



Presentation of clinical cases

***Candida lusitanae* sepsis in a patient with gastric adenocarcinoma: A case report**

Sepsis por *Candida lusitanae* en un paciente con adenocarcinoma gástrico: reporte de un caso

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ABSTRACT

Keywords:

Fungemia;
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Sepsis.

Candida lusitanae infection is a rare entity with a prevalence of 1% in the group of associated species, has also been recognized as a pathogen associated with infections acquired in health care in severely immunosuppressed patients. We present the case of a 55-year-old patient with a history of hospital admission due to localized abdominal pain in epigastrium, which was accompanied by nausea, vomiting, fullness, hair, anorexia, and weight loss, diagnosed by imaging and histopathological studies with advanced gastric carcinoma, which developed sepsis by *C. lusitanae*, a fungigram was obtained and management was given with fluconazole obtaining a satisfactory evolution in the patient. It is concluded case presented demonstrates that the clinical characteristics of this species are presented according to the natural history of sepsis.

RESUMEN

Palabras clave:

fungemia;
Candida;
neoplasias
gástricas;
inmunosupresión;
sepsis.

La infección por *Candida lusitanae* constituye una entidad poco frecuente con una prevalencia del 1% en el grupo de especies asociadas, además ha sido reconocido como un patógeno asociado a las infecciones adquiridas en la atención de salud en los pacientes de gravedad e inmunosuprimidos. Se presenta el caso de un paciente de 55 años con historia de ingreso hospitalario por dolor abdominal localizado en epigastrio, que se acompañaba de náuseas, vómitos, sensación de llenura, melenas, anorexia, y pérdida de peso, diagnosticada por estudios imagenológicos e histopatológicos con carcinoma gástrico avanzado, la cual desarrolló una sepsis por *C. lusitanae*, se obtuvo un fungigrama y se dio manejo con fluconazol obteniendo una evolución satisfactoria en la paciente. Se concluye caso presentado demuestra que las características clínicas de esta especie se presentan acordes a la historia natural de la sepsis.

INTRODUCTION

Candida species are opportunistic fungal pathogens in the normal skin and mucosal microbiota. However, *Candida* overgrowth can cause infections such as thrush or life-threatening invasive candidiasis in immunocompromised patients¹.

However, when discriminating by *Candida* species, the prevalence is marked by *Candida albicans* leaves other species aside, as demonstrated by the SENTRY Antifungal study surveillance Program, which showed that the frequency of *Candida albicans* accounted for 54% of the 2047 *Candida* bloodstream infections recorded, while the distribution of the other species was: *C. glabrata* (16%), *C. parapsilosis* (15%), *C. tropicalis* (10%), *C. krusei* (2%), *C. guilliermondii* (1%) and *C. lusitanae* (1%)².

The latter, called *C. lusitanae*, constitutes one of the less frequent species; Despite this, some authors, such as Sánchez *et al*³, have described colonization rates of up to 7% in patients undergoing bone marrow transplantation or admitted to intensive care units, possibly constituting a risk factor for the onset of infections in the hospital environment.

Other studies add that this species of *Candida* has emerged as an important nosocomial pathogen in the last 20 years, one of its most important characteristics being clinical and microbiological resistance to amphotericin B (intrinsic and acquired), which distinguishes it from other species⁴.

Sepsis generates a systemic immune response from the agent and host interaction. When caused by *Candida*, this opportunistic pathogen uses self-protection strategies, counteracting the host's immune responses provided by different subsets of immune cells, which can be seen affected if there are conditions of immunosuppression in the individual⁵ which, added to the above, constitutes necessary clinical isolation.

Another relevant aspect is that identifying cases of sepsis by this microorganism is significant in the clinical field, considering that in Colombia, there is only one described report of infection by this fungus, which generated endocarditis in a minor infant⁶. Likewise, in the international literature, there are few reported cases of fungemia or complications caused

by this pathogen, especially in solid tumors such as the one presented by the patient in the case presented.

Therefore, for global knowledge, this case shows that *C. lusitanae*, despite being an emerging nosocomial pathogen of low frequency and susceptible to conventional antifungal therapies, currently draws attention because some isolates are resistant to amphotericin B, 5-fluorocytosine or fluconazole, as well as the fact that Clinical data on invasive infections caused by *C. lusitanae* are scarce in the literature⁷.

The objective of this clinical case was to describe the clinical, microbiological, and epidemiological characteristics of a clinical case concerning a bloodstream infection by *C. lusitanae* in a cancer patient.

CLINICAL CASE

A 55-year-old white patient from Teorama, Norte de Santander, with a history of hospital admission for six months due to abdominal pain located in the epigastrium, accompanied by nausea, vomiting, a feeling of fullness, long hair, hyporexia, and loss of weight.

The patient reports that she had been treated with antacids and proton pump inhibitors but had not felt any improvement. As relevant background, she stated that she had been diagnosed with gastroesophageal reflux a few years ago.

