


## CASE REPORT

# Duration of antifungal therapy for septic pulmonary embolism caused by *Candida albicans* from a central venous catheter: A case report

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## Abstract

The treatment duration for candidemia with septic pulmonary embolism should be determined based on the clearance of fungus from the bloodstream and improvement of symptoms. The remaining lung nodules may not necessarily indicate persistent infection.

## KEYWORDS

*Candida albicans*, candidemia, endophthalmitis, invasive candidiasis, septic pulmonary embolism

## 1 | INTRODUCTION

We report a clinical course of a candidemia patient associated with septic pulmonary embolism. The treatment duration should be determined based on the clearance of fungus from

the bloodstream and appropriate source control regardless of remaining lung nodule as in our case.

Candidemia is the fourth most common nosocomial bloodstream infection<sup>1</sup> and accounts for approximately 4% of septic pulmonary embolism.<sup>2</sup> Invasive candidiasis has a high

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mortality rate of approximately 40% even in patients receiving antifungal therapies.<sup>1</sup> The delay of treatment is associated with higher mortality<sup>3,4</sup>; however, no clinical symptoms and signs are specific for invasive candidiasis, complicating early diagnosis. Furthermore, objective clinical targets for the treatment of septic pulmonary embolism of candidemia have not been established to inform optimal treatment duration. Here, we report a case of septic pulmonary embolism caused by *Candida albicans* that presented with mild symptoms despite serious bilateral lung abnormalities and successfully treated by appropriate management.

## 2 | CASE REPORT

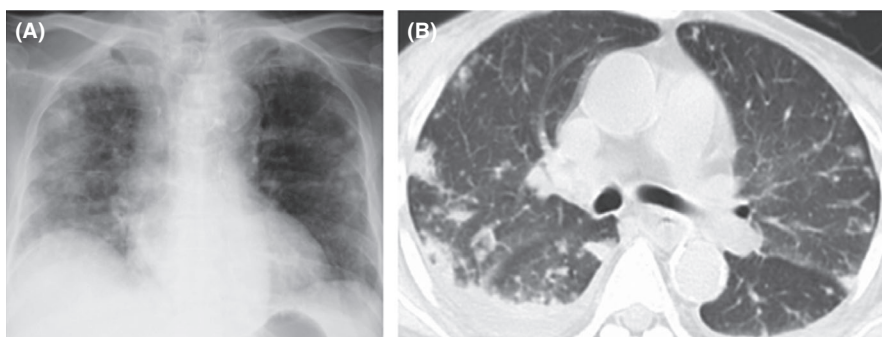
A 69-year-old woman presented with mild dyspnea and fever, which had persisted for one month. Ten months previously, she underwent a laparoscopy-assisted distal gastrectomy for gastric cancer and was subsequently admitted to a local hospital for rehabilitation. One month prior to presentation, she received total parental nutrition via an implantable central venous access device due to appetite loss. Her fever was resistant to antimicrobial therapy, and chest radiographs revealed random nodules in both lungs (Figure 1). For further examination, she was referred to our hospital (Day 1). Vital signs on admission were as follows: temperature 38.8°C, pulse rate 77 bpm, blood pressure 137/64 mm Hg, SpO<sub>2</sub> 97% (nasal cannula O<sub>2</sub> 1 L/min), and respiratory rate 18/min with clear consciousness. Laboratory tests revealed the following: white blood cell count (WBC) 8400/μL (neutrophil 84.0%, lymphocyte 5.0%), hemoglobin 7.0 g/dL, platelets 44 000/μL, albumin 1.8 g/dL, blood urea nitrogen 29.3 mg/dL, creatinine 1.27 mg/dL, C-reactive protein 13.72 mg/dL, prothrombin time-international normalized ratio 1.31, fibrinogen degradation products 25.2 μg/mL, procalcitonin 0.435 ng/mL, and β-D glucan >500 pg/mL (MK-II assay; negative cutoff value ≤20 pg/mL). Blood cultures were positive for *C. albicans*, and culture of her removed central venous catheter tip was positive for *C. albicans* and *C. glabrata*. No other pathogen was isolated from blood cultures or any other clinical specimen. Ocular examination revealed several white and border irregularity spots, suggesting bilateral endogenous

endophthalmitis. No verruca or valvular disease was detected by transthoracic and transesophageal echocardiography. Abnormalities of other organs such as liver, kidney, and brain were not detected in a systemic CT scan. The source of infection could not be positively identified, but the central venous catheter was suspected.

