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Scientific Letter

Extended-spectrum beta-lactamase–producing *Klebsiella pneumoniae* isolated in a patient with postoperative mediastinitis

Klebsiella pneumoniae productora de Betalactamasa de espectro extendido aislada en un paciente con mediastinitis posoperatoria

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Mr. Editor

Antimicrobial resistance constitutes a survival strategy developed by microorganisms against one or more antimicrobial agents through various mechanisms that reduce the microbicidal or inhibitory capacity of these drugs.[1] This capability may be intrinsic or acquired. Intrinsic resistance occurs through vertical transmission, whereas acquired resistance arises from chromosomal mutations or horizontal gene transfer. The World Health Organization considers antimicrobial resistance a major current threat to human health.[2]

This phenomenon, extensively studied in bacteria, includes several mechanisms, among which the production of antibiotic-inactivating enzymes stands out. Numerous bacteria have acquired resistance to a widely used group of antibiotics, namely beta-lactams, through the production of beta-lactamase enzymes that eliminate their efficacy.[2]

However, these pathogenic organisms have developed diverse resistance mechanisms to overcome even the most modern drugs of this family. An example is extended-spectrum beta-lactamase (ESBL)-producing bacteria such as *Klebsiella pneumoniae*, which has been included by the World Health Organization among the 12 families of bacteria considered most dangerous to human health, highlighting the importance of reporting its isolation in order to make timely clinical decisions.[2]

At *Hospital Universitario Cardiocentro «Ernesto Guevara»* of Santa Clara, Villa Clara, a patient was treated by the Department of Cardiovascular Surgery with a medical history of multiple cardiorespiratory diseases. During the clinical interview, it was determined that she had community-acquired pneumonia, empirically treated with antibiotics from the cephalosporin and fluoroquinolone classes.

The patient was admitted due to persistent nonspecific fever and suspected infectious endocarditis, based on symptomatology and echocardiogram findings.

To confirm the presumptive diagnosis, two blood culture samples were collected to identify the infectious microorganism and determine its *in vitro* susceptibility, as well as a nasal swab. These samples were sent to the Microbiology Laboratory of *Hospital Provincial Gineco-Obstétrico Universitario «Mariana Grajales»* of Santa Clara.

Two blood culture bottles containing broth media provided by *Scientifica* Company (CPM–Italy), were received, each inoculated with 10 milliliters of peripheral blood, along with the nasal swab, which tested negative.

Using standard biochemical techniques and conventional methods, *Staphylococcus* species other than *aureus* (SOSA) were identified in all subcultures.

Proper interpretation of the positive blood culture results confirmed the presence of infectious endocarditis involving the native mitral valve. Microbiological results acquire true value when combined with the patient's clinical findings and medical history, which fall under the responsibility of the attending physician, highlighting the need for professional collaboration,[3] as evidenced in this case.

An important aspect to note is that SOSA (formerly referred to as coagulase-negative *Staphylococcus*) are part of the normal commensal skin microbiota; therefore, it is necessary to distinguish between contamination and infection, even though they have been reported as the cause of 20–30% of patients with mediastinitis.[4] Recent studies have identified this group of microorganisms as significant potential pathogens causing septicemia, attributed to the increased use of intravascular and prosthetic devices. They predominantly affect immunocompromised patients and are capable of forming biofilms, a key factor contributing to pathogenicity. A fundamental concern is their antimicrobial resistance, which complicates medical treatment.[5, 6]

Once the microorganism was identified and repeatedly isolated from the collected samples, and with the clinical data provided by the attending physician, the case was interpreted as an infection and laboratory testing continued. Antibiogram was performed using the disk diffusion method and minimum inhibitory concentration determination. Disks of cefoxitin (30 µg), ciprofloxacin (5 µg), clindamycin (2 µg), erythromycin (15 µg), gentamicin (10 µg), linezolid (30 µg), penicillin (10 units), and tetracycline (30 µg) were used; vancomycin was tested using the E-test strip. Results were interpreted according to the breakpoints established by the Clinical and Laboratory Standards Institute (CLSI) 2024 guidelines,[7] as shown in the table.

