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# Successful therapy of *Candida pulcherrima* fungemia in a premature newborn with liposomal amphotericin B and micafungin

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ABSTRACT

New *Candida* species may cause bloodstream infections challenging current therapeutic approaches because of unpredictable susceptibility and virulence. In the present report, we describe a fungemia case due to *Candida pulcherrima* in a premature neonate. After full *in vitro* diagnostic workup, the neonate was successfully treated with liposomal amphotericin B and micafungin achieving rapid fungal eradication from blood.



## 1. Introduction

*Candida* species are the third most frequently isolated pathogens from blood cultures in neonatal late-onset sepsis (9–13%) [1]. The mortality rate due to *Candida* sepsis is high ranging from 25% to 54% and it can reach 70% in very low birth weight newborns [1,2]. *Candida albicans* has been historically the most frequent pathogen in neonates followed by *Candida parapsilosis* and other *Candida* species such as *Candida tropicalis*, *Candida glabrata* and *Candida krusei* [3,4]. However, rare *Candida* species have been increasingly recognized as potential pathogens for neonates [5]. Admission into a Neonatal Intensive Care Unit quadruples the risk of infection by these pathogens [6]. Given the recognition of increased number of bloodstream infections by uncommon opportunistic yeasts with variable susceptibility to antifungal drugs [7], identification of new potential pathogens is important for initiation of prompt and targeted antifungal therapy.

The most recent guidelines by ESCMID favor the use of amphotericin B (conventional and liposomal), fluconazole and micafungin (B-II) for the treatment of neonatal candidemia [8]. However, antifungal resistance to fluconazole is increased among *Candida* non-*albicans* species and particularly *C. glabrata*, whereas echinocandin resistance among *C. glabrata* isolates poses a therapeutic challenge in the treatment of candidemia [9]. While *C. albicans* and *C. parapsilosis* constitute the great majority of *Candida* species causing neonatal candidiasis, rare yeasts with variable susceptibility can occasionally be found and require special care [10].

In the present case report, we describe a rare case of fungemia by *Candida pulcherrima* in a premature neonate together with the diagnostic and therapeutic approaches followed.

## 2. Case

A male newborn born as a gemini B twin with a gestation age of 33 weeks was admitted to the Neonatal Intensive Care Unit at the General Hospital of Nikaia, Athens, Greece due to prematurity and respiratory distress syndrome. The neonate was delivered via spontaneous vaginal delivery following premature rupture of the amniotic membrane. The birth weight was 2080 g. He was initially treated empirically with ampicillin and gentamicin. All drugs were administered via a peripheral catheter, which was changed every

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three days. Parenteral nutrition was administered until day 3.

On day 0 he developed symptoms and sign of sepsis with fever to 38°C, paleness, indolence and acrocyanosis. His laboratory results demonstrated thrombocytopenia (min 21,000/mm$^3$) and increased CRP (max 51 mg/L). The antibiotic therapy was modified to meropenem and teicoplanin and on day 3 liposomal amphotericin B (7 mg/kg/d. i.v.) was added and maintained throughout the treatment after fungal growth was detected in four aerobic blood bottles (BacT Alert, Biomerieux, France) collected on day 0. *C. pulcherrima* was identified as described below and it was detected in all blood cultures collected on days 3, 6 and 7. Ultrasound of the head and abdomen, lumbar puncture, urine culture, ophthalmologic exam and echocardiogram did not indicate disseminated candidiasis.

Four days after initiation of liposomal amphotericin B, the blood cultures remained positive for the same yeast and micafungin 10 mg/kg/d i.v. was added on day 7. His general condition was improved progressively, CRP levels decreased ( $< 3$ mg/L) and after two days of combined antifungal therapy on day 9 the blood cultures became negative. The treatment continued for another 16 days. On day 30, the neonate was discharged from the hospital in good condition and with normal laboratory results.

### 2.1. Species identification

The isolate grew on Sabouraud Dextrose agar plates slowly at 37 °C and best at 25–30 °C (Fig. 1A). The colonies were slow growing, convex, cream colored with a reddish pigment developed after 48 h (Fig. 1A). Microscopically ovoid to ellipsoidal budding yeasts with chlamydospores but no pheudohyphae were found (Fig. 1B). Biochemical identification with VITEK 2 Compact automated system (Biomerieux, France) revealed *C. pulcherrima* (good identification with 90% confidence level). Identification was confirmed with ITS sequencing as previously described using ITS1 (5- TCCGTAGGTGAACCTGCGG-3), and ITS4 (5-TCCTCCGCTTATTGATATGC-3) primers (Fig. 2) [11]. High sequence alignment (99%) was found in Genbank Blast analysis with *Metschnikowia pulcherrima*, the sexual name of *C. pulcherrima* (GenBank Accession No KX276090).

