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Original Article

Community-onset candidemia at a university hospital, 1995-2005

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Background and Purpose: Although not all candidemias are hospital-acquired, data on clinical epidemiology for the community-onset candidemia are limited. This retrospective study was conducted to describe predisposing factors and outcomes of community-onset candidemias.

Methods: Medical records of patients who were admitted to the National Taiwan University Hospital between January 1, 1995 and May 31, 2005 and had *Candida* isolated from their blood in the outpatient setting and/or within 48 h of hospitalization (community-onset) were reviewed.

Results: A total of 56 episodes of candidemia were reviewed, which included 8 episodes (14.3%) of true community-acquired candidemia occurring in patients with no record of hospitalization within the previous 30 days and without histories of invasive procedures either just before or at the time of admission, and 48 episodes (85.7%) that were health care-associated. The latter included 24 episodes (42.9%) in patients recently discharged from hospitals (within 2-30 days of current admission), 23 episodes (41.1%) associated with invasive procedures and/or central intravascular lines placed for outpatient therapy, and 1 episode (1.8%) in patients admitted from nursing homes. Gastrointestinal bleeding (46.4%), immunosuppressive therapy (42.9%) and previous antibiotics use (37.5%) were the most common predisposing factors. Diabetes was the single most important predisposing factor in true community-acquired candidemia (62.5%) and had a significantly higher prevalence among these patients than in those with health care-associated candidemias (p=0.035). *Candida albicans* was the most common isolate (39.7%), followed by *Candida tropicalis* (22.4%) and *Candida glabrata* (17.2%). The overall case fatality rate was 55.4% (31/56), and 58.1% (18/31) of this was attributable to candidemia. Multivariate analysis identified higher severity score and lack of antifungal therapy as having an independent and adverse influence on outcome.

Conclusions: Up to 85.7% of community-onset candidemias are health care-associated. There is a conceptual and practical need for a new classification for the spectrum of acquisition of infection, wherein the new category of health care-associated infection will have implications for the selection of empirical therapy.

Key words: Candidiasis; Cross infection; Fungemia; Infections, community-acquired; Mortality; Risk factors

Introduction

Candida species are an important cause of nosocomial bloodstream infections [1,2]. However, 4 to 28% of candidemia cases are not hospital acquisitions and clinical epidemiology for these cases is limited [3-12]. Thus, diagnosis of candidemia might be delayed in patients with sepsis who are being treated in the outpatient setting, particularly in the emergency departments. Our previous study demonstrated that 20% of patients with candidemia died within 72 h and that lack of antifungal therapy is an independent factor associated with mortality [13]. Thus, the importance of

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being continually aware of this disease entity cannot be overemphasized.

In recent decades, certain immunosuppressive therapies, surgical procedures, dialysis, and parenteral nutrition supports have been conducted in the outpatient setting. Thus, the traditional classification of infection acquisition according to the definition of the Centers for Disease Control and Prevention (CDC) [14], i.e., community acquisition vs hospital acquisition, becomes inadequate in differentiating such diversity [15,16]. As a consequence, new classifications for community-acquired bacteremia have been proposed, which emphasize the effect that exposure to the health care system has on community-acquired infections [15,17]. The term "community-onset" infection is perhaps more technically appropriate for the description of candidemia detected in the outpatient setting and/or within 48 h of hospitalization than the currently used "community-acquired" infection [18]. This retrospective study was conducted to better understand the clinical presentations, predisposing factors, and outcomes of 56 cases of community-onset candidemia at a university hospital and to adapt a new classification for community-acquired infections.

Methods

Hospital setting

The National Taiwan University Hospital is a 2400-bed, major medical center in Taiwan, which offers both primary and tertiary medical care.

Patient selection

The medical records of patients who had *Candida* species isolated from blood collected in the outpatient setting or within 48 h of hospitalization between January 1, 1995 and May 31, 2005 were reviewed. These patients were identified during a prospective, hospital-wide, nosocomial infection surveillance program. Those who fulfilled the definition of hospital acquisition [14] were excluded.

