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Brief report

Clinical manifestations and prognostic factors of central line–associated candidemia

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From 2009-2012, a total of 281 episodes of central line–associated candidemia were identified, and the overall incidence was 2.05 episodes per 1,000 hospital admissions. More than half of the patients were classified as older adults, with an age ≥65 years. Cancer was the most common underlying disease (n = 231, 82.2%). Twenty patients had polycandidal candidemia, and 94 had concomitant bacteremia. The overall in-hospital mortality rate was 50.9%, and a multivariable analysis showed that this rate was only significantly associated with a Charlson comorbidity index score >5, jaundice, no antifungal agent use, and use of mechanical ventilators.

Bloodstream infections that are caused by *Candida* species have become a major cause of nosocomial infections worldwide.[1-3] Candidemia frequently develops in patients who are at risk for receiving invasive procedures or devices or intravascular catheters, broad-spectrum antimicrobial agents, mechanical ventilation, immunosuppressive agents, or parenteral nutrition.[3] Importantly, its associated mortality rate is high, ranging from 40%-56%.[1,4-7] Among these different types of candidemia, central line–associated candidemia compromises a significant proportion of cases. However, most studies that have been performed to date have broadly investigated invasive candidiasis, and few have focused on central line–associated candidemia specifically. Therefore, we retrospectively reviewed the clinical characteristics of central line–associated candidemia and investigated its associated prognostic factors at a hospital in Taiwan.

METHODS

This study was retrospectively conducted at a 900-bed hospital in southern Taiwan. From 2009-2012, patients with positive blood cultures for *Candida* species were identified from the database of the microbiology laboratory. The medical records of these individuals were retrospectively reviewed, and those with central line–associated candidemia were identified. Candidemia was defined as at least 1 set of positive blood cultures for *Candida* species in patients with compatible clinical signs and symptoms of infection. Central line–associated candidemia was defined as primary laboratory-confirmed candidemia in a patient with a central line at the time of (or within 48 hours prior to) the onset of symptoms that was not related to an infection at another site. Polycandidal candidemia were classified in patients whose blood samples were revealed to contain at least 2 *Candida* pathogens at the same time. Only those patients experiencing their first candidemia episode were enrolled in this study. Comparisons between each variable or category were performed using the χ^2 test. A multivariable forward logistic regression model was used to identify risk factors for mortality. All of the statistical analyses were conducted using the statistical package SPSS version 19.0 for Windows (SPSS Inc, Chicago, IL), and a P value <.05 was considered to be statistically significant.

RESULTS

During the 4-year period, a total of 281 episodes of central line–associated candidemia were identified, and the overall incidence was 2.05 episodes per 1,000 admissions. The hospital had a total of 136,831 admissions and 41,440 cancer patient admissions

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Table 1
Risk factors for mortality among 281 patients with central line–associated candidemia

Variable	Univariable			Multivariable		
	Odds ratio	*P* value	95% confidence interval	Odds ratio	*P* value	95% confidence interval
Charlson comorbidity index						
Charlson comorbidity index <5	Reference					
Charlson comorbidity index ≥5	3.13	.001	1.63-6.01	3.43	.001	1.70-6.91
Elevated bilirubin (>2 mg/dL)						
No	Reference					
Yes	2.59	.002	1.40-4.80	2.31	.013	1.20-4.46
Use of antifungal agents						
No	Reference					
Yes	0.36	.04	0.14-0.95	0.31	.03	0.11-0.88
Use of mechanical ventilator						
No	Reference					
Yes	3.21	<.001	1.95-5.31	3.02	<.001	1.78-5.11

during the study period spanning from January 2009-December 2012. The mean age of the patients was 65.9 years, over half of whom were classified as older adults, with ages ≥65 years. The mean Charlson comorbidity index score was 7.5. All of the episodes were classified as health care–associated infections. Cancer was the most common underlying disease (n = 231, 82.2%), followed by diabetes mellitus (n = 91, 32.4%), liver cirrhosis (n = 33, 11.7%), and end-stage renal disease (n = 24, 8.5%). Moreover, most of the patients had variable underlying conditions, such as prior exposure to broad-spectrum antibiotics (69%), and many were receiving immunosuppressants (72.2%).