He was admitted to the emergency department of the hospital center due to presenting asthenia, adynamia, and unquantified fever; on physical examination, they found vital signs as follows: heart rate of 87 beats per minute, respiratory rate of 16 breaths per minute, temperature 37.5 °C, blood pressure 120/80 mmHg, O2 saturation 97% and Glasgow scale 15/15. Likewise, a patient in regular general and nutritional status was detailed, with tolerance to ambient oxygen, hydrated, febrile, with a picnic constitutional biotype, and whose actual age did not match her apparent age.

In the physical examination by systems, it was found to be abnormal since it presented a 3 x 3 cm left supraclavicular adenopathy and a globose abdomen

due to a soft, adipose panniculus, with mild pain on palpation in the epigastrium and mesogastrium.

A complete blood count showed pancytopenia (anemia, leukopenia, and thrombocytopenia), neutrophilia, and lymphopenia.

Given the above, she was seen by the internal medicine service, in which the patient was considered to have a high risk of complications, including death, for which she was transferred to an intensive care unit, where a catheter was placed. The central venous system completed a 5-day stay after being stabilized and subsequently sent to the general hospital ward.

As diagnostic studies requested by the treater, an upper digestive tract endoscopy was performed, in which an infiltrative lesion was reported at the pyloric antrum level, and from which a sample was taken for the histopathological study, which concluded in a lesion compatible with infiltrating moderately undifferentiated squamous cell adenocarcinoma added to extensive areas of interstitial hemorrhage.

In addition, a thoracoabdominal computed tomography was performed, which reported a circumferential wall thickening of the gastric antrum and a lesion at the level of hepatic segment II of possible metastatic origin.

Stent was placed to manage gastric emptying by the gastroenterology service. However, the establishment of parenteral nutrition was requested due to gastric restriction for the typical passage of food and the patient's hyporexia, which conditioned the physical and functional deterioration.

On the ninth day of hospitalization, the patient had quantified fever spikes of 38.5°C and was asthenic, so it was decided to take blood and urine samples for cultures. Blood cultures processed with MALDITOF positive for *C. lusitaniae* with Vitek2 technology fungigram that reported sensitivity to antifungals, as well as a positive urine culture for *Escherichia coli* with characteristic extended-spectrum beta-lactamase (Table 1).

Table 1. Fungigram of *C. lusitaniae* made by *BioMérieux technology*.

Antifungal	MIC	Resistance profile
<i>fluconazole</i>	(≤0.5)	Sensitive
<i>Voriconazole</i>	(≤0.12)	Sensitive
<i>Caspofungin</i>	(0.25)	Sensitive
<i>Micafungin</i>	Not reported	Not reported
<i>Amphotericin B</i>	Not reported	Not reported
<i>Flucytosine</i>	(≤1)	Sensitive

*MIC: Minimum inhibitory concentration.

Regarding the previous findings and despite the estimate of the *Candida* Score for which the patient had obtained a score of 0.908 (low probability of candidiasis), it was decided to start treatment for fungemia based on the clinical practice guideline for managing candidiasis. From IDSA (Infectious Diseases Society of America)⁸ with fluconazole 200 mg intravenously every 12 hours and meropenem 1 gram intravenously every 8 hours for the management of urinary tract infection based on the sensitivity profile and the antibiotic therapy guidelines provided by the epidemiology group of the center hospitable.

After seven days of treatment, the patient completed the antifungal scheme with fluconazole, and serial blood cultures was again requested, which this time were negative for the growth of microorganisms, including *C. lusitaniae*.

Finally, the patient obtained an improvement in the septic condition and the accompanying symptoms; however, he died six months later due to complications related to the underlying pathology.

Declaration on ethical aspects

When carrying out and participating in this study, the signing of the patient's informed consent was considered. In addition, the procedures followed the ethical norms of Resolution 8430 of 1993 of the Ministry of Health and Social Protection of Colombia and the Declaration of Helsinki.

DISCUSSION

Candida is a species of commensal yeast that resides in the mucous membranes of the oral and vaginal cavities, as well as in the gastrointestinal tract of humans, allowing it to be classified as a harmless species in the healthy host; however, pathogenicity

increases in the immunocompromised host⁹ which generates complications, as is the case of the patient presented.

That is why some authors like Arikan *et al*¹⁰ have studied the risk factors associated with infections caused by this fungus, which they divide into two large groups: those related to health care such as the use of catheters, total parenteral nutrition, surgical interventions, and the use of antimicrobial drugs; and those associated with the patient's condition such as age, immunosuppressive diseases, clinical deterioration, and comorbidities.

Therefore, it must be taken into account when diagnosing infection by some species of *Candida*, such as *C. lusitanae*, which is a rare species; the conditions that act as risk factors must be evaluated, including individual factors in the diagnosis—clinical, epidemiological and microbiological area; which were identified in the present case report.

