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Case Report

Voriconazole Treatment for Fungal Chorioretinitis After Obesity Surgery

Fatma Savur, Havva Kaldirim, Kursat Atalay

Department of Ophthalmology, Istanbul Health Sciences University, Bagcilar Training and Research Hospital, Istanbul, Turkey

Abstract

Presently described is a case of fungal septicemia diagnosed based on a fundus examination and successfully treated with voriconazole. A 48-year-old woman who had undergone sleeve gastrectomy 20 days prior due to obesity was referred to the ophthalmology clinic for blurred vision in the right eye. The initial examination indicated visual acuity of only light perception in the right eye and 0.00 logMAR in the left eye. Anterior segment examination and light reaction results were normal in both eyes. The vitreous was clear. A central, hemorrhagic, hypopigmented lesion 1/3 optic disc diameter in size, was located in the right fovea, bulging from the retina. There were 3 or 4 small hypopigmented lesions in both peripheral retinas. The examination findings and patient history suggested fungal chorioretinitis. The patient was treated with intravenous voriconazole at a maintenance dose of 200 mg 2 times a day following a loading dose of 6 mg/kg 2 times a day for 48 hours according to the recommendation of the infectious diseases clinic. Multimodal imaging using fundus photography, fluorescein angiography, and spectral domain optical coherence tomography was performed throughout treatment. The patient's daily follow-up revealed no deterioration and improvement was seen on the third day. Endogenous fungal chorioretinitis is a rare infection, but it remains important in ophthalmology due to the high potential to cause severe visual loss and the limited diagnosis and treatment options. Patients who are susceptible to fungemia and have a recurrent fever may be referred to an ophthalmologist. Many clinical tests may have negative results but a careful fundoscopic examination can determine signs of fungemia-related chorioretinitis.

Keywords: Bariatric surgery, chorioretinitis, fungemia, voriconazole

Introduction

Fungal chorioretinitis is a rare ocular disorder; however, it can manifest endogenously as a result of hematogenous fungus dissemination or exogenously through direct infection, and may lead to vision loss. The most common etiological pathogen is a Candida infection, particularly Candida albicans (1-3). Normal human flora includes Candida albicans and in a healthy individual it does not demonstrate significant virulence. Yet, Candida spp. can cause fungal septicemia and chorioretinitis when the host's defenses are weakened due to conditions such as prolonged hospitalization, abdominal surgery, cancer, diabetes, or intravenous drug abuse (3,4). Some diagnostic procedures, such as blood cultures, can yield negative results. Early recognition and prompt treatment of chorioretinitis due to fungal septicemia can improve both visual and systemic outcomes.

Both local and systemic treatments are necessary to cure fungal septicemia and chorioretinitis. The azole group of antifungals is the first line of treatment. Voriconazole, a potent synthetic derivative of fluconazole, is a second-generation

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Address for correspondence: Fatma Savur, MD. Istanbul Saglik Bilimleri Universitesi, Bagcilar Egitim ve Arastirma Hastanesi, Goz Hastaliklari Klinigi, Istanbul, Turkey
Phone: +90 212 440 40 00 **E-mail:** drfatmagezer@hotmail.com

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azole antifungal medication. However, there is little in the literature about the use of intravenous voriconazole to treat chorioretinitis. The diagnosis and treatment of endogenous fungal chorioretinitis can be challenging if the clinical findings are limited. The present case of fungal septicemia was diagnosed based on a fundus examination and successfully treated with voriconazole. A brief review of the literature is also provided.

Case Report

A 48-year-old woman who had undergone sleeve gastrectomy for obesity 20 days prior to presentation was referred to the ophthalmology clinic due to blurred vision in her right eye. Her medical records indicated that she had to be reoperated on 6 days after the gastrectomy due to wound evisceration and remained in the intensive care unit for 13 days. The patient had systemic hypertension, type 2 diabetes mellitus, chronic obstructive pulmonary disease, and sleep apnea syndrome. Intravenous (IV) cefazolin for prophylaxis was initiated in the postoperative period. The patient had a recurrent fever, though blood, urine, and rectal swab cultures were negative. Growth of Klebsiella pneumonia and Acinetobacter baumannii in catheter tip cultures prompted administration of 150 mg colistin, IV 3 times a day. A clinical improvement was not observed in follow-up, the cultures were repeated, and 2 g meropenem, IV 3 times a day was added to the treatment. The patient was referred for blurred vision in the right eye persisting for 3 days.