Data collection

Medical records were retrospectively reviewed and a standardized case record form was used to collect the following data: age, gender, underlying diseases, predisposing conditions, clinical presentations, and clinical outcomes. Underlying diseases included hematological malignancies, solid tumors, diabetes, cardiovascular diseases, chronic lung diseases, liver cirrhosis, chronic kidney diseases, and urinary tract obstructions. Data were also collected on the use of systemic antifungal drugs and potential predisposing conditions occurring within 30 days before the onset of candidemia. These included immunosuppressive therapy, total body irradiation, gastrointestinal bleeding, central venous catheterization, parenteral nutrition, urinary catheterization, and the use of antibiotics, H_2 receptor blockers, or proton pump inhibitors.

Definitions

Candidemia was defined as the isolation of *Candida* species from at least 1 blood culture collected from a patient showing signs and symptoms of infection. Candidemias detected in the outpatient setting or within the first 48 h of hospitalization (including candidemias detected on admission to another hospital, if the patient was transferred) were classified as "community-onset" candidemias according to the CDC definition [14] and further subclassified into community-acquired (A) or health care-associated (B-D) — Table 1 (modified from the study by Siegman-Igra et al [15]).

"Group A" candidemia included true community-acquired candidemias occurring in patients who were admitted to the hospital from their homes with no hospitalization in the preceding 30 days or histories of invasive procedures either just before or at the time of admission. Candidemias occurring in patients receiving long-term dialysis or in patients admitted with intravascular devices were excluded from this group. "Group B" consisted of candidemias diagnosed in patients who were recently discharged from hospital. Candidemia that occurred in patients who were discharged from hospital a day before the present admission was classified as a hospital-acquired infection and excluded from this study. "Group C" included candidemias associated with invasive procedures. This group was further classified into 5 subgroups: "group C1" included candidemias that occurred in patients who underwent an invasive procedure (endoscopy, urethral dilatation, etc.) shortly before admission to the hospital and who were admitted because of an infectious complication that resulted from this procedure. "Group C2" consisted of candidemias that occurred in patients with non-infectious problems who had undergone invasive procedures (Foley's catheter insertion, intravascular line insertion, etc.) at the time of admission to the hospital and developed complicating candidemia within the first 48 h of admission. "Group C3" included candidemias that occurred in patients with long-term, central intravenous

Table 1. Classification of 56 episodes of candidemia that occurred in the outpatient setting or within 48 h of hospitalization (community-onset candidemia)

Classification of candidemia	Circumstances of acquisition	No. of episodes (%)
A	True community-acquired candidemia	8 (14.3)
B	Candidemia in patients recently discharged from hospital (within 2-30 days of current admission)	24 (42.9)
C	Procedure-related candidemia	23 (41.1)
C1	Invasive procedure performed before admission	6 (10.7)
C2	Invasive procedure performed after admission	2 (3.6)
C3	Central intravascular lines placed for home therapy	15 (26.8)
D	Nursing home-acquired candidemia	1 (1.8)
Total		56 (100.0)

devices in place who were receiving chemotherapy, hemodialysis or parenteral nutrition, and who were admitted to the hospital with candidemias that resulted from the presence of these intravenous devices. "Group D" consisted of candidemias that occurred in patients who were admitted to the hospital from nursing homes.

For patients who had more than 1 episode of candidemia, the second episode was defined as an incident if it occurred at least 2 months after the first. The duration of candidemia was defined as the time interval (days) between the first and the last positive blood cultures. Concomitant bacteremia was defined as the isolation of bacteria from blood within 24 h of the first blood cultures being positive for *Candida*.

