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CASE REPORT

# *Candida lipolytica* candidemia as a rare infectious complication of acute pancreatitis: A case report and literature review



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## KEYWORDS

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*Candida lipolytica* candidemia is a rare but an emerging pathogenic yeast infection in humans. It can gain access to the bloodstream through intravascular catheterization, especially through central venous catheters in immunocompromised or critically ill patients during hospitalization. In this report, we present a noncatheter-related *C. lipolytica* candidemia infection in an 84-year-old man who was admitted due to acute pancreatitis. The possible pathogenesis and management of *C. lipolytica* candidemia are highlighted. It was an unusual infectious complication of acute pancreatitis. Clinicians should be aware that such an opportunistic pathogen can lead to invasive candidemia infection. In clinical practice, systemic antifungal therapy and the removal of the potentially infected central venous catheter might be recommended for the treatment of *C. lipolytica* candidemia.

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## Introduction

*Candida* species are some of the most common causes of bloodstream infections in hospitals.<sup>1</sup> Incidences of candidemia have been increasing significantly in recent years. The risk factors of candidemia are central venous catheterization, parenteral hyperalimentation, broad-spectrum antibiotics, and an immunocompromised status.<sup>2</sup> Despite *Candida albicans* being a major pathogen for candidemia, non-*albicans* candidemia has been responsible for 36–63% of all candidemia cases.<sup>2,3</sup>

*Candida lipolytica* was not included in the long list in Hazen's careful 1995 review of emerging yeast pathogens.<sup>4</sup> *C. lipolytica* infection was first reported by Wehrspann and Füllbrandt in 1985.<sup>5</sup> Since then, *C. lipolytica* candidemia has been increasingly reported and strongly associated with intravascular catheterization. In this case, candidemia attributed to *C. lipolytica* infection occurred during the treatment of acute pancreatitis, without a central venous catheter, parenteral nutrition, and broad spectrum antibiotics. We sought to deepen our understanding of the clinical characteristics and management of *C. lipolytica* candidemia.

## Case report

An 84-year-old man presented to our emergency department with a sudden onset of severe epigastric pain, which radiated to the back after 1 day. Upon arrival, physical examinations showed an oral temperature of 37.8 °C and epigastric tenderness without rebound tenderness. Results of laboratory analysis revealed a white blood cell count of  $15.4 \times 10^3/\text{mm}^3$  (normal range:  $4.5\text{--}11.0 \times 10^3/\text{mm}^3$ ), C-reactive protein of 5.32 mg/dL (normal range:  $<0.5$  mg/dL), amylase of 1597 U/L (normal range: 28–100 U/L), and lipase concentration of 3000 U/L (normal range: 13–60 U/L). A computed tomography of the abdomen revealed diffuse swelling with surrounding fatty stranding and an accumulation of peripancreatic fluid. The patient's

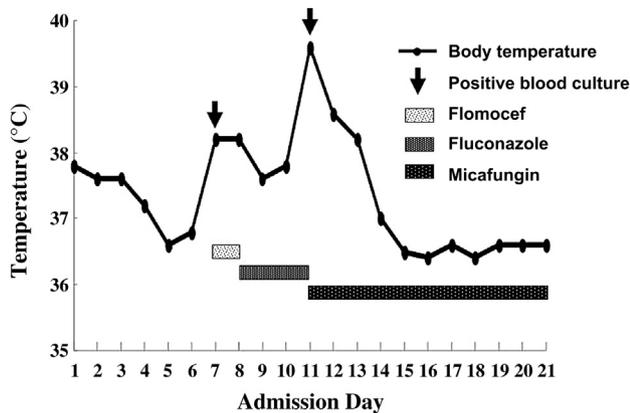
treatment included temporary fasting, fluid resuscitation, and pain control. The clinical symptoms improved gradually and enteral feeding was started on the 5th day of his admission.

