*Case Report*

# Successful Treatment of an Infant Infected with Refractory *C. parapsilosis* with Caspofungin

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**Summary**

**Neonatal *Candida* infections are the leading cause of invasive fungal infections that might cause severe morbidity or mortality in a large majority of those affected. Although *Candida albicans* has been the most common species, *Candida parapsilosis* is increasingly being recognized as an important cause of invasive candidiasis in neonates. Among the *Candida* species, *C. parapsilosis* has been commonly isolated and shown to be less susceptible *in vitro* to echinocandins than other *Candida* species. We report an infant who had refractory *C. parapsilosis* septicemia cured with caspofungin.**

**Key words: *Candida parapsilosis*, caspofungin, infant.**

## Introduction

Invasive candidiasis is a common problem in premature infants that may lead to death or severe neurodevelopmental impairment [1, 2]. Previously, most fungal infections in neonates were caused by *Candida albicans*, but *Candida parapsilosis* is now identified as a significant pathogen in this population [3]. *Candida parapsilosis* is associated with higher minimum inhibitory concentrations (MICs) of echinocandins, raising concerns about their role in therapy for invasive disease [4]. In this case report, we present the case of an infant having refractory *C. parapsilosis* despite fluconazole and amphotericin B therapy.

## Case Report

A male infant was born weighing 800 g at 26 weeks with cesarean section owing to placenta detachment. Apgar scores were three and five at the first and fifth minute, respectively. Exogenous surfactant was administered owing to progressive respiratory distress. Therapy including sulbactam, ampicillin and cefotaxime was initiated at birth; later, on the fifth day of life, the infant had apnea, acute renal failure and abdominal distension. Laboratory study showed thrombocytopenia ($99 \times 10^3/\mu l$) and elevated C-reactive protein (5.24 mg/dl). On abdominal radiography, pneumatosis intestinalis was detected; stool contained occult blood, and the patient was diagnosed with necrotizing enterocolitis stage 2. Vancomycin, metronidazole and amikacin were added to the therapy. As his apnea increased in frequency with accompanying bradycardia, he was intubated. Cefotaxime was switched with meropenem and sulbactam and ampicillin were stopped. Blood culture yielded *C. parapsilosis* on Day 18, so fluconazole (8 mg/kg/day) was initiated. He was admitted to our center for follow-up and treatment on the 20th day of life; a central venous catheter was placed on admission. Antibiotic therapy including meropenem, vancomycin, amikacin, metronidazole and fluconazole was continued through the peripheral intravenous route in our hospital until *C. parapsilosis* was cultivated; despite fluconazole therapy, on the 22nd day of life, the catheter was removed. Liposomal amphotericin B was added (3 mg/kg/day) to the patient's antibiotic therapy instead of fluconazole. Although susceptibility testing for *C. parapsilosis* showed resistance to fluconazole and susceptibility to both amphotericin B and caspofungin (susceptibility testing and MICs to amphotericin B and fluconazole were determined by a broth microdilution method according to the recommendations of the National Committee for Clinical Laboratory Standards; MIC results were as follows: for amphotericin B, $<8\,\mu g/ml$; for caspofungin, $<2\,\mu g/ml$; for fluconazole, $>64\,\mu g/ml$). Two more blood cultures

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drawn after 72 h of amphotericin B therapy indicated presence of *C. parapsilosis* on Day 11 of therapy, and patient was still thrombocytopenic with no clinical improvement. Also, there was no sign of central nervous system involvement, so antifungal therapy was switched to caspofungin (50 mg/m$^2$/day). Control blood culture was negative. After caspofungin therapy, thrombocytopenia resolved; patient tolerated oral feeding. On Day 32, meropenem and other antibiotics were discontinued. Caspofungin was stopped after 14 days of therapy.

## Discussion

Among non-albicans species, *C. parapsilosis* is the second leading cause of candidemia in children, and in some centers, it has overtaken *C. albicans* as the leading species in invasive disease [5, 6]. There are concerns about echinocandin resistance in *C. parapsilosis* isolates [7], which may be associated with acquired mutations of the *fks* gene that encodes $\beta$-D-glucan synthase [8]. It has been stated that *C. parapsilosis* might have decreased susceptibility to echinocandins without displaying *fks* gene mutations; yet, in our case, we successfully treated the patient with caspofungin after failure with fluconazole and amphotericin B. Although *C. parapsilosis* was susceptible to amphotericin B *in vitro*, we could not eradicate the microrganism *in vivo*. But data concerning use of echinocandins in neonates are limited and it is not approved for this age-group, so reserving use of echinocandins for situations involving treatment failure, such as in our case, or toxic side effects with other antifungal medications is recommended [9], and further controlled studies are needed for this issue.

Reported factors that increase the risk for invasive *C. parapsilosis* infection are use of cephalosporins [10], presence of an indwelling central venous catheter [11, 12] and receipt of parenteral nutrition (total parenteral nutrition) [12]. Our patient had a central venous catheter placed and received total parenteral nutrition and cephalosporin therapy, in addition to having common risk factors for candidemia such as prematurity and intubation [2].

Thrombocytopenia was reported as a marker for invasive candidiasis in low-birth-weight newborns [13]. Similarly, our patient had thrombocytopenia, which resolved with caspofungin therapy.

In conclusion, in refractory *C. parapsilosis* infections, caspofungin could be a good alternative in resistant patients not having central nervous system involvement, but further randomized controlled studies are required, and in these patients, thrombocytopenia could be the only symptom or sign before the fungemia is diagnosed.

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