

CANDIDEMIA IN A BRAZILIAN HOSPITAL: THE IMPORTANCE OF *Candida parapsilosis*

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SUMMARY

The aim of this study was to perform a retrospective analysis of cases of candidemia in a Brazilian hospital in the city of Fortaleza, Ceará. A total of 50 blood cultures were analyzed from 40 candidemic patients. The mycological diagnosis was based on the phenotypical analysis and the patients' data were recorded in appropriate files. The most frequent species were *Candida parapsilosis* (n = 18), followed by *C. albicans* (n = 14), *C. tropicalis* (n = 8), *C. guilliermondii* (n = 6), *C. glabrata* (n = 2), and *Candida* spp. (n = 2). A detailed descriptive study was undertaken with 21 patients whose medical records were complete. The candidemia episodes occurred in eight male patients and 13 female patients. The most representative risk factors implicated in candidemia were prior antibiotic therapy, central venous catheters, parenteral nutrition, gastric probes and mechanical ventilation. Death occurred in 13 of the 21-candidemic patients. This study demonstrated the emergence of candidemia caused by *C. parapsilosis* in a Brazilian hospital in the city of Fortaleza, Ceará.

KEYWORDS: Candidemia; *Candida* species; Epidemiology; *C. parapsilosis*.

INTRODUCTION

Candidemia is defined as a clinical illness associated with the presence of *Candida* in patients' bloodstream²². In recent years, a progressive increase in the frequency of fungemia has been seen, particularly among patients receiving antibiotics, immunosuppressive therapy or parenteral nutrition, as well as among patients exposed to invasive medical procedures²⁷. *Candida* is the most important genus of yeast implicated in human infections, and is associated with almost 80% of all nosocomial fungal infections, representing the major cause of fungemia¹.

Candidemia is the fourth most common cause of hospital blood infection worldwide²³, being associated with extended hospital stays²⁶ and with high mortality rates among critically ill patients¹⁴. The worldwide candidemia rate has increased in many tertiary hospitals over the past few decades².

Candida albicans is the main pathogen implicated in candidemia, being responsible for more than 50% of all *Candida* bloodstream infections in the USA, Canada and Europe^{10,18,21}. *C. glabrata* is the second leading cause of both blood fungal infections and mucosal candidiasis in the USA^{2,14}.

Brazilian reports have revealed that *C. albicans* is the main species implicated in candidemia^{4,19} and among the non-*albicans* species, *C.*

*parapsilosis*¹¹ and *C. tropicalis*^{7,15} are considered the most important pathogens. The emergence of non-*albicans* species as important agents of candidemia has been linked to a prophylactic or an empiric use of antifungal drugs²⁶.

The aim of this investigation was to perform a retrospective study of 21 candidemia cases in a reference hospital in Fortaleza, Ceará (Northeast Brazil), emphasizing the mycological and epidemiological aspects.

MATERIAL AND METHODS

This study was performed at a tertiary hospital in the city of Fortaleza, Ceará, Brazil. The study began by surveying all hemocultures processed by the hospital's microbiology laboratory from June 2000 to June 2002. During this period, 4,376 hemocultures were processed by the Bactec system (Becton Dickinson, Diagnostic Instrument Systems, Sparks, MD, USA).

From a total of 4,376 hemocultures examined, 50 yeast-positive materials were sent to the Medical Mycology Specialized Center at the Federal University of Ceará, Brazil. The following tests were conducted for yeast identification: germinative tube, microculture in *Corn-meal* agar with Tween 80 (DIFCO, Detroit), CHROMagar-Candida[®] (Company, Paris, France) growth, auxonogram, zimogram subcultures and nitrogen assimilation tests¹².

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After the involvement of *Candida* species had been confirmed by the laboratory, a through search of each patient's medical record was made to collect the following information: age, gender, underlying condition and antimicrobial prophylaxis (use of therapeutic protocols with antibiotics and/or antifungals previous to laboratorial confirmation of sepsis). Invasive procedures, such as dissection of veins, introduction of catheters and probes, surgery and other possible predisposing factors were also investigated. This study was conducted with qualitative analysis of mycological and patient data.