On the 7th day of admission, he developed an unexpected fever. The trend of the highest daily body temperature during the whole hospitalization is shown in Fig. 1. A re-evaluation of the patient's general condition showed no pustules or skin lesions, no signs of phlebitis in the peripheral venous catheter, no ophthalmological abnormality, no oral thrush or mucositis, no respiratory symptoms, no cardiac murmur, no abdominal tenderness, and no dysuria. Results of laboratory tests revealed a white blood cell count of  $17.7 \times 10^3/\text{mm}^3$ , C-reactive protein of 9.57 mg/dL, and lipase concentration of 150 U/L. Two sets of blood cultures from peripheral veins were obtained with an interval of 30 minutes. Empiric antibiotics with intravenous flomoxef (1.0 g) four times daily were administered immediately. On the 8th day, 24 hours after the blood cultures were taken, non-*albicans Candida* was discovered by the BacT/ALERT Microbial Detection System (bioMérieux, France). An antifungal agent with intravenous fluconazole (800 mg) loaded, followed by 400 mg daily was initiated. The flomoxef treatment was discontinued. On the 11th day, a spiking fever developed again, accompanied by general weakness and drowsiness. The blood culture was repeated again, and antifungal therapy was shifted to intravenous micafungin (100 mg) daily. Later, *C. lipolytica* was identified by the VITEK 2 YST system (bioMérieux, France) (bionumber: 5710124000025511, 97% probability). The minimum inhibitory concentrations of five antifungal agents against the *C. lipolytica* isolates were  $\leq 1$  µg/mL for fluconazole,  $<0.125$  µg/mL for itraconazole,  $\leq 0.06$  µg/mL for voriconazole,  $\leq 4$  µg/mL for 5-flucytosine, and  $\leq 0.5$  µg/mL for amphotericin B (ATB Fungus 3 system, bioMérieux, France). On 15th and 19th day, the repeated blood cultures were all sterile. After a 14-day course of intravenous antifungal therapy, the patient was discharged uneventfully.

## Discussion

*C. lipolytica*, also known as *Yarrowia lipolytica*, is a strictly aerobic and ubiquitous inhabitant in the environment, and is capable of producing important metabolites and has an intense secretory activity. It is widely used in the detergent, food, and pharmaceutical industries. Several processes based on *C. lipolytica* are classified as "Generally Recognized As Safe" by the Food and Drug Administration.<sup>6</sup> How such a yeast microorganism invades human hosts, even causing severe bloodstream infections is an interesting issue that is yet to be elucidated.

*C. lipolytica* candidemia occurs most frequently in immunocompromised or critically ill patients during hospitalization. By reviewing relevant studies in English from PubMed, we found that 16 cases, including ours, were reported over the past decades. The age, gender, admission diagnosis, whether the patient was neutropenic, whether there was an infected vascular catheter, management and outcomes are summarized in Table 1.<sup>5,7–15</sup> Indwelling catheter devices, especially central venous catheters, were strongly correlated in almost all cases of *C. lipolytica*



**Figure 1.** The trend graph of the highest daily body temperature during the whole hospitalization period. *Candida lipolytica* candidemia was identified on the 7th and 11th day, respectively. The fever subsided after antifungal therapy with micafungin.

**Table 1** Clinical characteristics of patients with *Candida lipolytica* candidemia

No.	Age	Gender	Admission diagnosis	Neutropenia <sup>a</sup>	Infected catheter	Main management	Outcome	Reference
1	57 y	F	Brain infarction	No	PVC	Ketoconazole Removal of vascular catheter	Remission	5
2	54 y	M	Cholelithiasis	No	PVC	Removal of vascular catheter	Remission	7
3	1 mo	M	Necrotizing enterocolitis	No	CVC	Fluconazole Removal of vascular catheter	Remission	8
4	2 mo	M	Bacterial meningitis	Yes	None	None	Remission	8
5	8 y	F	Acute myeloid leukemia	Yes	Hickman	Amphotericin B	Remission	8
6	14 y	M	Acute myeloid leukemia	Yes	Hickman	Amphotericin B	Remission	8
7	4 y	M	Aplastic anemia	Yes	CVC	Fluconazole Removal of vascular catheter	Remission	8
8	15 y	F	Acute myeloid leukemia	Yes	CVC	Removal of vascular catheter	Remission	9
9	18 y	F	Acute leukemoid leukemia	Yes	CVC	Amphotericin B Removal of vascular catheter	Remission	10
11	2 d	M	Intestinal obstruction	No	CVC	Caspofungin Removal of vascular catheter	Remission	11
12	4 mo	F	Nosocomial pneumonia	No	CVC	Caspofungin Removal of vascular catheter	Remission	11
10	2 y	M	Tubercular meningitis	No	CVC	Amphotericin B Removal of vascular catheter	Remission	12
13	13 y	M	Acute leukemoid leukemia	Yes	CVC	Fluconazole Removal of vascular catheter	Remission	13
14	9 y	M	Neuroblastoma	Yes	CVC	Caspofungin Antifungal-locked therapy	Remission	14
15	61 y	M	Adenocarcinoma of lung	No	Port-A	Micafungin Removal of vascular catheter	Remission	15
16	84 y	M	Acute pancreatitis	No	None	Micafungin	Remission	Our case

