who received antibiotic therapy for a long period; patients who required invasive medical devices such as mechanical ventilation and a central line; and patients with malignant tumors, diabetes, renal disease, cardiovascular disease, among others (12-14). In the present case, the patient's risk factors included age >65 years, prolonged hospital stay, use of a peripheral vascular catheter, diabetes mellitus, and cardiovascular complications.

Although the automated VITEK 2 system has a high positive predictive value (15) and is commonly used to identify pathogens and determine their susceptibility to antimicrobials (3,6,8), it may yield a variable number of false positives when identifying *E. meningoseptica,* so it should be used with caution. Therefore, to identify this microorganism, more advanced techniques are recommended, such as mass spectrometry, known as MALDI-TOF (Matrix-Assisted Laser Desorption/ Ionization Time-of-Flight), as well as molecular techniques such as 16S rRNA gene sequencing, and whole genome sequencing (WGS) (2,15).

In the treatment of *E. meningoseptica* infections, broad-spectrum antibiotics should be considered for the elimination of the most common gram-negative bacteria in the hospital setting. This approach is important because *Elizabethkingia* are highly resistant to antimicrobials, including extended-spectrum beta-lactams, tetracycline, aminoglycosides, and chloramphenicol (6). Likewise, it is worth mentioning that *E. meningoseptica* has shown variable susceptibility to some antibiotics such as piperacillin, piperacillin/tazobactam, trimethoprim/ sulfamethoxazole, minocycline, and fluoroquinolones (10). These resistance and susceptibility properties have been extensively documented in previous studies, such as the ones carried out by Chen *et al.* (6) and Zajmi *et al.* (10).

Acknowledging *E. meningoseptica* as the cause of a bacteremia is critical in order to provide a timely and successful treatment.

CONCLUSIONS

E. meningoseptica is an opportunistic pathogen that is potentially fatal because it is difficult to treat. Consequently, recognizing its presence in hospital settings and establishing clinical criteria to facilitate early detection are essential for initiating timely and appropriate treatment.

ETHICAL CONSIDERATIONS

For the development of this case report, the standards established in Resolution 8430 of 1993 of the Colombian Ministry of Health (16) were followed, and approval was obtained from the Ethics Committee of the Clinica Avidanti in Ibagué, in accordance with the minutes No. R-CCAL-06-12.

CONFLICTS OF INTEREST

None stated by the authors.

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