Successful treatment of fungal endophthalmitis using intravitreal caspofungin

Ciprian Danielescu, Alina Cantemir, Dorin Chiselita

ABSTRACT

Fungal endophthalmitis is a rare condition, accounting for 8%-18% of culture-positive endophthalmitis (1) and often has a poor prognosis. Given its low incidence, evidence-based data are unavailable (2). To our knowledge, this is the first report of Stephanoascus ciferrii endophthalmitis and its successful treatment with intravitreal caspofungin.

Keywords: Endophthalmitis; Phacoemulsification/adverse effects; Candida; Intravitreal injections; Lipopeptides

INTRODUCTION

Fungal endophthalmitis is a rare condition, accounting for 8%-18% of culture-positive endophthalmitis (1) and often has a poor prognosis. Given its low incidence, evidence-based data are unavailable (2). We report a case of endophthalmitis caused by an unusual yeast-like fungus, Stephanoascus ciferrii (a teleomorph of Candida ciferrii), that only responded to intravitreal caspofungin therapy.

CASE REPORT

In October 2014, a 57-year-old otherwise healthy woman presented to our clinic 2 weeks after an uneventful cataract surgery at another center. The best corrected visual acuity (BCVA) in her right eye was 0.2 on the logarithm of the minimum angle of resolution (logMAR) scale. Anterior pole examination revealed ciliary injection, 4+ anterior chamber cells, and a 1-mm hypopyon. Examination of the retina was possible (albeit difficult because of moderate anterior vitritis), and no white choroidal lesions or vitreous snowballs were visible. Anterior chamber paracentesis was performed (however, the subsequent culture was negative), and 0.1 mg of vancomycin was injected into the vitreous cavity (repeated at 48 h). We acknowledge that, according to the guidelines (3), a vitreous tap should have been performed multiple intravitreal injections, first with 50 μg/0.1 ml and then with 250 μg/0.1 ml caspofungin. Despite the recurrence of symptoms, intravitreal injection of caspofungin finally abolished the inflammation and achieved ambulatory vision that persisted until 1 year of follow-up. To our knowledge, this is the first report of Stephanoascus ciferrii endophthalmitis and its successful treatment with intravitreal caspofungin.

Keywords: Endophthalmitis; Phacoemulsification/adverse effects; Candida; Intravitreal injections; Lipopeptides

RESUMO

Endoftalmite fúngica é uma ocorrência rara, muitas vezes associada com mau prognóstico. Apresentamos um caso de endoftalmite fúngica aguda pós-operatória causada por fungo de levedura incomum, Stephanoascus ciferrii (Candida ciferrii). O fungo foi resistente ao fluconazol, ao voriconazol e à anfotericina B e susceptível à caspofungina. Dado que a penetração vítrea de caspofungina após administração intravenosa não é clara, optou-se por realizar múltiplas injeções intravitreas, primeiro de 50 μg e depois de 250 μg de caspofungina, e finalmente obteve-se a resolução da inflamação e a visão recuperada foi mantida por pelo menos um ano após o acidente. No nosso conhecimento, este é o primeiro relato de endoftalmite por Stephanoascus ciferrii e o primeiro relato de endoftalmite fúngica tratada com sucesso com caspofungina intravitréa.

Descritores: Endoftalmite; Facoemulsificação/efeitos adversos; Candida; Injeções intravitreas; Lipopeptides

Submitted for publication: September 13, 2016
Accepted for publication: February 12, 2017

1 Department of Ophthalmology, University of Medicine and Pharmacy “Gr.T.Popa,” Iasi, Romania.

Funding: No specific financial support was available for this study.
Disclosure of potential conflicts of interest: None of the authors have any potential conflict of interest to disclose.

Corresponding author: Ciprian Danielescu. Department of Ophthalmology, University of Medicine and Pharmacy “Gr.T.Popa” str. Universitativi 16, Iasi - 700111 - Romania
E-mail: ciprian.danielescu@umfiasi.ro
ting revealed that the fungus was resistant to fluconazole, voricona-
zole, and amphotericin B, but sensitive to caspofungin (minimum inhibitory concentration: 2 µg/ml). Concurrently, the patient had a counting fingers VA, diffuse corneal edema, and 4+ anterior chamber cells. Based on a literature search we recommended intravitreal injections of caspofungin as a salvage therapy to the patient. She signed an informed consent form adapted to her situation.

Lavage of the anterior chamber and vitreous cavity was performed. Intravitreal injections of 50 µg/0.1 ml caspofungin were administered. Given the clinical response and lack of an alternative therapy, five intravitreal injections were administered at 48-h intervals (the total duration of the treatment was 8 days). The patient demonstrated a prompt response to this therapy, exhibiting a BCVA of 0.8 on the logMAR scale, minimal corneal edema, 1+ anterior chamber cells, and good visibility of the fundus (Figure 1 B). She was discharged, and minimal fluctuations in BCVA and clinical findings were recorded at monthly follow-up visits.

