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LETTER

Yarrowia lipolytica fungemia in patients with severe polytrauma requiring intensive care admission: analysis of 32 cases

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Dear Editor,

Systemic fungal infections are a significant cause of morbidity and mortality in hospitalized patients. Incidences of candidemia have been increasing significantly in recent years [1]. Critically ill medical and surgical patients often undergo surgery, receive total parenteral nutrition, require central venous catheters and/or are administered broad spectrum antibiotics—all factors which predispose them to develop blood stream infections caused by *Candida* spp. [1–5]. *Yarrowia lipolytica*, also known as *Candida lipolytica*, is a ubiquitous and opportunistic yeast [3, 4]. However, to the best of our knowledge, the development of *Y. lipolytica* fungemia in severe polytrauma patients has not been reported to date. Between 6 October 2012 and 15 June 2014, we collected 32 *Y. lipolytica* isolates from blood samples obtained from 32 trauma patients admitted to the intensive care unit (ICU) of a single institution (Habib Bourguiba University Hospital). In all cases, blood cultures were drawn from peripheral punctures.

Here we describe the clinical and epidemiological data and impact outcomes related to this atypical fungemia. In total, 55 episodes of *Y. lipolytica*-septicemia were diagnosed during the study period. The patient cohort comprised 32 patients admitted for post-traumatic injury. The median age of the patients was 39 (range 18–82) years [see Electronic Supplementary Material (ESM) Fig. 1]. The mean Simplified Acute Physiology Score II score on admission was at 38 ± 11 (median 37.7). The mean Sequential Organ Failure Assessment (SOFA) score on ICU admission was at 7.47 ± 3 (median 7). All patients had a polytrauma. Epidemiological and clinical characteristics of these 32 polytrauma patients with fungemia caused by *Y. lipolytica* are given in Table 1. The mean duration of onset of candidemia in the ICU was 20 ± 13 (median 18 days) days. The Pittet index calculated on the day of fungemia diagnosis was <50% in 71% of cases. Moreover, the *Candida* score calculated the day of fungemia diagnosis was >3 in 38% of cases (ESM Fig. 2). In terms of the overall antifungal susceptibility profiles of the commonest species, 96.9% of isolates were sensitive to amphotericin B, and 68.8% were sensitive to fluconazole.

The mean delay in initiating antifungual treatment was at 4.9 ± 4 (median 4 days) days. The mean antifungual treatment duration was at 13.4 ± 5 (median 14) days. The mean delay of bloodstream sterilization was 5.29 ± 4 (median 4) days. The evolution of all population groups was marked by the deaths of 12 patients (37.5%). Examination of the hands of healthcare providers, intravenous injection samples, infusion pumps and central venous catheters suggested that the cause of this fungemia was vasucular catheter-associated candidemia. This suspicion was supported by the isolation of *Y. lipolytica* in the central venous catheter culture of seven patients diagnosed with this fungemia. Moreover, *Y. lipolytica* was also isolated from the hands of one healthcare provider and in the infusion pump of one patient. All of these findings suggest that the outbreak was due to cross-transmission. Analysis of the isolated strains confirmed that it was the

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Table 1 Epidemiological and clinical characteristics of 32 polytrauma-patient with fungemia caused by *Yarrowia lipolytica*

Parameters	Values
Mean age (years)	41 ± 18 (18–82)
Gender (female)	2 (6.3%)
Head trauma	25 (78%)
Chest trauma	20 (62.5%)
Abdominal/pelvis trauma	10 (31%)
Fracture of long bones trauma	9 (28%)
Mean Injury Severity Score	26.2 ± 8.5 (13–43)
Mean Glasgow Coma Scale score	7 ± 4 (3–15)
Mean SAPS II	38 ± 11 (21–61)
Mean SOFA score	7.4 ± 3 (1–14)
Comorbidities	
Cancer	0
Immunocompromised status	0
Pulmonary disease	0
Cardiac disease	1 (3.1%)
Diabetes mellitus	0
Renal failure	0
Other associated risk factors	
Central venous catheterization	31 (96.9%)
Hemodialysis	3 (9.4%)
Prior surgery	0 (0%)
ARDS	15 (46%)
Shock	19 (59%)
Disseminated intravascular coagulopathy	1 (3.1%)
Mechanical ventilation	31 (96.9%)
Parenteral nutrition	28 (87.5%)
Antibiotics	27 (84%)
Steroids	11 (34.4%)