For the clinical aspect, Lazo *et al*¹¹ proposed that the symptoms due to *C. lusitanae* can vary according to the location and the entity to which it is presented (sepsis, endocarditis, localized infection) because the performance of blood cultures is of vital importance to avoid the increase in mortality in critically ill patients, as was achieved with the patient studied who, despite having a complex picture, reached the diagnosis through microbiological identification.

On the other hand, from the epidemiological point of view, it should be taken into account that the prevalent risk factors for developing candidemia by this species have been described in frequency by the use of central venous catheter 93.9%, use of antibiotics 93%, use of antifungal agents 79.6% and parenteral nutrition 60.2%, added to the factors involved in mortality such as the presence of solid cancer and the female gender,¹² which were found in the case described.

However, in the microbiological field, this species proliferates on Sabouraud agar and is indistinguishable from other *Candida species*, for

which biochemical tests must be used to identify it¹³, just as they were used with the patient through the isolation in CHROMagar™ *Candida*, the use of the MALDITOF technology and the VITEK method, which allowed the identification of the species and the estimation of the antifungal susceptibility for the orientation of the treatment, respectively.

In the same way, for the microbiological process, it was possible to recognize that the reported microorganism has a sensitive resistance profile despite the current resistance mechanisms and its epidemiological characteristics that are affirmed in the present case, considering the risk factors described in the literature.

Consequently, considering the low frequency of the case, the proposals regarding the management are still being debated; some researchers, for example, Favel *et al*¹⁴ studied the in vitro susceptibility of 80 clinical isolates of *C. lusitanae* against five systemic antifungal agents and found that all isolates were susceptible to fluconazole and voriconazole.

However, Runco¹⁵ proposes that due to the low frequency of the isolation of *C. lusitanae* clinically, there are no conclusive data on the antifungal treatment of choice, so when strains resistant to amphotericin B appear, the recommended treatment is fluconazole at a dose of 6-12 mg/kg/day or voriconazole (6 mg/Kg/12 h), as given to the patient.

Indeed, the new azoles show in vitro activity against this yeast, so it seems reasonable to assume that they can be used to treat infections caused by *C. lusitanae*¹⁵. Zurita¹⁶ adds that, due to this species' rapid development of resistance to amphotericin B, it is recommended to treat the patient with azoles.

However, the few cases reported in the literature show that the conditions are variable and do not have a similar pattern regarding semiology to treatment, as shown in the following table summarizes the case reports where said microorganism is involved (Table 2).

Table 2. Summary of cases reported in the literature by *C. lusitaniae*.

Authors	Patient	Type of infection	Clinical manifestations	Treatment
Raja <i>et al</i> ¹⁷	77-year-old man	Fungemia associated with the use of a urinary catheter	Dysarthria, right-sided facial droop, and right-sided weakness	Micafungin
Apsemidou <i>et al</i> ¹⁸	17-year-old male	Hematopoietic cell transplant-associated fungemia	Fever and anemia	Caspofungin and liposomal amphotericin B
Rahmati <i>et al</i> ¹⁹	41-year-old woman	Fungemia and endocarditis associated with intravenous drug use	Afebrile, normotensive and tachycardic	Micafungin
Mishra <i>et al</i> ²⁰	82-year-old man	Kidney cancer-associated fungemia	Worsening back pain, fever progressing to hypotension	Fluconazole and caspofungin
Pietrucha <i>et al</i> ²¹	52-year-old woman	Fungemia associated with pancreatitis and cholecystectomy and use of a central venous catheter.	Fever and abdominal abscess	Fluconazole

Therefore, the development of this clinical case shows that there needs to be more evidence regarding the characteristics defined in the clinical and microbiological part for developing sepsis by *Candida* species, especially by *C. lusitaniae*. However, there are defined risk factors that can guide the diagnosis and timely management, to provide optimal management, such as that provided to the patient and suggest proposals that tend to minimize the appearance of this type of fungemia that increase the risk of complications and mortality.

However, considering the practical implications of the present case report, the importance of using national and international clinical practice guidelines for the management of *Candida* infections is valued to reduce microbial resistance and favor the patient recovery as well as timely identification of patients at high risk of *Candida* infections through the use of previously validated scores such as the one applied to the patient.

As a conclusion focused on the evidenced findings, the importance of the microbiological isolation of this type of microorganisms is exposed, taking into account the current considerations of international organizations such as the World Health Organization, which proposes the importance of expanding the knowledge of the species circulating and resistance patterns of each institution, in order to help the health professional to choose the best treatment for the patient.

It is recommended for future research to carry out more extensive, multicenter studies with greater statistical and epidemiological strength, such as cross-sectional studies that allow a detailed characterization of the event, as well as studies that propose strategies to avoid the appearance of this type of fungemia as an associated infection. to health care, in order to avoid the morbidity and mortality caused by them, especially in patients like the one reported.

DECLARATION ON CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

AUTHORS' CONTRIBUTION

First author: Analysis, writing of the manuscript, and final approval.

Second author: Analysis, writing of the manuscript, and final approval.

Third author: Analysis, writing of the manuscript, and final approval.

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