RESULTS

From June 2000 to June 2002, 50 hemocultures from 40 candidemic patients were analyzed. *Candida* species were detected in all 50 yeast-positive hemocultures. The most frequent agent was *C. parapsilosis* (n = 18), followed by *C. albicans* (n = 14), *C. tropicalis* (n = 8), *C. guilliermondii* (n = 6), *C. glabrata* (n = 2) and *Candida* spp. (n = 2).

A total of 40 patients medical records were evaluated for candidemia. However, only 21 patients with available and complete medical records were included in our research. The analysis of medical records from these patients revealed that eight were male and 13 were female, age ranged from 0 to 76 years old, with nine newborn children and 12 adults. Candidemia episodes occurred mainly in patients from intensive care units (19 cases); *C. parapsilosis* was responsible for the fungemia of

seven patients, of which three were premature children. Two patients were referred from other Medical Care Centers (Table 1).

Of the 21 patients analyzed with positive *Candida* cultures, 10 presented only candidemia episodes, of which three suffered two recurrences (Table 1), and 11 showed additional bacteremia episodes. Of these, four cases of candidemia were prior to bacteria isolation, while in seven patients, bacteremia episodes preceded *Candida* isolation.

The most important underlying conditions were gastrointestinal disease (n = 5), neoplasm (n = 5) and prematurity (n = 6). There were no differences in risk factors or underlying diseases in candidemia caused by *C. parapsilosis*, *C. tropicalis*, and *C. albicans*. *C. tropicalis* was infrequent among premature children with *C. albicans* being the most frequent species among this patient group (Table 1).

From the analysis of 21 patients' records, it was considered that the most important coexisting exposures in candidemia development were prior antibiotic therapy (n = 18), central venous catheters (n = 17), parenteral nutrition (n = 15), gastric probes (n = 17), mechanical ventilation (n = 15) and surgery (n = 16). Each patient analyzed was subject to at least one risk factor.

Systemic antifungal drugs were used as prophylactic therapy before the occurrence of candidemia in only one patient (patient no. 20), with

Table 1
Clinical, epidemiological and laboratorial features of candidemic patients in tertiary care hospital from Northeast Brazil

Patient	Age (years)/ Sex	Underlying illness	Coexisting exposures	Species	Antifungal therapy (days)	Outcome
1*	NB/ F	Prematurity	B, E, G, K, N, O	<i>C. parapsilosis</i>	Amphotericin B(1)	Died during treatment
2	NB/ F	Prematurity	A, B, E, G, K, N, O	<i>C. albicans</i>	No	Died
3	36/ F	Complications of childbirth	D, E, G, L, N, O	<i>C. tropicalis</i>	No	Alive
4	63/ F	Gastrointestinal disease	A, B, C, D, E, F, G, I, N, O	<i>C. albicans</i>	Fluconazole(16)	Died during treatment
5	28/ F	Miscellaneous conditions	A, B, D, E, I, K, L, M, N, O	<i>C. guilliermondii</i>	No	Alive
6	NB/ M	Prematurity	A, B, D, E, G, K, N, O	<i>C. albicans</i>	Amphotericin B(14)	Died during treatment
7	NB/ F	Respiratory disease	D, E, G, N, O	<i>C. albicans</i>	No	Died
8	62/ F	Circulatory disease	B, D, G, K, N, O	<i>C. guilliermondii</i>	No	Died
9	24/ F	Surgery complications	A, B, E, G, K, L, N, O	<i>C. tropicalis</i>	Fluconazole(9)	Alive
10	NB/ F	Gastrointestinal disease	A, B, D, E, G, F, I, K, N, O	<i>C. tropicalis</i>	No	Died
11	NB/ F	Prematurity	A, B, E, K, O	<i>C. albicans</i>	No	Died
12	49/ M	Neoplasms	A, B, C, D, E, F, G, N, O	<i>C. glabrata</i>	No	Alive
13	25/ M	Gastrointestinal disease	A, B, C, D, E, G, H, N, O	<i>C. parapsilosis</i>	No	Died
14	NB/ F	Infectious disease	D, E, N, O	<i>C. parapsilosis</i>	No	Died
15*	NB/ F	Prematurity	A, B, C, D, N, O	<i>C. parapsilosis</i>	No	Died
16	76/ M	Neoplasms	B, C, D, E, G, J, K, N, O	<i>C. tropicalis</i>	Fluconazole(12)	Alive
17*	52/ M	Neoplasms	A, D, E, I, K	<i>C. tropicalis</i>	No	Alive
18	57/ M	Gastrointestinal disease	A, B, C, E, K, L	<i>C. tropicalis</i>	Fluconazole(9)	Alive
19	NB/ M	Prematurity	A, B, G, D, N, O	<i>C. albicans</i>	Amphotericin B(25)	Alive
20	75/ F	Neoplasms	A, B, C, D, E, F, G, J, L, N, O	<i>C. parapsilosis</i>	No	Died
21	44/ M	Gastrointestinal disease	A, B, D, G, L, N, O	<i>C. albicans</i>	Fluconazole(13)	Died during treatment