Immunosuppressive therapy was defined as present if there was at least one of the following: neutropenia (absolute neutrophil count <1000 per mm^3), corticosteroid therapy (equivalent of >20 mg prednisolone per day), or cancer chemotherapy. Acute renal failure was defined as the need for hemodialysis or the presence of elevated creatinine levels >2.5 mg/dL. Significant liver dysfunction was defined as liver function test levels >3 times the upper limits of normal. Multiple organ failure was defined as the failure of more than 3 organs. Concomitant bloodstream infection was defined as the isolation of another non-*Candida* microorganism from the blood within a 48-h period before or after the first isolation of *Candida* in blood culture.

The severity of candidemia was scored using the following clinical criteria observed within 3 days of the positive blood culture: mental status, presence of fever (a single temperature measurement of >38.5°C or 3 measurements of >38.0°C within a 24-h period), hypotension (systolic blood pressure <90 mm Hg or a drop in systolic blood pressure by >40 mm Hg), requirement for mechanical ventilator and vasopressor support, and cardiac arrest. This scoring system has been proven to be highly predictive of survival in previous prospective studies on Gram-negative bacteremia [19,20] and candidemia [13,21]. Severity of illness was quantified as follows: temperatures >38°C (1 point), temperatures >39°C (2 points), mental status (alert, 0 points; disoriented, 1 point; stupor, 2 points; coma, 4 points), hypotension (2 points), mechanical respiratory support (2 points), and cardiac arrest (4 points). Patients who accumulated 4 or more points were defined as critically ill.

Outcome was defined at discharge. Candidemia was considered to be the primary or contributory cause of death if patients died within 7 days of candidemia without other evident reasons for death, or patients remained in septic conditions before death. Death was considered to be due to another cause when candidemia was cleared at the time of death (as indicated by a lack of fever or positive cultures) and there was another likely cause (usually the underling disease).

Candida species was identified by standard microbiological methods in our microbiology laboratory.

Statistics

In univariate analyses, categorical variables were compared with the chi-squared test or Fisher's exact test, and continuous variables were analyzed using Student's *t* test. A p value <0.05 was considered to be statistically significant, and all probabilities were 2-tailed. Multivariate analyses were conducted by a stepwise logistical regression method. All statistical analyses were performed with the Statistical Package for the Social Sciences for Windows (Version 14.0; SPSS Chicago, IL, USA).

Results

From January 1, 1995 to May 31, 2005, 2017 episodes of candidemia satisfied the definition of hospital acquisition

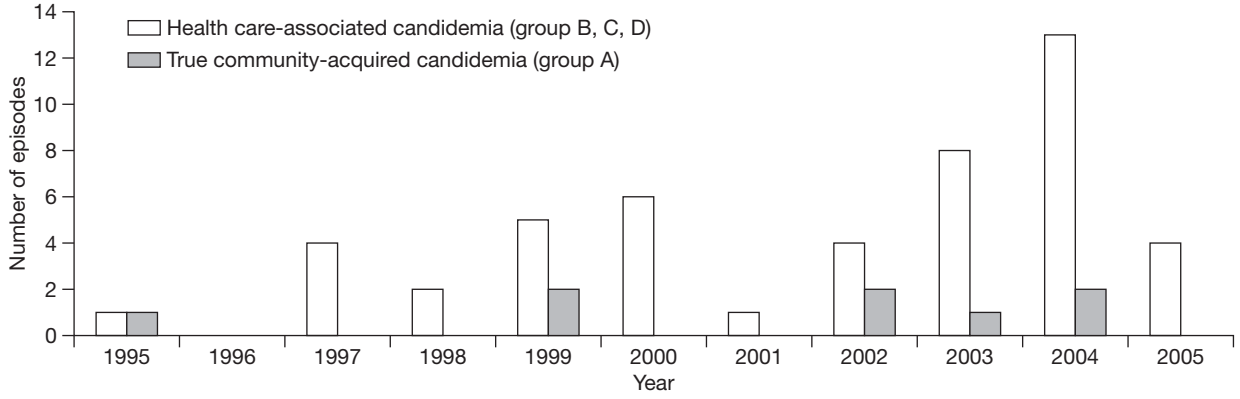

Fig. 1. Episodes of community-onset candidemia from January 1, 1995 to May 31, 2005 at the National Taiwan University Hospital.