Values in table are presented as the mean ± standard deviation with the range in parenthesis, or as a number with the percentage in parenthesis, as appropriate

SAPS II Simplified Acute Physiology score II, *SOFA score* Sequential Organ Failure Assessment score, *ARDS* acute respiratory distress syndrome

same strain in all cases, and molecular biology tests confirmed its genotype to be *Y. lipolytica* BC507. In vitro analysis of the virulence factors of this isolated species of *Y. lipolytica* showed that this fungus had developed the selective ability to adhere to—and form a biofilm on—catheter medical devices. In comparison with *Candida albicans* and *C. glabrata*, the biofilms of *Y. lipolytica* tend to be more compact, with a structured hyphal layer. Also, in one study on *Y. lipolytica* BC507, after 48 h the fungal biofilm biomass had increased by fivefold in comparison with an earlier stage [3]. In that same study, the in vitro estimation of capacities of *Y. lipolytica* BC507 to produce hydrolytic enzymes showed a good capacity to produce a number of hydrolytic enzymes, such as phospholipase and hemolytic enzymes. Such enzymes are always considered to act as a protective barrier against antifungal treatment and an excellent mechanism to trick the host's defense system [3].

Our comparison of survivors and deceased patients showed that the factors associated with poor outcome were age, SOFA score on the day of candidemia diagnosis, high SAPSS II score on ICU admission, renal failure and the mean delay in initiating antifungual treatment (See ESM Tables 2, 3). Multivariate analysis showed that the only factor associated with poor outcome was the delay in initiating antifungual treatment for >3 days ($p = 0.02$; odds ratio 5.9; 95% confidence interval 1.8–18.9).

This study is the first to describe an atypical candidemia caused by *Y. lipolytica* strains in severe polytrauma patients requiring ICU admission. Our ICU reported a particularly high infection rate due to *Y. lipolytica* during the period from October 2012 to June 2014. This was notable because this species of *Candida* had, up to that time, never been reported at Habib Bourguiba University Hospital or in our ICU.

Our study suggests that *Y. lipolytica* fungemia can occur in polytrauma patients. It was associated with a poor outcome in our patient population. The cause of this fungemia is vascular catheter-associated candidemia, likely due to cross-transmission. As a consequence, we strongly recommend vigilance in the use of medical implants, particularly in ICUs.

Electronic supplementary material
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Compliance with ethical standards

Conflicts of interest
The authors declare that they have no competing interests.

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References

1. Lortholary O, Renaudat C, Sitbon K, Madec Y, Denoeud-Ndam L, Wolff M, Fontanet A, Bretagne S, Dromer F, French Mycosis Study Group (2014) Worrisome trends in incidence and mortality of candidemia in intensive care units Paris area, (2002–2010). Intensive Care Med 40:1303–1312
2. Tak V, Mathur P, Varghese P, Gunjiyal J, Xess I, Misra MC (2014) The epidemiological profile of candidemia at an Indian trauma care center. J Lab Phys 6:96–100
3. Abbes S, Amouri I, Trabelsi H, Neji S, Sellami H, Rahmouni F, Makni F, Rebai T, Ayadi A (2017) Analysis of virulence factors and in vivo biofilm-forming capacity of *Yarrowia lipolytica* isolated from patients with fungemia. Med Mycol 55:193–202
4. Liu WC, Chan MC, Lin TY, Hsu CH, Chiu SK (2013) *Candida lipolytica* candidemia as a rare infectious complication of acute pancreatitis: a case report and literature review. J Microbiol Immunol Infect 46:393–396
5. Pappas PG, Kauffman CA, Andes D, Benjamin DK Jr, Calandra TF, Edwards JE Jr et al (2009) Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 48:503e35