Table 1. Antibiogram results for isolated staphylococci other than *Staphylococcus aureus* (SOSA)

Antimicrobials	Reading*	Interpretation
Cefoxitin	23mm	Resistant
Ciprofloxacino	23 mm	Susceptible
Clindamicina	23 mm	Susceptible
Eritromicina	25 mm	Susceptible
Gentamicina	18 mm	Susceptible
Linezolid	28 mm	Susceptible
Penicilina	22 mm	Resistant
Tetraciclina	20 mm	Susceptible
Vancomicina	3 µg/ml†	Susceptible
D-test		Negative

* Measurement of the diameter of the zone of inhibition of bacterial growth around the tested antibiotic disk. These breakpoint values correspond to those established by the Clinical and Laboratory Standards Institute (CLSI) in 2024 and remain in force.
† Dilution number that inhibits bacterial growth of the tested antibiotic.

Overall, high susceptibility to the tested antimicrobials was observed, although resistance to cefoxitin was detected. Intravenous treatment with vancomycin plus gentamicin was administered according to institutional protocol, followed by urgent surgery for replacement of the affected valve. The microbiology of the infection is a determining criterion; however, patient-related factors such as comorbidities, renal function, and previous antibiotic exposure must also be considered.

Empirical antimicrobial therapy should be broad-spectrum until culture results are available; thus, vancomycin is used to cover methicillin-resistant staphylococci, in addition to gentamicin for Gram-negative bacteria, as in the present case where both indications coincided.[8, 9]

During the acute postoperative period (eighth day), the patient developed purulent discharge from the drain sites, along with thoracic pain and sternal crepitus. Samples were collected for culture and *in vitro* susceptibility testing. *Klebsiella pneumoniae* (Figure 1A) producing an extended-spectrum beta-lactamase (ESBL) was isolated.

Antibiogram results are shown in figure 1B, demonstrating resistance to third- and fourth-generation cephalosporins such as ceftriaxone, ceftazidime, and cefepime, evidenced by bacterial growth around each antibiotic disk. Re-

sistance to monobactams (aztreonam), aminopenicillins combined with inhibitors (amoxicillin–clavulanic acid), and fluoroquinolones was also observed. Sensitivity was noted to cephamycins, aminoglycosides, and carbapenems The infectious process persisted for 28 days, leading to initiation of treatment with meropenem.