and were excluded. A total of 56 episodes of community-onset candidemia in 52 patients were reviewed (56/2073; 2.7%). Up to 48 episodes (85.7%) occurred in the emergency department, 4 (7.1%) were detected in the outpatient clinics, and 2 episodes (3.6%) each occurred within 48 h of admission to the surgical and medical wards, respectively. These episodes, traditionally classified as community-acquired infections [14], included only 8 episodes (14%) of true community-acquired candidemia. Forty eight episodes (85.7%) among the 56 reviewed were health care-associated (Table 1). The latter included 24 episodes (42.8%) in patients recently discharged from hospital, 23 episodes (41.1%) associated with invasive procedures and/or central intravascular lines placed for outpatient therapy, and 1 episode (1.8%) in a patient admitted from a nursing home. Invasive procedures performed either before or at the time of admission included Foley's catheter insertion (n = 2), closure of enterocutaneous fistula (n = 1), peripheral vein line insertion (n = 5), and central vein line insertion (n = 2). The study showed an increase in the number of health care-associated candidemia episodes during the study period (Fig. 1).

Table 2 summarizes the clinical characteristics of patients with candidemias. The median age of patients was 60.5 years old, and all patients with true community-acquired candidemia, except 1, were male. There was no significant difference in the clinical characteristics of the 4 groups.

All patients had underlying diseases, such as hematological malignancies or solid tumors (57.1%), diabetes (28.6%), chronic renal failures (26.8%), and cardiovascular diseases (25.0%) [Table 3]. Diabetes was the single most important predisposing factor in community-acquired candidemia and was more prevalent in these patients than among those with health

Table 2. Clinical characteristics of patients with community-onset candidemia

Variable	No. of episodes of candidemia (%)				
	Group A (n = 8)	Group B (n = 24)	Group C (n = 23)	Group D (n = 1)	Total (n = 56)
Age (years) [median (range)]	55.5 (31-74)	62.5 (25-81)	63 (24-89)	94 (94)	60.5 (24-94)
Gender (male/female)	7/1	12/12	14/9	0/1	33/23
Fever	7 (87.5)	18 (75.0)	19 (82.6)	1 (100.0)	45 (80.4)
Hypotension	3 (37.5)	9 (37.5)	10 (43.5)	1 (100.0)	23 (41.1)
Aminotransferase elevation	5 (62.5)	11 (45.8)	8 (34.8)	1 (100.0)	25 (44.6)
Leukocytosis >10,000/L	6 (75.0)	14 (58.3)	11 (47.8)	1 (100.0)	32 (57.1)
Thrombocytopenia <100,000/L	2 (25.0)	2 (8.3)	6 (26.1)	0 (0.0)	10 (17.9)
Mechanical respiratory support	2 (25.0)	3 (12.5)	7 (30.4)	0 (0.0)	12 (21.4)
Worsening azotemia	1 (12.5)	9 (37.5)	8 (34.8)	0 (0.0)	18 (32.1)
Multiple organ failure	2 (25.0)	3 (12.5)	5 (21.7)	0 (0.0)	10 (17.9)
Severity of illness >4 points	2 (25.0)	9 (37.5)	11 (47.8)	1 (100.0)	23 (41.1)
Death, all causes	5 (62.5)	14 (58.3)	11 (47.8)	1 (100.0)	31 (55.4)
Death due to candidemia	1 (12.5)	10 (41.7)	6 (26.1)	1 (100.0)	18 (32.1)

Table 3. Underlying diseases and predisposing conditions of patients with community-onset candidemia

