**Candida glabrata Endophthalmitis Treated Successfully with Caspofungin**

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A 39-year-old man with *Candida glabrata* endophthalmitis was successfully treated with a 28-day course of intravenous caspofungin. Presence of underlying renal insufficiency and infection with a drug-resistant strain precluded use of amphotericin B or fluconazole. Intravitreal administration of antifungals and vitrectomy were not required. The role of caspofungin in *Candida* endophthalmitis is discussed.

Both amphotericin B, often combined with flucytosine, and fluconazole have been recommended as preferred antifungals for treatment of *Candida* endophthalmitis on the basis of limited supportive evidence [1]. Unfortunately, use of these agents has been associated with poor outcomes, suboptimal intraocular penetration, toxicity, and emergence of drug resistance. We report a case of *Candida* endophthalmitis treated successfully with intravenous caspofungin, a novel echinocandin antifungal. A discussion of available pharmacokinetic and clinical data on the use of echinocandins in intraocular *Candida* infections is presented.

**Case report.** A 39-year-old man underwent exploratory laparotomy for peritonitis secondary to a ruptured Meckel’s diverticulum. He experienced multiple postoperative complications, including small bowel obstruction, enterocutaneous fistula formation, and hepatic and renal insufficiency. The patient required extensive resection of his small bowel, and total parenteral nutrition was started. He then successively developed episodes of intravenous catheter–related bloodstream infection caused by *Staphylococcus aureus*, *Enterobacter* species, and *Candida albicans*, which was managed with catheter exchanges and treatment with broad-spectrum antibiotics and fluconazole.

Several weeks later, the patient developed a bloodstream infection caused exclusively by *Candida glabrata* that required catheter removal and therapy with intravenous caspofungin. The drug was initially given at a dosage of 50 mg per day, which was then reduced to 35 mg per day because of the presence of moderate hepatic insufficiency. An echocardiogram appeared normal. A funduscopic examination revealed vitreitis and a retinal lesion in the left eye (figure 1). Visual acuity was normal. The patient was diagnosed with focal endogenous endophthalmitis caused by *C. glabrata*. Follow-up funduscopic examinations performed 10 days after and 3 weeks after the completion of a 28-day course of caspofungin showed improvement (figure 2) and resolution (figure 3) of ocular involvement. Drug susceptibility testing performed on the blood isolate by broth microdilution according to NCCLS method showed the following MICs: amphotericin B, 1 μg/mL; caspofungin, 0.25 μg/mL; fluconazole, 64 μg/mL; flucytosine, ≤0.03 μg/mL; itraconazole, 2 μg/mL; and voriconazole, 0.125 μg/mL at 24 h of fungal incubation and 1 μg/mL at 48 h. Intravitreal antifungal therapy and vitrectomy were deferred because of patient’s excellent vision, mild vitreitis and retinal lesion, and favorable clinical course. At a 7-month follow-up visit, findings of funduscopic examination were normal.

**Discussion.** Even though a number of studies have demonstrated excellent distribution of echinocandins into most types of tissue, little is known about the intraocular or CNS penetration of these drugs, and existing data on this subject are limited to experimental animal models. In a rabbit model of endotoxin-induced uveitis, intravenously administered caspofungin penetrated into inflamed eyes and reached levels in the cornea and aqueous humor that exceeded the MICs for many pathogenic fungi [2]. In a pharmacokinetic study of persistently neutropenic rabbits with disseminated candidiasis, micafungin demonstrated significant dosage-dependent clearance of *C. albicans* from the vitreous (*P* < .01) and the brain (*P* < .001). This agent successfully reduced the burden of *C. albicans* in the vitreous by >100-fold, and no organisms were detectable in either the vitreous or the brain in animals treated for up to 10 days with dosages of ≥1 mg/kg per day [3]. In another study, in which mice were administered radioactive caspofungin, radioactivity was detectable in the brain [4]. Concentrations of micafungin and anidulafungin were also measurable in
Figure 1. Initial color and red-free funduscopic images showing an exudative lesion with indistinct borders in the superotemporal portion of the posterior pole of the left retina.

the brains of rabbits by other investigators [5, 6]. Furthermore, anidulafungin treatment resulted in significant clearance of \( C. albicans \) from the brain in a neutropenic rabbit model of disseminated candidiasis [7].

Clinical experience with caspofungin in endophthalmitis is limited. In a prospective trial comparing caspofungin \((n = 109)\) and amphotericin B \((n = 115)\) as treatment for invasive candidiasis, 0 patients in the caspofungin group and 1 patient in the amphotericin B group developed new ocular lesions while receiving therapy [8]. In this study, 7 patients had Candida endophthalmitis at enrollment. Of these, 2 patients were treated with caspofungin. One of them was infected with \( C. albicans \) and had no evidence of endophthalmitis at the end of study therapy. The other patient was infected with \( C. tropicalis \) and had no follow-up funduscopic examination because he died. Other investigators have reported adequate clinical responses to caspofungin in fungal infections of the CNS [9–11]. However, some of these patients received caspofungin as part of combination regimens [10, 11]. We are not aware of clinical experience with other echinocandins for treatment of Candida infections of the eye or CNS.

Taken together, these pharmacokinetic and clinical data suggest that caspofungin may play a role in the management of intraocular Candida infections. We caution that this statement should be interpreted in the context of the limited and observational nature of the available evidence. A number of questions merit further investigation. These include comparative evaluations of treatment with caspofungin and other antifungals, their use in severe infections, dosing schedules, duration of therapy, and whether to use intravitreal administration. In summary, the case we describe suggests that caspofungin may be an alternative therapeutic option for selected patients with \( C. glabrata \) endophthalmitis for whom first-line therapies cannot be used because of toxicity or drug resistance.

Figure 2. Initial color and red-free funduscopic images obtained 10 days after the initiation of intravenous caspofungin show that the size of the retinal lesion decreased.
Figure 3. Initial color and red-free funduscopic images obtained 3 weeks after completion of a 28-day course of caspofungin show complete resolution of ocular involvement.

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References