We started antifungal therapy with liposomal amphotericin B (150 mg/day) and flucytosine (2000 mg/day) without the use of anticoagulants. Antimicrobial agents (meropenem and teicoplanin) were also administered empirically but discontinued early when no bacteria were detected. The antifungal therapy was effective, leading to negative blood cultures immediately and a reduction in the bilateral lung nodules from Day 14. However, the endogenous endophthalmitis fundus lesions did not improve. Accordingly, we increased the dose of liposomal amphotericin B (200 mg/day) and flucytosine (4000 mg/day). By Day 30, the fundus lesions had ameliorated, and the fever had resolved by Day 50. The duration of antifungal therapy was determined based on documented clearance of *Candida* species from the bloodstream and resolution of symptoms attributable to candidemia and ophthalmological findings. Although the lung nodules remained detectable in chest radiographs (Figure 2), the antifungal agents were discontinued after the fundus lesions resolved on Day 70. In total, the patient was treated with liposomal amphotericin B and flucytosine for approximately 8 weeks followed by step-down therapy to oral fluconazole for 10 days. The β-D glucan levels were sustained at >500 pg/mL for 7 weeks and then gradually decreased (307 pg/mL on Day 70). Despite the detection of residual lung nodules, no recurrence of lung or eye diseases was observed after the cessation of treatment and the patient was discharged on Day 91.

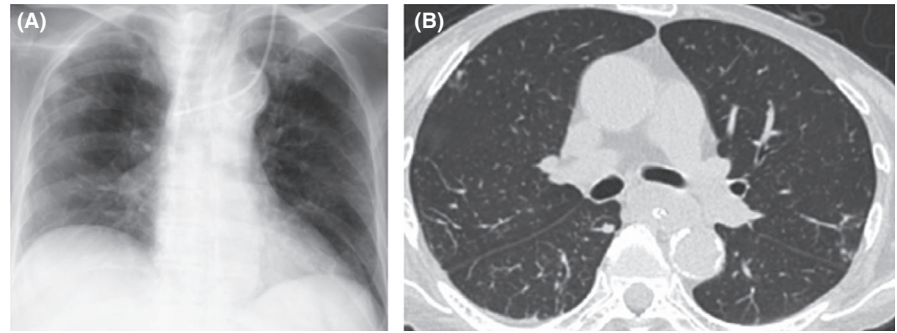
## 3 | DISCUSSION

We present the case of septic pulmonary embolism caused by *C. albicans*. The patient had mild symptoms despite diffuse lung abnormalities. The mortality of candidemia is significantly higher than those of bacterial blood infections,<sup>5</sup> and delay of initial treatment and inappropriate antifungal therapy are associated with the increased mortality.<sup>3,4,6,7</sup> Hence, the



**FIGURE 1** Chest X-ray (A) and CT scan (B) on admission. Multiple random nodules without cavitation were present in bilateral lungs. An associated halo of ground-glass opacity, areas of air-space consolidation, and right pleural effusion were also identified

**FIGURE 2** Chest X-ray (A) and CT scan (B) after 8 wk of antifungal treatment. Overall improvement was observed, but some nodules persisted