Variable	No. of episodes of candidemia (%)				
	Group A (n = 8)	Group B (n = 24)	Group C (n = 23)	Group D (n = 1)	Total (n = 56)
Underlying disease					
Solid tumors	3 (37.5)	12 (50.0)	7 (30.4)	0 (0.0)	22 (39.2)
Hematological malignancy	1 (12.5)	2 (8.3)	7 (30.4)	0 (0.0)	10 (17.9)
Diabetes[a]	5 (62.5)	6 (25.0)	5 (21.7)	0 (0.0)	16 (28.6)
Chronic renal failure	0 (0.0)	5 (20.8)	9 (39.1)	1 (100.0)	15 (26.8)
Cardiovascular disease	1 (12.5)	8 (33.3)	5 (21.7)	0 (0.0)	14 (25.0)
Liver cirrhosis	2 (25.0)	4 (16.7)	2 (8.7)	0 (0.0)	8 (14.3)
Chronic lung disease	0 (0.0)	2 (8.3)	1 (4.3)	0 (0.0)	3 (5.4)
Urinary tract obstruction[b]	3 (37.5)	5 (20.8)	0 (0.0)	1 (100.0)	9 (16.1)
Predisposing condition					
Immunosuppressive therapy	3 (37.5)	11 (45.8)	10 (43.5)	0 (0.0)	24 (42.9)
Neutropenia	0 (0.0)	2 (8.3)	3 (13.0)	0 (0.0)	5 (8.9)
Steroid usage	2 (25.0)	7 (29.2)	7 (30.4)	0 (0.0)	16 (28.6)
Chemotherapy	2 (25.0)	6 (25.0)	8 (34.8)	0 (0.0)	16 (28.6)
Total body irradiation	1 (12.5)	3 (12.5)	0 (0.0)	0 (0.0)	4 (7.1)
Gastrointestinal bleeding	3 (37.5)	12 (50.0)	11 (47.8)	0 (0.0)	26 (46.4)
Central venous catheterization	0 (0.0)	12 (50.0)	16 (69.6)	0 (0.0)	28 (50.0)
Parenteral nutrition	0 (0.0)	7 (29.2)	4 (17.4)	0 (0.0)	11 (19.6)
Urinary catheterization	1 (12.5)	7 (29.2)	4 (17.4)	1 (100.0)	13 (23.2)
Drainage tube	0 (0.0)	1 (4.2)	0 (0.0)	0 (0.0)	1 (1.8)
Antibiotics use	3 (37.5)	9 (37.5)	9 (39.1)	0 (0.0)	21 (37.5)
H_2 blocker or proton pump inhibitor	1 (12.5)	7 (29.2)	8 (34.7)	0 (0.0)	16 (28.6)

[a] p=0.035.

[b] p=0.108.

care-associated candidemia (62.5% vs 22.9%, p=0.035). Gastrointestinal bleeding (46.4%), immunosuppressive therapy (42.9%), and prior antibiotics use (37.5%) were the most common predisposing factors.

Candida albicans was the most common isolate (39.7%), followed by isolates of *Candida tropicalis* (22.4%), *Candida glabrata* (17.2%), *Candida parapsilosis* (15.5%), and 1 each of *Candida guilliermondii*, *Candida krusei* and *Candida famata.* In true community-acquired candidemia (group A) [Table 4], *C. albicans* was the most common isolate (n = 3), followed by *C. tropicalis* (n = 2), *C. glabrata* (n = 2), and *C. parapsilosis* (n = 1). In health care-associated candidemia (groups B, C, and D), *C. albicans* was the most common isolate (n = 20), followed by *C. tropicalis* (n = 11), *C. glabrata* (n = 8), *C. parapsilosis* (n = 8), and others (n = 3). Six of 28 candidemias (21.4%) associated with central lines were caused by *C. parapsilosis*, compared with 3 out of 28 (10.7%) in the other group (p=0.469).