The first examination revealed visual acuity of light perception in the right eye and 0.00 logMAR in the left eye. An anterior segment examination and light reaction results were normal in both eyes. The vitreous was clear. There was a central, hemorrhagic, hypopigmented lesion 1/3 the optic disc (OD) diameter in the right fovea, bulging from the retina. There were 3 or 4 small, hypopigmented lesions in both peripheral retinas. Spectral-domain optical coherence tomography (SD-OCT) showed hyperreflective vitreous dots and elevated subfoveal lesion. This hyperreflective foveal lesion appeared to originate in the choroidea with hyperreflective dots in the nearby vitreous. Fluorescein angiography (FA) revealed early hypofluorescence and late phase leakage in the foveal lesion (Fig. 1).

Risk factors, such as diabetes, abdominal surgery, prolonged hospitalization, intravenous catheterization, intensive care unit treatment, and fever despite broad-spectrum antibiotic therapy, in addition to the eye examination findings led us to suspect fungal chorioretinitis. After repeating the cultures, the patient was treated with IV voriconazole at a maintenance dose of 200 mg 2 times a day following a loading dose of 6 mg/kg 2 times a day for 48 hours according to the recommendations of the infectious diseases clinic. There was no deterioration seen in the patient's daily follow-up and improvement in the ocular findings was observed on the third day. Her visual acuity was counting fingers from 1 meter in the right eye and a significant decrease in the retinal lesions was noted in an ophthalmologic examination performed after 1 week. No growth was observed in the final cultures. The response of the retinal lesions to antifungal therapy and improvement in systemic findings led us to believe the suspicion of fungal chorioretinitis was correct. IV voriconazole treatment was administered for 10 days, followed by oral administration for 4 weeks.

At the first-month control visit, the right eye vision was 0.20 logMAR, the left eye vision was 0.00 logMAR, the anterior segment of both eyes was natural, and pigment changes in the right eye fovea were observed in the ophthalmological examination. SD-OCT examination revealed disruption of the retinal pigment epithelium layer and inner segment/outer segment junction. A window defect was present in FA images (Fig. 2).

Discussion

Dissemination of fungal organisms can occur in the eye via hematogenous fungal seeding of small retinal and choroidal capillaries (5).The majority of these patients develop chorioretinitis, and progression to endophthalmitis is seen in 1.6% of cases (6). Chorioretinitis is much more common than endophthalmitis in patients with fungemia, and chorioretinitis is often asymptomatic. In a prospective, multicenter study of 118 hospitalized patients with candidemia, 9% of the patients were found to have chorioretinitis. Few had eye symptoms, and none had endophthalmitis (7). The diagnosis and treatment of chorioretinitis can be delayed due to an asymptomatic course and the high rate of culture negativity. In our patient, reduction in visual acuity as a result of a foveal lesion allowed us to identify the disease at the chorioretinitis stage. A delayed diagnosis can result in the development of endophthalmitis, which can adversely affect visual acuity. Culture negativity may occur in cases of endophthalmitis. Binder et al. (8) reported 70% positive results in cultures of eye samples and 33% positive in blood cultures. Another study that evaluated 31 eyes of 28 patients with endogenous endophthalmitis yielded a positive rate in vitreous cultures of 81%, 32% in aqueous samples, and 33% in blood cultures (9). Therefore, clinical findings and patient history are important guidelines for starting treatment in order to prevent vision loss, In our case, treatment was initiated based on the patient's history and ophthalmological examination findings.

Fungal chorioretinitis is treated with the systemic administration of antifungal drugs, and intravitreal injections or vitrectomy can be performed when necessary. If the lesion is treated early, the prognosis for visual acuity im-

proves (10,11). Fungal chorioretinitis treatments include intravenous amphotericin B (AmB), fluconazole, and the recently introduced voriconazole. AmB achieves a very poor concentration in the posterior segment of the eye, but fluconazole concentrations are high. Therefore, endogenous fungal chorioretinitis usually responds well to treatment with intravenous fluconazole. Although fluconazole has adequate efficacy in many cases, it should be noted that there are resistant Candida spp. and it is less effective than AmB in Aspergillus infections (12). Voriconazole is a broad-spectrum antifungal agent that is more effective than fluconazole in the treatment of Aspergillus spp. and fluconazole-resistant species, such as Candida glabrata and Candida krusei (13,14). Biju et al. (15) reported good results in the treatment of endogenous fungal endophthalmitis with oral voriconazole. The authors also posited that oral voriconazole was a more effective and tolerable drug than AmB in fungal endophthalmitis. Due to concerns about arrangements for oral voriconazole treatment in a patient with a history of complicated bariatric surgery, we