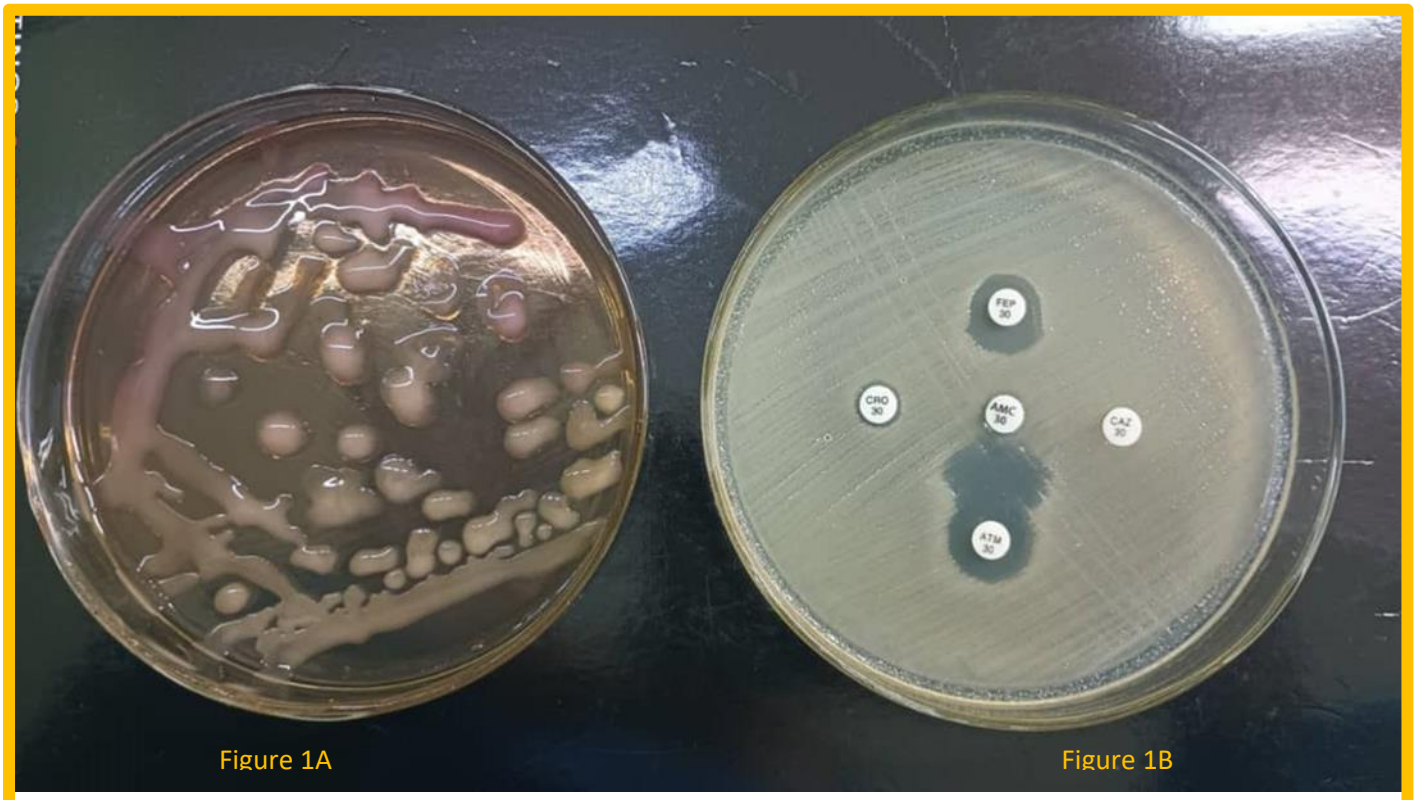

Figure 1 A. *Klebsiella pneumoniae* culture on MacConkey agar showing bacterial growth.
Figure 1 B. Antibiogram of ESBL-producing *Klebsiella pneumoniae*.
Legend: CRO (ceftriaxone), FEP (cefepime), AMC (amoxicillin/clavulanic acid), CAZ (ceftazidime), ATM (aztreonam).

In response to laboratory findings, strict epidemiological measures were implemented, including isolation in a single-patient room. Clinical evolution was favorable, although multiple interventions were required for complete resolution of the infectious process and subsequent surgical wound reconstruction, allowing hospital discharge with outpatient follow-up. The final diagnosis was postoperative mediastinitis.

Klebsiella pneumoniae, as a Gram-negative bacterium, produces beta-lactamase enzymes as its most common mechanism of antimicrobial resistance. These enzymes inactivate penicillins, third- and fourth-generation cephalosporins, and monobactams (aztreonam), leaving carbapenems as the only useful class of beta-lactam antibiotics for treatment. Meropenem offers the broadest coverage in Cuban hospitals. Detection of ESBLs in laboratories is essential for appropriate antibiotic selection and for determining epidemiological measures to prevent dissemination of these microorganisms.[10]

Adults are more susceptible to colonization by these microorganisms due to the high diversity of the human intestinal microbiome.[11] The patient presented multiple predisposing factors favoring infection with ESBL-producing Enterobacterales: prior antibiotic treatment in the community; exposure to cardiac surgery followed by several reinterventions with excessive manipulation and invasion of anatomical barriers, compromising immune system function; use of cavity drains; prolonged mechanical ventilation, and vasopressors. Similar cases were reported by Jiménez et al. [12] in Mexico and by Zukowska et al.[4]

Moreover, prior and often prolonged use of broad-spectrum antibiotics, including carbapenems, exerts strong selective pressure favoring the emergence and dissemination of resistant strains. The plasmid localization of

resistance genes facilitates horizontal transfer among different bacteria within the intestinal microbiome or through contact in the hospital environment, leading to rapid spread of resistance even among different bacterial species.[13]

Postoperative mediastinitis is one of the most severe complications in cardiovascular surgery. It is associated with high morbidity, mortality, prolonged hospital stay, and increased healthcare costs. One limitation of this study was the inability to determine the species within the SOSA group, as its diagnosis requires a high index of clinical suspicion on physical examination, positive microbiological test results, and early multidisciplinary management to modify prognosis. Antimicrobial resistance is a global phenomenon, unstoppable and rapidly progressing, compared to the emergence of new antibiotics, which requires a faster pace to combat bacterial infections.

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