The overall case fatality was 55.4% (31/56) and the 14-day mortality rate was 33.9% (19/56). Mortality directly attributable to candidemia was 58.1% (18/31). Univariate analysis identified older age, solid tumors, higher severity scores, hypotension, and lack of antifungal therapy as the 5 factors associated with 14-day mortality (Table 5). Among the 28 patients with central catheterization, catheter removal was associated with lower case fatality rates (0%; 0/16) than in those who had no removal of catheters (66.7%; 8/12, p<0.001).

Of all the variables associated with mortality in the univariate analysis, only lack of antifungal therapy (odds ratio [OR], 34.6; 95% confidence interval [CI], 3.6-333.4; p=0.0022) remained strongly predictive of death in the multivariate analysis. Higher severity scores (≥4) had a borderline impact (OR, 1.38; 95% CI, 0.99-1.92; p=0.0548).

Discussion

This is the first study series on community-onset candidemia in Taiwan, emphasizing the need for a change in the traditional definition of community-acquired infections. Previous studies have reported that 4 to 28% cases of candidemia are not hospital-acquired [3-12]. Richet et al reported that 15% of

Table 4. Clinical characteristics of the 8 patients with true community-acquired candidemia

Patient no.	Age (years)/ gender	Underlying medical conditions	Duration of candidemia	Previous admission	Portal of entry	*Candida* species therapy	Severity score	Duration of antifungal therapy	Outcome
1	31/M	Diabetes mellitus, renal stone with hydronephrosis, aortic regurgitation s/p aortic valve replacement, IV drug abuser	10 months	3	Urine, IE	*Candida tropicalis*	2	52 weeks (AmB 4 weeks, then fluconazole)	Survived
2	48/M	Diabetes mellitus, iatrogenic Cushing's syndrome with adrenal insufficiency	8 months	2	NA	*Candida glabrata*	5	Fluconazole 1 week, AmB 2 weeks	Death (51 days)
3	34/M	Rectal cancer with cancerous peritonitis s/p Hartmann's procedure	9 months	1	NA	*Candida parapsilosis*	2	Fluconazole 2 weeks	Death (41 days)
4	58/M	Diabetes mellitus, renal stones with hydronephrosis, chronic renal insufficiency	Nil	6	Urine, IE	*Candida albicans*	3	Fluconazole 1 week	Death (7 days)
5	71/M	Adenocarcinoma of unknown origin with spine/liver metastasis, gastric ulcer	42 days	1	Sputum	*Candida tropicalis*	7	Fluconazole 5 weeks	Death (34 days)
6	74/M	Non-Hodgkin's lymphoma, coronary artery disease s/p CABG, HBV carrier	2 months	1	NA	*Candida albicans*	3	Fluconazole 2 weeks	Survived
7	53/M	Diabetes mellitus, duodenal ulcer, liver cirrhosis, hepatoma with portal vein thrombosis	5 months	2	NA	*Candida albicans*	2	Micafungin 7 weeks	Survived
8	68/F	Diabetes mellitus, renal stone, HCV-related liver cirrhosis, upper gastrointestinal bleeding	4 months	>3	Urine, IE	*Candida glabrata*	1	Fluconazole 1 week	Death (9 days)

Abbreviations: M = male; F = female; s/p = status post; IV = intravenous; CABG = coronary artery bypass graft; HBV = hepatitis B virus; HCV = hepatitis C virus; IE = infective endocarditis; NA = not applicable; AmB = deoxycholate amphotericin B

the 156 candidemias noted in a year at 25 French hospitals were community-acquired, and 70% of the candidemias were hospital-acquired infections. The type of acquisition could not be determined in 15% of the patients [7].

