

## Hemodialysis Device-Associated Infections, Report of Two Cases

Silva Rojas Glen Andrés<sup>1</sup>, Farfán Cano Galo Guillermo<sup>2\*</sup>, Silva Rojas Kevin Joshua<sup>1</sup>, Christian Mateo and Castillo-Jaramillo Christian Mateo<sup>3</sup>

<sup>1</sup>Catholic University of Santiago de Guayaquil, Faculty of Medicine, Guayaquil, Ecuador

<sup>2</sup>Society of Infectious Diseases of Guayas, Guayaquil, Ecuador

<sup>3</sup>Central University of Ecuador, Faculty of Medicine, Quito, Ecuador.

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### ABSTRACT

VADIs constitute an important morbidity and mortality factor among HAIs, because of the complications derived from them, such as endocarditis, sepsis, and patient's death. Mostly caused by pathogens of the *Staphylococcus* genus, especially *S. aureus*. We present two cases of endocarditis in diabetic patients hospitalized in the ICU, who were on RRT. Reporting these cases is important from the perspective of infection prevention and control to reduce the occurrence of endocarditis, in addition to highlighting the observable limitations in public health systems.

**Keywords:** *Staphylococcus aureus*, Candida, Hemodialysis, Sepsis

### INTRODUCTION

A vascular access device (VAD) is a tool that facilitates administration of drugs, fluid therapy, hemodynamic monitoring, total parenteral nutrition, sampling, or hemodialysis using one of the great vessels; within this group of devices are central venous catheters, percutaneous catheters or distal access central venous catheters and hemodialysis catheters [1]. Vascular access device-associated infections (VADIs) are an important cause of morbidity and mortality due to healthcare associated infections (HAIs), especially in patients with chronic renal failure undergoing renal replacement therapy (RRT) using hemodialysis catheters (HDC). Most isolated agents belong to the genus *Staphylococcus*, with *S. aureus* and *S. epidermidis* being frequent, with or without methicillin resistance; in turn, the presence of gram-negative agents such as *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *Serratia marcescens* has been reported, with predominant resistance patterns producing extended-spectrum beta-lactamase (ESBL), resistance to fluoroquinolones, without excluding reports of carbapenemase-producing strains [2-5]. Among the microorganisms reported in VADIs, the presence of fungal agents is less frequently evidenced, especially of the genus *Candida*, of which certain strains represent a challenge due to their resistance to azoles [6].

### PATIENTS AND METHODS

#### Ethical aspects

To prepare case reports, written informed consent was requested from the patients' relatives.

#### Case A

A 68-year-old female, with a history of hypertension, type 2 diabetes mellitus (NIDDM) (insulin-requiring), chronic kidney disease (CKD) in RRT by means of right jugular HDC (placed in June 2019). She went for assessment on July 15, 2020, for presenting general malaise, fatigue, accompanied by generalized pain (non-specific pain characteristics on questioning) of 15 days of evolution, accompanied by purulent discharge at the HDC insertion site, and epigastralgia. On admission, vital signs without alterations (**Table 1**), physical examination showed no neurological deterioration, pale face, chest without alterations, painful abdomen in hypogastrium, symmetrical limbs with preserved tone and sensitivity.

**Corresponding author:** Galo Guillermo Farfán Cano, Society of infectious diseases of Guayas, Faculty of Medicine, Guayaquil, Ecuador, Tel: (+593) 97 875 9899; E-mail: dr.galo.farfán.cano@gmail.com

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**Table 1.** Vital signs of the cases. The values at admission of each patient are shown.

Vital Signs	Case A	Case B
Blood temperature	36°C	39,7°C
Blood pressure	110/50	95/51
Pulse	54	96
Respiratory rate	19	20
Pulse oximetry saturation	98%	91%

Evaluated by a nephrology specialist, to whom she reported thermal rise and discomfort at home prior to admission, which correlated with the last hemodialysis session,

establishing presumptive diagnosis of sepsis associated with HDC, indicating empirical scheme with ceftriaxone, after taking blood culture samples. The infectious disease department evaluated her the second day of hospitalization, indicating therapeutic adjustment to meropenem and vancomycin, blood culture sampling from the catheter, removal of the VAD with a change of insertion site and catheter tip culture; additionally, because of risk factors, a cardiological evaluation was agreed upon to consider echocardiography, which would be performed with the results of the blood cultures.

Laboratory results showed leukocytosis, neutrophilia, and elevated acute phase reactants; blood cultures isolated *Candida albicans* and *Staphylococcus aureus* (Table 2).