Patient presented two positive blood cultures at different times; * NB: newborn, A- parenteral nutrition; B- gastric catheter; C- colostomy; D- surgery; E- central venous access; F- thoracic drain; G- mechanical ventilation; H- peritoneal drain; I- gastrostomy; J- hemodialysis; K- hemotransfusion; L- vesical probe; M- abdominal drain; N- antibiotic treatment, O- intensive care unit (ICU)

fluconazole (200 mg per day) for 10 days. Even after candidemia had been confirmed, only eight patients received antifungal treatment. Three candidemic patients (patients no. 1, 6, 19) were treated with amphotericin B (0.5-1 mg/kg/day) for 13 days and the remaining five patients (patients no. 4, 9, 16, 18, 21) were treated with fluconazole (150 - 400 mg per day) for an average of 12 days. The remaining 13 patients were not treated with antifungal drugs (Table 1).

Candidemia was responsible for the death of 13 of the 21 patients. *C. albicans* was implicated in the death of six of them and *C. parapsilosis* was responsible for the death of five patients. Four of these patients had been treated with antifungal drugs (Table 1).

DISCUSSION

It was found that all the fungal blood infections at the reference tertiary hospital were caused by yeast of the *Candida* genus. These data corroborate some studies in which *Candida* species were the most involved in fungemia cases^{1,15}.

In this study, non-*albicans* species of *Candida*, were responsible for a total of 72% of fungemia cases. *C. parapsilosis* (n = 18) was the most isolated agent, followed by *C. albicans* (n = 14), *C. tropicalis* (n = 8), *C. guilliermondii* (n = 6), *C. glabrata* (n = 2) and *Candida* spp. (n = 2). Brazilian reports have revealed that *C. albicans* is the main agent of candidemia (20 - 50%), followed by *C. parapsilosis* (17 - 35%), *C. tropicalis* (12 - 27%), and *C. guilliermondii* (2 - 10%)².

The increased use of invasive medical procedures as well as the prophylactic and empirical use of antifungal drugs, especially those of azolic derivation, has been blamed for the emergence of the non-*albicans* species of *Candida*^{13,14,20}.

C. parapsilosis is widely recognized as a cause of fungemia among hospitalized patients¹⁷. *C. parapsilosis* is part of the endogenous microbiota of human beings and is a commensal organism, which penetrates the blood by rupturing the skin. The yeast is capable of forming biofilm in glucosylated solutions and adhering to plastic materials, such as catheters used for parenteral nutrition. Over the last few years, outbreaks and clusters of cross-transmission, total parenteral nutrition solutions, intravascular devices, and medications have been related to *C. parapsilosis* fungemia^{6,10}.

