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LETTER TO THE EDITOR

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Clinical features of patients with candidemia in sepsis

To the Editor:

Invasive candidiasis remains a critical problem in intensive care units (ICUs) throughout the developed world.[1] Nonetheless, differentiating between those with and without invasive candidiasis among critically ill ICU patients, especially during the early phase of the clinical course, remains challenging. In these situations, it is helpful to be familiar with both the epidemiology of the disease and the typical clinical characteristics of patients with candidemia complicated by sepsis, one of the most common risk factors for candidemia.[2] Our aim was to describe the characteristics and clinical features of patients with candidemia admitted to the ICU due to sepsis.

This is a case series analysis from a sepsis substudy of the Focused Outcomes Research in Emergency Care in Acute Respiratory Distress Syndrome, Sepsis and Trauma (FORECAST) study, a multicenter, prospective cohort study of patients with sepsis. FORECAST was conducted in 59 ICUs from January 2016 to March 2017 in Japan.[3] Adult patients (≥16 years) with severe sepsis or septic shock based on Sepsis-2 criteria and admitted to a participating ICU were included. Among this population, we selected patients with candidemia diagnosed from blood culture results.

Of 1184 patients with sepsis, fifteen patients with candidemia were identified (Table 1). Baseline characteristics are shown in Table S1. Six patients died prior to discharge from hospital. Among nine survivors, only one patient was able to return home after discharge (Table S2). The most common species among monomicrobial isolates was *C. albicans* (six patients). Three of the six patients with *C. albicans* and three of the nine patients with non–*C. albicans* died prior to discharge. Catheter-related blood stream infection (CRBSI) was the most commonly identified source of infection (five patients), followed by lung and abdomen (four patients each). Among five patients with CRBSI, four patients were under 60 years old. All patients with CRBSI survived to discharge, while all patients with fungal pneumonia or empyema died.

The incidence of candidemia among patients with sepsis in the FORECAST study [3] was 1.3%, which was comparable with previous studies[4] despite significant geographical differences in the Candida species.[5] Candidemia should always prompt a search for the source despite the possibility of reflecting colonization of an indwelling intravenous catheter. Our results showed differences in patients with candidemia complicated by sepsis. Deep-seated infections, which lead to secondary candidemia, were associated with high mortality compared to CRBSI. However, underestimation of patients with candidemia is likely as rates of fungal blood culture positivity are lower than for bacteria. Although there is not yet a magic bullet for the diagnosis of this elusive disease, clinical information, such as comorbidities, need for mechanical ventilation, elevated severity score, and low albumin, remains crucially important in providing clues to the diagnosis of candidemia.[1]

In conclusion, this is the first report to provide a detailed description of septic patients with candidemia in ICU in Japan. In terms of nosocomial infections, candidemia from deep-seated sources had poorer outcomes compared to those with candidemia caused by CRBSI. Early recognition of fungal infection remains key.

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CONFLICT OF INTERESTS

The authors have stated explicity that there are no conflict of interest in connection with this article.

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TABLE 1 Characteristics and outcome of fifteen patients with candidemia complicated by sepsis (n = 15)

Age	Gender	Infection site	Admission source	Shock	Medication	Comorbidities	Antibiotic use before diagnosis	MV	Vasopressor use	SOFA score	APACHE II score	Blood culture		Antifungal drug	Antibiotics	LOS (d)	ICU-FD (d)	Disposition
67	M	Abdomen	ED	Yes	No	COPD	Yes	Yes	Yes	11	23	*C albicans*	*E faecium* *E coli*		MEPM, VCM	17	0	Dead
46	M	CRBSI	Ward (transfer)	No	No		Yes	No	No	8	23	*C albicans*		F-FLCZ		74	8	Transfer
76	M	Lung	Ward (transfer)	Yes	Anticancer drug	Metastatic malignant tumor	Yes	Yes	No	12	37	*C tropicalis*		MCFG	MEPM, VCM	27	0	Dead
45	M	Lung	Ward (transfer)	Yes	Steroid	Connective tissue disease, Peptic ulcer disease, DM	Yes	No	Yes	12	28	*C albicans*	*C striatum*	F-FLCZ	MEPM, VCM	15	0	Dead
46	M	CRBSI	Ward (transfer)	Yes	No		No	NA	Yes	NA	NA	*C glabrata*		FLCZ		11	23	Transfer
78	M	Abdomen	Ward (transfer)	No	Steroid	Connective tissue disease	No	No	No	3	20	*C glabrata*	*E coli*	MCFG	MEPM	27	8	Transfer
60	M	CRBSI	Ward (transfer)	Yes	No	Cerebrovascular disease, DM, hemiplegia	No	Yes	Yes	17	31	*C tropicalis*	*P mirabilis*		MEPM, VCM	27	15	Transfer
85	W	Abdomen	ED	Yes	Anticoagulant	Dementia	No	No	Yes	8	15	*C parapsilosis*	*Pseudomonas sp.*		CMZ	96	9	Transfer
30	W	CRBSI	Ward (transfer)	No	No		Yes	Yes	Yes	9	30	*C parapsilosis*		F-FLCZ	CFPM	142	22	Home
62	W	Wound	Ward (transfer)	Yes	No		No	Yes	Yes	11	13	*C glabrata*	*P mirabilis*	VRCZ, MCFG	CTRX, MEPM, VCM, DAP	19	0	Dead
86	M	CRBSI	Ward (transfer)	Yes	No	Cerebrovascular disease, COPD	Yes	No	Yes	NA	23	*C tropicalis*			MEPM	47	23	Transfer
46	W	Abdomen	Ward (transfer)	Yes	No		Yes	Yes	Yes	7	18	*C albicans*			MEPM	165	0	Transfer
75	M	Lung	Ward (transfer)	Yes	No	Malignancy (solid)	Yes	Yes	Yes	8	17	*C glabrata*		L-AMB	CZOP	149	0	Dead
71	W	Lung	Ward (transfer)	No	No	Cerebrovascular disease, DM, liver disease	Yes	No	Yes	11	32	*C albicans*			PIPC/TAZ	6	0	Dead
71	M	Other site	Ward (transfer)	No	No	DM, malignancy (solid)	Yes	Yes	Yes	11	32	*C albicans*			PIPC/TAZ, CLDM	90	11	Transfer

APACHE II, acute physiology and chronic health evaluation II; CFPM: cefepime; CLDM: clindamycin; CMZ: cefmetazole; COPD: chronic obstructive pulmonary disease; CRBSI: catheter-related blood stream infection; CTRX: ceftriaxone; CZOP: cefozopran; DAP: daptomycin; DM: diabetes mellitus; ED: emergency department; F-FLCZ: fosfluconazole; FLCZ: fluconazole; ICU-FD: ICU-free days; L-AMB: liposomal amphotericin B; LOS: length of hospital stay; VRCZ: voriconazole; M: men; MCFG: micafungin; MEPM: meropenem; MV: mechanical ventilation; PIPC/TAZ: piperacillin/tazobactam; SOFA: Sequential Organ Failure Assessment; VCM: vancomycin; W: women.

Other site was not lung, abdomen, urinary tract, soft tissue, central nervous system, osteoarticular, endocardium, wound, and implant device.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

APPENDIX

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