**Table 2.** Comparison of laboratory parameters at admission and discharge of case A.

Laboratory	Admission	Discharge	Unit of measure
Procalcitonin	42,100	-	ng/mL
C-reactive protein	19.92	-	mg/mL
Leukocytes	39.50	34.70	x10 <sup>3</sup> /ul
Total neutrophils	31.57	29.63	x10 <sup>3</sup> /ul
Prothrombin time	14.2	-	Sec
INR	1.17	-	
Thromboplastin time	121.9	-	Sec
Platelets	181	336	x10 <sup>3</sup> /ul
Mean platelet volume	8.8	7.9	fl
Hemoglobin	10.9	8.2	g/dl
Glucose	237	-	mg/dl
Chlorine	98	99	mmol/L
Potassium	4.4	4.7	mEq/L
Sodium	133.4	138.2	mmol/L
Glycosylated hemoglobin	8.85	-	%
Urea	44	83	mg/dl
Creatinine	2.82	3.20	mg/dl
July 4, 2019 blood culture sample.	<i>Staphylococcus aureus</i> , oxacillin-resistant		>100.000 UFC/ml
Urine culture specimen from July 12, 2019	<i>Candida albicans</i>		
Sputum culture from July 12, 2019	<i>Candida albicans</i>		
Retrograde blood culture (from catheter) and peripheral specimen (right lower extremity) from July 18, 2019	<i>Staphylococcus aureus</i>		
Catheter tip culture	No bacterial growth until 48 h of incubation.		
Blood cultures for fungi, aerobes and anaerobes.	<i>Candida albicans</i>		

Following the microbiological isolations, an echocardiogram was performed reporting a mass in the right atrium, for which referral to a tertiary care unit was recommended for excision of the mass (for biopsy and culture) and comprehensive management, upon diagnosis of severe mixed sepsis due to coinfection of *Candida albicans* and *Staphylococcus aureus*, compounding and vancomycin were indicated, pending biopsy, she was referred to a tertiary level unit, however, upon follow-up of the case, the patient's death was reported without the possibility of performing the biopsy.

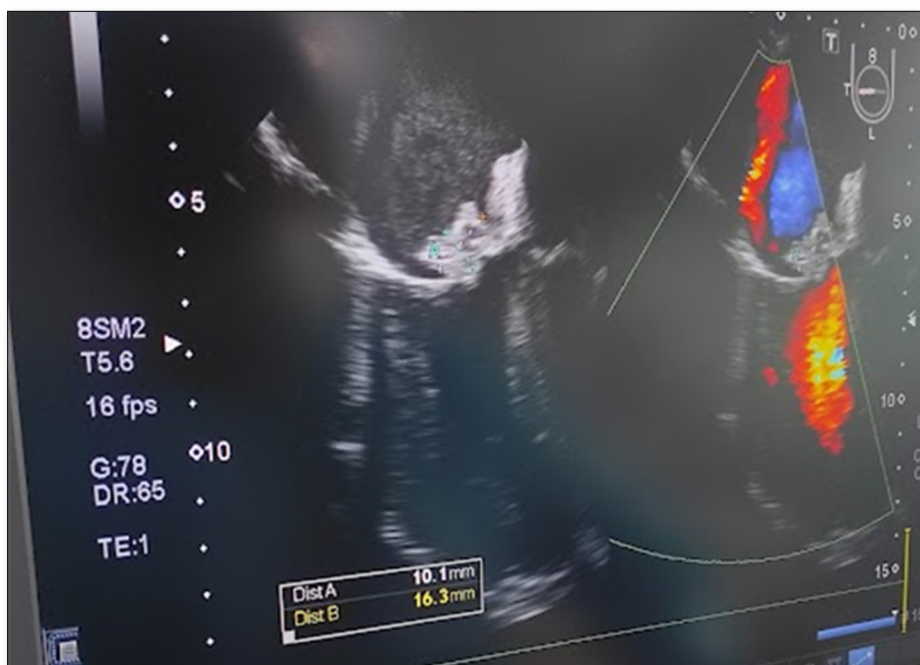
**Case B**

An 82-year-old male, with a history of hypertension, NIDDM and CKD, who started hemodialysis sessions at a private center (December 2021). Attended on January 26, 2022, for presenting 3 days of thermal rise above 40°C, general malaise, asthenia, hyporexia, after a hemodialysis session, classifying his condition as sepsis associated with HDC; levofloxacin and ibuprofen were prescribed; vital signs can be seen in **Table 1**. Physical examination on admission revealed a foul odor in the vicinity of the HDC insertion site, with erythema, heat and flushing. Upon his deterioration, diagnosis of septic shock associated with HDC was established and the admission to the intensive care unit (ICU) was decided; to establish the diagnosis and therapeutic management of the case, the clinical method was applied. He was admitted to the ICU from January 29 to February 19, 2022, the laboratory results of his evolution can be seen in **Table 3**, blood cultures were requested for aerobes, anaerobes and fungi, without obtaining samples for lack of institutional reagents and limited economic resources of the family, due to the COVID-19 pandemic.