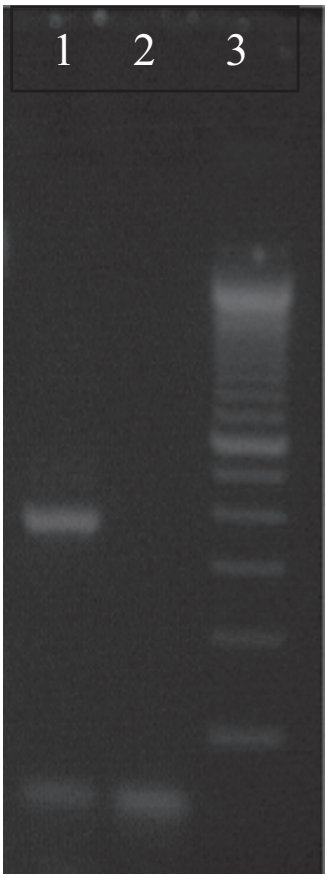


**Fig. 2.** Gel electrophoresis of PCR products after amplification of *C. pulcherrima* DNA with ITS1 (5-TCCGTAGGTGAACCTGCGG-3) and ITS4 (5-TCCTCCGCTTATTGATATGC-3) primers, 1: *C. pulcherrima* 368 bp PCR product, 2: negative control, 3: 100 bp DNA ladder.

### 2.2. In vitro susceptibility testing

*In vitro* antifungal susceptibility was tested with Sensititre YeastOne and the minimal inhibitory concentrations (MICs) were

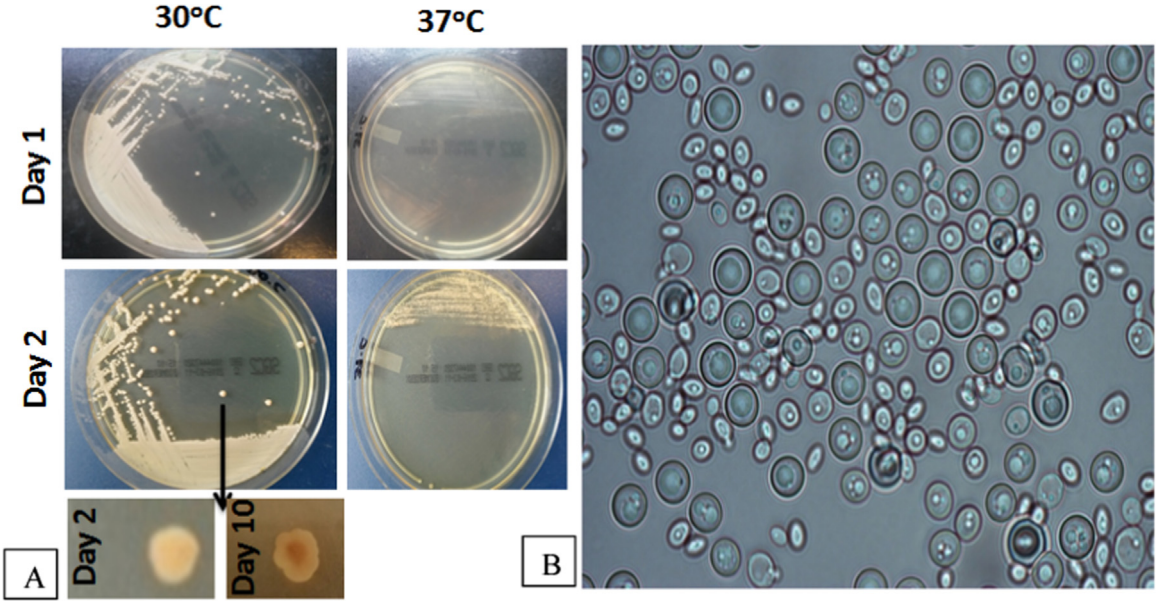


**Fig. 1.** Macroscopic (A) and microscopic (B) photos of *C. pulcherrima*. A. Cream colored colonies with reddish pigment on the reverse of Sabouraud Dextrose Agar. B. Chlamydospores, budding yeast and no pseudohyphae were observed in corn-meal agar after incubation at 37 °C for 48 h. (Magnification 400 ×).