The following were not included in this research: the presence of *C. parapsilosis* on the hands of the medical team and on substances which come into contact with patients, such as catheters and solutions for intravenous use. However, the information from the literature corroborates the hypothesis that the medical team could be involved, in some way, in the contamination of patients, in as much as *C. parapsilosis* could be isolated on the hands of healthy professionals^{9,28}. In addition, *C. parapsilosis* is an important pathogen of onychomycosis in fingernails^{4,6,25}.

Most of the patients involved in this study (n = 19) were from Intensive Care Units (ICU); *C. parapsilosis* were related to candidemia in three premature children from this unit. However, such episodes occurred on different dates (case 1: 06/12/2000; case 2: 08/13/2000; case 3: 04/27/2001). Such high rates of fungal infection in ICUs corroborate the findings of several authors^{3,19}. These data may be explained by the fact that these

patients are usually considered high risk, depending on life support, thus subject to multiple invasive procedures which make them more susceptible to a rapid microbial invasion.

It is important to state that, in addition to the seven strains of *C. parapsilosis* isolated from patients with complete medical records (Table 1), the remaining strains were isolated from patients treated in the following units: emergency (n = 3), cardiology (n = 2), gastroenterology (n = 3), intensive care unit (n = 2) and nursing (n = 1). It was observed during this study that the presence of candidemia cases associated with episodes of bacteremia was considerable (n = 11), especially when the bacteremia preceded candidemia. These data may be considered a new risk factor, according to ELLIS *et al.*¹¹, due to the indiscriminate use of antibiotics in high-risk patients.

The risk factors assessed in our study are also quoted by several authors^{7,27}. It was seen that prior antibiotic treatment, central venous access, parenteral nutrition, surgery, mechanical ventilation and gastric catheterization were all associated with candidemia. From the therapeutic point of view, it was observed that, of the 21 patients, 13 were not treated with any antifungal agent and of these, four patients were cured after risk factors had been removed as described above.

Although the literature states an association of risk factors such as central venous catheter and parenteral nutrition, with *C. parapsilosis*⁶, this was not seen in this study, due to the limited number of samples, which did not allow statistical analysis.

The species which showed the highest mortality rates were *C. albicans* (n = 6) and *C. parapsilosis* (n = 5). However, HUANG *et al.*¹⁴ reported that *C. parapsilosis* showed high involvement in cases of mortality and morbidity, especially in neonates. In our study, cases of mortality as a result of this agent were observed in untreated patients, who were diagnosed at a later stage.

This study shows that among all the found yeasts, *C. parapsilosis* was the main isolated agent and evidences the importance of *C. parapsilosis* in candidemia episodes in a Brazilian tertiary care hospital in Northeast Brazil.

RESUMO

Candidemia em hospital terciário brasileiro: a importância da *Candida parapsilosis*

O presente estudo objetivou desenvolver uma análise retrospectiva de casos de candidemia em hospital brasileiro na cidade de Fortaleza, Ceará. Um total de 50 hemoculturas foram analisadas de 40 pacientes com quadros de candidemia. O diagnóstico micológico foi baseado na análise morfológica e bioquímica e os dados dos pacientes foram coletados das histórias clínicas. As espécies mais frequentes foram *Candida parapsilosis* (n = 18), seguida por *C. albicans* (n = 14), *C. tropicalis* (n = 8), *C. guilliermondii* (n = 6), *C. glabrata* (n = 2) e *Candida* spp. (n = 2). Um estudo descritivo foi realizado com apenas 21 pacientes os quais possuíam dados clínicos completos. Os episódios de candidemia aconteceram em oito pacientes do sexo masculino e 13 do feminino. Os fatores de risco implicados em candidemia foram antibioticoterapia prévia, uso de cateter venoso central, nutrição

parenteral, sondagem gástrica e ventilação mecânica. A morte aconteceu em 13 dos 21 pacientes com candidemia. Este estudo demonstrou a emergência de candidemia causada por *C. parapsilosis* em um hospital brasileiro na cidade de Fortaleza, Ceará.

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