Macphail et al reported that although 17% of 202 candidemias reported in 5 years at 3 Canadian hospitals were not nosocomial, most of the patients had identifiable risk factors [6]. A population-based study done by Kao et al in Atlanta and San Francisco showed that 20.2% of patients with candidemias developed infections in the outpatient setting [4]. The demographic and clinical characteristics of these patients were similar to those of patients who developed candidemia while being hospitalized, suggesting that they have similar risk factors. Our study demonstrated that up to 85.7% of community-onset candidemias were health care-associated. This finding might explain the great disparity

Table 5. Univariate predictors of 14-day mortality in patients with candidemia

Characteristics	Survived (n = 37) No. (%)	Died (n = 19) No. (%)	Odds ratio (95% confidence interval)	*p*
Community-acquired (group A)	6 (16.2)	2 (10.5)	0.61 (0.11-3.36)	0.703
Age (years) [mean±standard deviation]	56.4 ± 18.7	67.8 ± 11.3	4.11 (1.22-13.83)[b]	0.018
Underlying disease				
Hematological malignancy	9 (24.3)	1 (5.3)	0.17 (0.02-1.48)	0.139
Solid tumor	11 (29.7)	11 (57.9)	3.25 (1.03-10.28)	0.050
Diabetes mellitus	9 (24.3)	7 (36.8)	1.82 (0.55-6.01)	0.362
Urinary tract obstruction	5 (13.5)	4 (21.1)	1.71 (0.40-7.28)	0.470
Liver cirrhosis	5 (13.5)	4 (21.1)	1.71 (0.40-7.28)	0.470
Predisposing factors				
Immunosuppression	18 (48.6)	6 (31.6)	0.49 (0.15-1.56)	0.264
Steroid	14 (37.8)	2 (10.5)	0.19 (0.39-0.97)	0.059
Neutropenia	4 (10.8)	1 (5.3)	0.46 (0.05-4.42)	0.652
Central catheterization	20 (54.1)	8 (42.1)	0.62 (0.20-1.89)	0.573
Others				
Concomitant bacteremia	7 (18.9)	2 (10.5)	0.50 (0.09-2.71)	0.703
Non-*Candida albicans*	22 (59.5)	11 (57.9)	0.94 (0.31-2.88)	1.00
Prior fluconazole therapy	4 (10.8)	6 (31.6)	3.81 (0.92-15.73)	0.073
Severity of illness				
Severity score (range)	2.7 ± 1.9	5.7 ± 3.2	8.71 (2.45-30.94)[c]	<0.001
Hypotension	10 (27.0)	13 (68.4)	5.85 (1.75-19.60)	0.004
Mechanical respiratory support	6 (16.2)	6 (31.6)	2.39 (0.65-8.78)	0.302
Worsening azotemia	9 (24.3)	9 (47.4)	2.8 (0.87-9.045)	0.130
Treatment				
Removal of catheter[a]	16 (43.2)	0 (0.0)	0.57 (0.43-0.75)	<0.001
No antifungal therapy at all	1 (2.7)	12 (63.2)	61.71 (6.87-554.07)	<0.001

[a]Twenty eight evaluable patients with central catheterization.

[b]Divided by age more than 60 years old.

[c]Divided by severity score more than 4 points.

seen in the proportion of candidemias that are not nosocomial in origin.

This is the largest study series of candidemia in the outpatient setting. In the existing English literature, only Pasqualotto et al have described detailed clinical characteristics of 18 candidemias in the outpatient setting between 1995-2003 [12]. Both studies showed major underlying diseases to be cancer and chronic renal failure, with high mortalities in both groups. According to our studies, there was no difference in the 14-day mortality of patients with community-onset candidemia (33.9%; 19/56, this study) and those with hospital-acquired infections (34.6%; 65/188) [22]. However, other studies have shown that nosocomial acquisition of candidemia is a risk factor for adverse outcomes [9,10].

This study showed 15.5% of community-onset candidemias were caused by *C. parapsilosis*. Population-based studies have demonstrated that species other than *C. albicans*, mainly *C. parapsilosis*, are more prevalent in the community [4,11,12]. Up to 83.7% of candidemias occurring in the outpatient setting in Brazil were caused by species other than *C. albicans*, primarily *C. parapsilosis* (36.8%) [12]. This finding may reflect the high proportion of procedure-related candidemias in the study population, as *C. parapsilosis* fungemia is associated with the presence of a central line [23].