Transthoracic echocardiogram compatible with endocarditis of etiology to be determined reports findings of vegetation affecting the anterior leaflet of the mitral valve of 1.4 x 1.0 cm (**Figure 1**), generating insufficiency jet running attached to the posterolateral side of the left atrium, additionally, aortic valve calcification with jet of mild tricuspid valvular insufficiency, without record of ventricular dilatation. Concentric hypertrophy, preserved systolic function (55-60%), without regional contractility disorders. Mild bilateral atrial dilatation. No pericardial effusion. Facing a severe sepsis, empirical regimen was started with meropenem and vancomycin adjusted to renal function and hemodialysis session for tentatively 4 weeks; colistin and fluconazole were added after 2 weeks, due to the presumption of fungal infection and probability of infection by strains resistant to carbapenemics; however, the patient's death was reported without diagnosis of causal microorganism after 4 weeks of antibiotic treatment and 2 weeks of antifungal treatment.

**Table 3.** Laboratory values of case B during his stay in the ICU.

Parameters	Values at ICU admission	Values at follow-up		
Date	29-01-2022	31-01-2022	01-02-2022	19-02-2022
Leukocytes	29.8	41.5	24.8	22.5
Hemoglobin	8.3	9.6	8.7	7.8
Neutrophils	24.8	38.4	22	15.3
Urea	53	147	167	111
Creatinine	3.03	6.01	6.26	4.13
pH	7.378	7.411	7.39	7.37
HCO3	18.9	21.8	20.5	20.2
PO2	175.3	128.2	121.4	182
PCO2	29.1	32.9	31.4	32
pH V		7.426		
HCO3 V		22.9		
PO2 V		33.9		
PCO2 V		44.6		
DELTA CO2		1		
SERUM LACTATE		7.7		



**Figure 1.** Transesophageal echocardiography photograph. The size of the mass attached to the anterior leaflet of the mitral valve is striking.

## DISCUSSION

VADIs account for 10-20% of all nosocomial infections and complicate the stay of more than 10% of intensive care patients [7]. Given the usefulness of VADs, it is important implementing preventive measures to reduce pathogen exposure in healthcare settings [7-9]. The incidence of VADIs from 1992 to 2004 in the United States ranged from 1.8 to 5.2 events per 1000 days of catheter use (10); while in other parts of the world the incidence can range from 0.48 to 8.75 per 1000 days of device use, and a mortality of 12 to 25% [9]. In both hospital emergency and ICU areas, the microorganism most frequently associated was *Staphylococcus aureus* [3,8-10].

Presence of infections prior to the use of VADs, mainly due to methicillin-resistant *Staphylococcus aureus* (MRSA), is considered a highly predisposing factor for reinfection; additionally, the history of NIDDM and duration of the catheter use may condition the development of VADIs [3,10].

Risk factors frequently mentioned as causes of VADIs include device tip colonization, catheter luminal contamination, hematogenous dissemination from a distal infectious focus, and device compromise secondary to device manipulation, drugs or contaminated infusions [8,9]. Microorganisms considered as causal agents include bacterial agents belonging to the usual microbiota of the skin (highlighting *S. aureus* and coagulase negative staphylococci), as well as transient microbiota (seen in

cross-infections in sanitary environments, especially when there is inadequate hand hygiene adherence), *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae* and *Acinetobacter baumannii*; VADIs of fungal etiology has been mentioned, mainly by *Candida* sp. [8-11]. Among clinical manifestations in patients with VAD are fever, chills and hypotension, allowing presumption of the presence of VADIs, which must be confirmed with the detection of the microorganisms [7-9,12]. Recommendations to reduce VADIs include aseptic measures such as hand hygiene and preparation of the insertion site with iodine-based solutions, 70% alcohol or chlorhexidine gluconate, the removal and change of the device is considered controversial despite reports of therapeutic benefit in several studies and staff training, choice of devices according to the duration of treatment, avoiding femoral access [7,8,13]. Culture of the catheter tip is recommended to confirm colonization of the device (as the cause of the infection), stating that figures higher than 15 CFU in a semiquantitative culture, or higher than  $10^2$  on sonication (quantitative study) can be considered as positive [7-9,11,14]. However, microorganism ability to form biofilms and, consequently, the possibility of polymicrobial reports should be evaluated. Therapeutic approach to VADIs involves using empirical and targeted regimens, whose application depends on the clinical conditions of the patient and availability of blood culture isolates. Coverage for gram-positive, gram-negative agents and yeasts should be prioritized, especially when facing signs of septic shock, femoral catheter and prolonged stay in the ICU [7-9,11]. Use of vancomycin is recommended when

MRSA infections are suspected, and its substitution by daptomycin when antibiotic minimum inhibitory concentrations (MIC) are higher than 1.5, antifungal therapy and antipseudomonics (carbapenem, piperacillin-tazobactam, etc.) when candidemia or gram-negative agents are suspected in the empirical scheme [7].

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