Between the fourth and fifth visits, the patient experienced a progressive recurrence of symptoms, and returned with a hand motion VA. She presented with corneal edema, and the inferior half of the anterior chamber was occupied by a dense, organized exudate (Figure 2 A). Considering the previous efficacy of caspofungin and lack of alternative treatment options, we repeated the intravitreal injections at a higher dose. After aspiration of the exudate in the anterior chamber and lavage of the vitreous cavity, five intravitreal injections of 250 µg/0.1 ml caspofungin were administered at 48-h intervals. The response to treatment was slow, but after 4 weeks, her BCVA increased to 1.1 on the logMAR scale, with 1+ anterior chamber cells, and fixed mydriasis (Figure 2 B). Further episodes of minimal cellular reactivity in the anterior chamber were treated with topical steroids, and the patient maintained the same BCVA (even after the occurrence of a secondary macular pucker) until 1 year of follow-up.

**DISCUSSION**

Although immunocompetent and lacking risk factors related to the initial cataract surgery, our patient presented with endophthalmitis caused by a yeast-like fungus. *S. ciferrii (C. ciferrii)* is an opportunistic pathogen that causes superficial infections in otherwise healthy individuals, but systemically invasive infections in immunocompromised patients. The first case of invasive infection in humans was reported in 2001 in a patient with acute leukemia who was already fluconazole-resistant. *S. ciferrii* strains have been described that are resistant to fluconazole, flucytosine, and itraconazole.

Caspofungin is an echinocandin antifungal drug that inhibits the enzyme β(1,3)-d-glucan-synthase, which is necessary for synthesis of the fungal cell wall. Because of its high protein-binding capacity and molecular mass, it is administered intravenously and exhibits minimal penetration into the eye. When caspofungin was administered intravenously in a rabbit model of uveitis (therefore with a disrupted blood-ocular barrier), it reached therapeutically relevant levels in the aqueous humor and cornea, but not the vitreous humor, of inflamed eyes. In a patient with *Candida* endophthalmitis, the disease progressed after monotherapy with intravenous caspofungin, and intraoperative vitreous sampling found that the concentration of caspofungin was undetectable. Systemic caspofungin was used in association with voriconazole for the treatment of three cases of endogenous fungal endophthalmitis.

In another case report, fungal endophthalmitis was successfully treated with intravenous caspofungin in a patient with candidemia associated with vitritis and a small retinal lesion in whom VA remained normal throughout 4 weeks of therapy. A response to intravenous caspofungin was also observed in 12 of 21 patients with endogenous fungal endophthalmitis included in controlled trials of echinocandins for the treatment of candidemia and invasive candidiasis, although detailed clinical information on these patients is unavailable.

In a study on the pharmacokinetics and safety of intravitreal injection of 50 µg/0.1 ml caspofungin, the concentrations of the drug in the vitreous humor at 1 and 16 h after injection were 6.06 and 2.04 µg/ml, respectively. After injecting up to 300 µg (corresponding to concentrations of up to 200 µg/ml in the 1.4-ml volume of the rabbit vitreous humor), no statistical differences were evident in a- and b-wave responses on scotopic electroretinography compared with control eyes.

In our patient, repeated intravitreal injections of 50 µg/0.1 ml caspofungin elicited a good clinical response, but the disease recurred after several months. Therefore, five injections of 250 µg/0.1 ml caspofungin were administered, and long-term remission of the infectious process and ambulatory vision were obtained. It is important to note that the injections were administered in a vitrectomized eye; thus, the clearance rate of the injected drugs was much faster.

The manufacturer of caspofungin recommends reconstitution of a 50 mg vial to a solution of 5 mg/ml followed by further dilution to 0.5 mg/ml (suitable for intravenous use and corresponding to 50 µg/0.1 ml). For the higher intravitreal dose, we diluted the reconstituted solution of 5 mg/ml to 2.5 mg/ml (corresponding to 250 µg/0.1 ml and still lower than the doses used in the safety study).

We were unable to distinguish the relative contributions of possible toxic effects and effects of the disease to the occurrence of sequelae (fixed mydriasis, low vision, and macular pucker formation), and we did not perform electroretinography in our patient.

To our knowledge, this is the first report of *S. ciferrii* endophthalmitis and its successful treatment using intravitreal caspofungin therapy. This case report provides clinicians with an alternative method of treating eyes unresponsive to conventional antifungal therapies.

**REFERENCES**


3. Bany B, Cordovés L, Gardner S. ESCRS Guidelines for prevention and treatment of en-
Successful treatment of fungal endophthalmitis using intravitreal caspofungin