Different criteria have been used for the definition of community-acquired infections. While many studies have employed the 48 h following hospital admission criteria [3,5,6,9], others have chosen 72 h [12,24] or even 24 h [4,10,11]. According to the guidelines published by the CDC, nosocomial infections are those that are not present or incubating at the time of admission to a hospital [14]. However, dramatic changes have taken place in the health care system in recent years, which have shifted a significant share of the load of caring for sick patients from the hospital to the community. As a result, the sharp distinction that existed between the characteristics of hospital- and community-acquired infections has become less clear, with some infections even having mixed characteristics of both types of

acquisitions. In this study, 85.7% of candidemias, traditionally classified as community-acquired infections, were reclassified as health care-associated. Health care-associated infections are similar to nosocomial infections in terms of the frequency of the various comorbid conditions, source of infection, pathogens and their susceptibility patterns, and mortality rates at follow-up [15,17]. There is a conceptual and practical need for a new classification for the spectrum of acquisition of infection [15,17], wherein the new category of health care-associated infection will have many implications on the selection of empirical therapy and infection control surveillance [17].

Criteria for the definition of recent hospitalization remain controversial. Pasqualotto et al showed that 52.6% of patients with outpatient-acquired candidemias had previous hospitalization in the 60 days preceding candidemia [12]. In this study, we chose the interval of 30 days to define recent hospitalization before identification of candidemia (group B). However, 7 of 8 patients with true community-acquired candidemia (group A) showed histories of hospitalization in the preceding 10 months (median, 5 months) [Table 4]. In the case of community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) infections, however, a 1-year interval is suggested instead, as MRSA colonization has been known to persist from months to years [18]. Colonization is a prerequisite for the development of candidiasis and colonization increases during hospitalization [23]. It is possible that patients become colonized during repeated hospitalizations and become predisposed to candidemia because of their underlying conditions, and the use of antibiotics and invasive procedures.

Diabetes mellitus is found in 15 to 30% of the patient population with candidemia [4,25,26]. This study demonstrated that 3 of 8 patients with true community-acquired candidemia had candiduria, renal stone, and hydronephrosis; all 3 had diabetes (Table 4). *Candida* is frequently isolated from the urine of patients, even in the absence of symptoms [27,28], and the prevalence of diabetes mellitus and urinary catheterization was significantly higher in this group when compared to the general hospital population [27]. On the other hand, candiduria may rarely be the source of subsequent dissemination in high-risk patients [29]. Urinary tract abnormalities were present in 23 of 26 patients with candidemia secondary to urinary tract infections (88%); 19 (73%) had urinary tract obstruction, and 19 had undergone urinary tract procedures before the onset of candidemia [29].

A unique finding of this study was that 3 of 8 patients with true community-acquired candidemia had endocarditis (Table 4). This finding was similar to that found by studies on community-acquired *S. aurues* bacteremia [30]. The duration of community-onset candidemias could also be longer than that of the nosocomial ones, predisposing the patients to endocarditis.

Although this was a retrospective study, medical records obtained from the hospital were comprehensive enough for the reclassification of community-onset candidemias. However, there is a possibility that health care-associated practices in other hospitals might be underestimated by similar studies, if transfer notes are not provided at the time.

In conclusion, candidemia is a potential cause of community-onset infections and is associated with high mortality rates. Up to 85.7% of community-onset candidemias are health care-associated. Health care professionals must recognize that *Candida* is no longer a pathogen acquired by inpatients alone and that it must be kept in mind during the differential diagnoses of patients from the community hospitalized with clinical evidence of sepsis. True community-acquired candidemia is known to occur in patients with malignancies, diabetes, or urinary tract obstructions. New classifications for the spectrum of bloodstream infection acquisition should be considered.

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