<sup>a</sup> Absolute neutrophil count < 1000/mm<sup>3</sup>.

CVC = central venous catheter; d = days; m = months; PVC = peripheral venous catheter; y = year.

candidemia. It could introduce the yeast pathogen into the blood stream easily. In addition, D'Antonio et al claimed that *C. lipolytica* produced large amounts of viscous slime materials, which are responsible for its capability to adhere to and colonize the central catheter.<sup>10</sup> These cases were proven directly by the catheter tip culture, indirectly by the discharge culture from the venipuncture site or by the blood culture obtained from the catheter. Therefore, *C. lipolytica* might be considered one of the causative agents of catheter-related candidemia.

In this report, *C. lipolytica* candidemia developed after acute pancreatitis. Fungal infections manifesting as infectious complications in severe acute pancreatitis have been increasingly recognized in recent years. Kochhar et al suggested that acute pancreatitis was associated with increased gut mucosal permeability, which makes it

predisposed to septic complications. The translocation of fungal flora from the gastrointestinal tract to extra-intestinal sites plays an important role in the pathogenesis of fungal infections in acute pancreatitis.<sup>16,17</sup> We speculated that *C. lipolytica* gains access to the bloodstream from gastrointestinal tract mucosa. To confirm our hypothesis, a further fungus survey or culture from the intestine was necessary theoretically, but would be impractical to perform in reality.

Proper management of *C. lipolytica* candidemia is still controversial. Only two studies suggested that the removal of the infected vascular catheter alone without intensive antifungal therapy could resolve candidemia.<sup>7,9</sup> Consistent with the current guideline for the management of candidiasis,<sup>18</sup> most studies suggest systemic antifungal therapy as well as the removal of the potentially infected vascular

catheter as the best treatment. In our case, systemic antifungal therapy played a crucial role in treating *C. lipolytica* candidemia infection. Our results showed that most *C. lipolytica* isolates are susceptible to fluconazole and amphotericin B.<sup>10,11,14,15</sup> However, the drug–drug interaction and toxicity of azoles or polyene might lower the tolerance and limit clinical applications. Furthermore, *in vitro* susceptibility testing results could not be used to predict *in vivo* response.<sup>15</sup> Echinocandins are noncompetitive inhibitors of the synthesis of 1,3-beta-D-glucan, which is an integral component of the fungal cell wall. Based on broad-spectrum activity against the *Candida* species, the echinocandins were used extensively for invasive candidiasis, which was refractory to other antifungal therapy in adults or when patients do not tolerate other antifungal agents.<sup>18,19</sup> Recent reports suggested that echinocandins have good therapeutic effects on *C. lipolytica* candidemia.<sup>11,14,15</sup> In the present case, micafungin was used as an alternative antifungal therapy to fluconazole, which had failed to eliminate *C. lipolytica*, and led to the resolution of the candidemia effectively.

In conclusion, *C. lipolytica* is an opportunistic and emerging human yeast pathogen. It can gain access to the blood stream through intravascular catheterization and possibly through the gastrointestinal tract in immunocompromised or critically ill patients during hospitalization. Administration of echinocandins as an alternative antifungal therapy is associated with successful treatment of *C. lipolytica* candidemia infection. Based on current evidence, intensive antifungal therapy combined with the removal of the potentially infected vascular catheter might be recommended for the management of *C. lipolytica* candidemia.

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