Twenty patients had polycandidal candidemia. Among them, 9 had concomitant *C albicans* and *C glabrata*, 4 had *C albicans* and *C tropicalis*, 4 had *C albicans* and *C parapsilosis*, 2 had *C tropicalis* and *C parapsilosis*, and 1 had *C tropicalis* and *C glabrata*. Overall, *C albicans* (n = 156, 55.5%) was the most common pathogen, followed by *C tropicalis* (n = 58, 20.6%), *C parapsilosis* (n = 39, 13.9%), *C glabrata* (n = 35, 12.4%), and *C guilliermondii* (n = 6, 2.1%). In addition, 94 patients had concomitant bacteremia. Among these 94 cases, coagulase-negative staphylococcus (n = 37, 39.4%) was the most common bacteria, followed by enterococcus (n = 19, 20.2%), *Staphylococcus aureus* (n = 13, 13.8%), and *Escherichia coli* (n = 11, 11.7%). Moreover, antibiotic-resistant pathogens, including methicillin-resistant *S aureus*, vancomycin-resistant enterococci, extended-spectrum β-lactamase-producing *E coli*, and multidrug-resistant *Acinetobacter baumannii* were found.

Although >90% of the patients received variable antifungal agents and 70.8% experienced catheter removal, >40% of patients required intensive care unit (ICU) admission or mechanical ventilation. The overall in-hospital mortality rate was 50.9%. Table 1 summarizes the risk factors for mortality among the 281 patients with central line–associated candidemia. Multivariable analysis showed that in-hospital mortality was only significantly associated with a Charlson comorbidity index ≥5 (odds ratio [OR], 3.43; 95% confidence interval [CI], 1.70-6.91; $P = .001$), elevated bilirubin levels (OR, 2.30; 95% CI, 1.20-4.46; $P = .013$), use of antifungal agents (OR, 0.31; 95% CI, 0.11-0.88; $P = .028$), and use of a mechanical ventilator (OR, 3.02; 95% CI, 1.78-5.11; $P < .001$). In addition, other factors (eg, age, sex, *Candida* species, underlying diseases, concomitant bacteremia, removal of catheter, ICU admission) were not significant associated with mortality.

DISCUSSION

This large study investigating the clinical features of 281 episodes of central line–associated candidemia at a single institution had several significant findings. First, central line–associated candidemia is not an uncommon health care–associated infection, displaying an incidence of 2.05 per 1,000 admissions in this study. Most of the infections developed in patients with variable underlying comorbidities (eg, cancer, diabetes mellitus), in addition to those who were currently receiving immunosuppressants or who had recently received broad-spectrum antibiotics. Overall, our findings suggest that clinicians should consider the *Candida* species to be an important pathogen causing central line–associated bloodstream infections, especially for patients with risk factors.

Second, the present work showed that central line–associated candidemia is associated with a high mortality rate, which was estimated to be >50%. However, we used the overall in-hospital mortality rate for the outcome analysis in this study. Therefore, our findings could have overestimated the attributable or 14- or 28-day mortality rate, which may be used in other studies. Moreover, we found that comorbidity and no antifungal agent use were significant risk factors associated with mortality. In contrast, catheter removal was not found to significantly affect mortality rates, as was observed in a previous study. This may be because of the lack of evaluation of the timing of catheter removal in this study, which prevented the determination of the association between early catheter removal and the outcome of patients with central line–associated candidemia.

Third, this study found that approximately 33% of patients had concomitant bacteremia, which is not uncommon for patients with candidemia. This finding is consistent with a previous study[8] and indicates that antibiotics should be considered for the treatment of possible concomitant bacteremia in addition to that of candidemia in these patients. Moreover, broad-spectrum antibiotics should initially be considered if an antibiotic-resistant bacterium is prevalent in the environment.

Finally, we noted that *C albicans* remained the most common causative agent of central line–associated candidemia, accounting for more than half of the episodes of our hospital. Additionally, *C tropicalis* (n = 58, 20.6%), *C parapsilosis* (n = 39, 13.9%), and *C glabrata* (n = 35, 12.4%) were the most frequently isolated non-albicans *Candida* species. Although this epidemiologic feature may be different in other countries, these findings are in accordance with several previous studies[9,10] investigating candidemia in Taiwan, which showed that *C tropicalis* was the second most common *Candida* species that caused invasive infections.

This study had several limitations. First, we did not perform a routine antifungal susceptibility test for all of the clinical isolates that were found at our institution. Therefore, we cannot provide data regarding antifungal resistance patterns. Second, we did not record the timing of antifungal agent use. Therefore, we cannot clarify the association between the outcome and timing of the antifungal therapy. Third, we did not have data describing the use