prognosis of patients with candidemia worsens when physicians do not recognize the symptoms and provide treatment promptly. However, candidemia can present with milder symptoms than bacteremia<sup>8</sup> and the symptoms reported in 168 patients with septic pulmonary embolism include fever (85.7%), chest pain (48.8%), dyspnea (48.2%), and cough (41.1%), which are not disease-specific.<sup>2</sup> In our case, the patient presented with only persistent fever and mild dyspnea. It took 1 month from appearance of symptoms to diagnosis in this case. *Candida* septic embolism may not be found until it progresses as occurred in our case due to its mild symptoms. Our patient had risk factors for invasive candidemia such as old age, broad-spectrum antibiotics, central venous catheter, gastrointestinal surgery, and total parenteral nutrition.<sup>1,5,8</sup> Candidemia should have been suspected earlier in this case due to multiple risk factors and persistent antibiotic-resistant fever. The gold standard for diagnosis of invasive candidiasis is positive blood or other sample cultures, but blood cultures are positive in only approximately 50 percent of patients.<sup>9</sup> Furthermore, blood cultures may become positive late in the disease course and the median time to positivity is 2–3 days.<sup>10</sup> Hence, physicians should suspect candidemia when risk factors are present and use nonculture diagnostic tests such as  $\beta$ -D glucan levels as an adjunct to culture tests for early detection of candidemia.

Although the appropriate duration of intravenous therapy for candidemia and timing of step down to oral therapy has not been determined,<sup>11</sup> the international guidelines recommend 2 weeks of antifungal therapy after documented clearance of *Candida* species from the bloodstream and resolutions of symptoms attributable to candidemia.<sup>10</sup> Longer duration of therapy is needed in patients who have a metastatic lesion such as endophthalmitis and infective endocarditis. If endophthalmitis is detected, a minimum of 4–6 weeks of therapy is required to resolve the fundus lesions.<sup>10</sup> However, appropriate duration of therapy for septic pulmonary embolism of candidemia remains to be clarified. In our case, antifungal therapy was effective; clinical features improved, blood cultures became negative, and the fundus lesions resolved. The exact source of the infection was not identified, but the central venous catheter was suspected and removed. The patient was administered antifungal agents for a total of 10 weeks

and had no recurrence despite high levels of  $\beta$ -D glucan and the lung nodules remaining. The chest radiological findings and  $\beta$ -D glucan levels were not a reliable guide for cessation of treatment.

Theoretically, it is unable to determine whether remaining lung nodules are due to active *Candida* infection unless a diagnostic procedure approaching directly to lung lesions, such as bronchoscopy and CT-guided lung biopsy, is performed. In previous reports, transbronchial lung biopsy of septic pulmonary embolism sometimes revealed organizing pneumonia.<sup>12,13</sup> These findings and our present case suggest that the remaining lung nodules may not necessarily indicate persistent infection after appropriate management such as appropriate source control and clearance of fungus from the bloodstream. It is reported that T2 Magnetic Resonance *Candida* Panel (T2MR), which detects *Candida* DNA in blood, has a benefit for supporting early discontinuation of empiric antifungal therapy in ICU patients with suspected candidemia compared with  $\beta$ -D glucan.<sup>14</sup> Although we did not use it in the present case, T2MR will be useful for deciding the duration of antifungal therapy in the future. Nevertheless, this case report provides evidence of safe and early discontinuation of antifungal therapy for a non-neutropenic candidemia patient with remaining lung nodules. To determine the appropriate time to discontinue antifungal therapy without recurrence, our approach was based on the following three findings: (a) confirmed clearance of the fungus from the bloodstream, (b) appropriate source control, and (c) resolutions of symptoms and ophthalmologic findings.

## 4 | CONCLUSIONS

We present a case of septic pulmonary embolism caused by *C. albicans*. This case presented with mild symptoms despite lung abnormalities. As candidemia can present with more mild symptoms than bacteremia, physicians must consider invasive candidiasis early to prevent any delay to diagnosis, especially in patients with known risk factors. The lung nodules remaining after treatment do not necessarily indicate persistent *Candida* infection; the treatment duration should be determined based on the clearance of fungus from the

bloodstream, appropriate source control, and resolutions of symptoms attributable to candidemia.

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## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

## AUTHOR CONTRIBUTIONS

DO: wrote the initial manuscript. KO and TM: revised the manuscript. All authors: contributed to the patient care and approved the final manuscript.

## ETHICAL APPROVAL

Written informed consent was obtained from the patient, and the approval of the Institutional Review Board of Nagasaki University Hospital was waived.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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