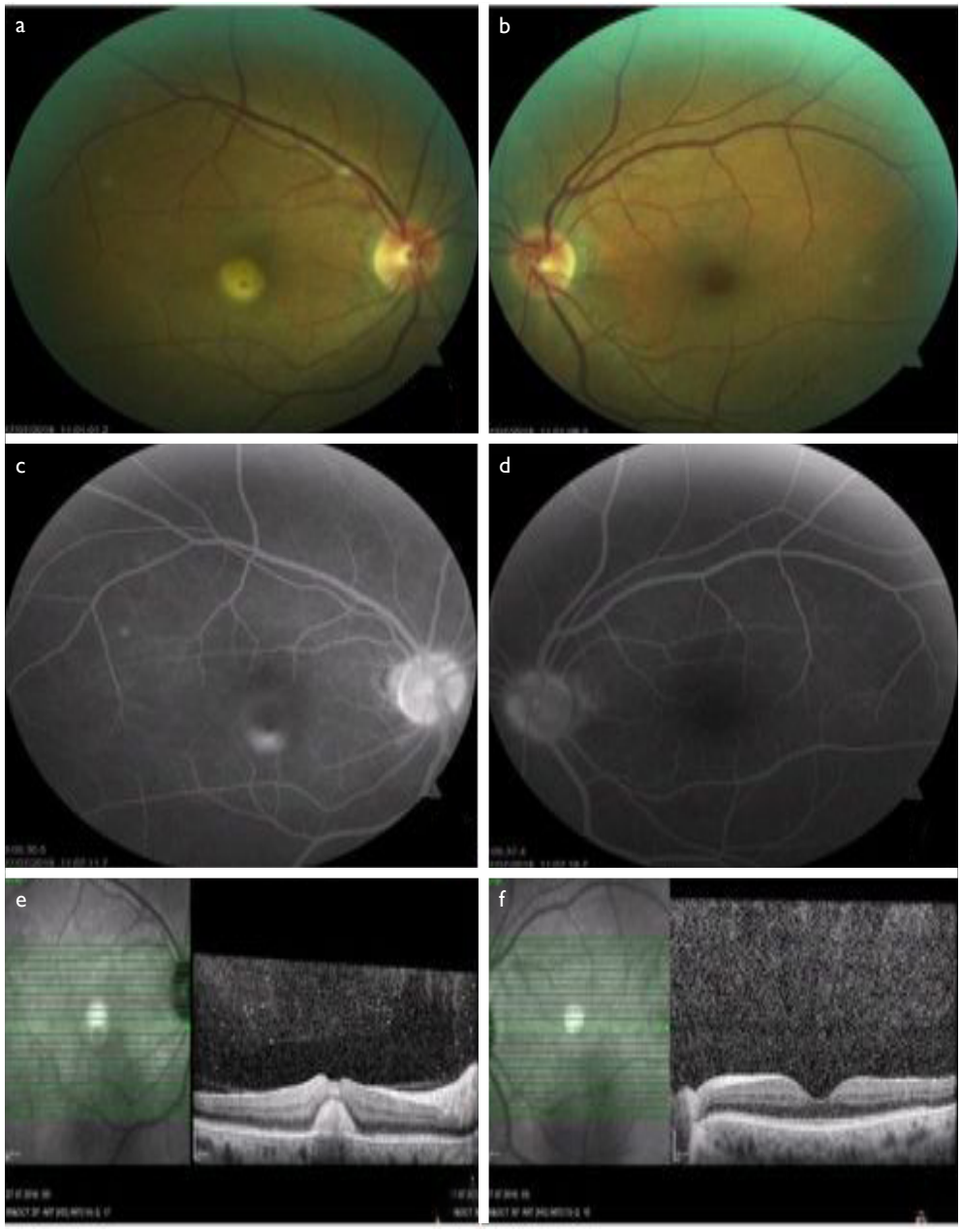

Figure 1. Fundus images of the first day. **(a, b)** Color fundus photographs showing a raised, white, chorioretinal lesion in the right eye; **(c, d)** Fluorescein angiography revealing hyperfluorescence in the foveal lesion and optic disc in the right eye at 5 minutes; **(e, f)** Spectral-domain optical coherence tomography images illustrating a subretinal lesion in the right eye and hyperreflective dots in the vitreous.

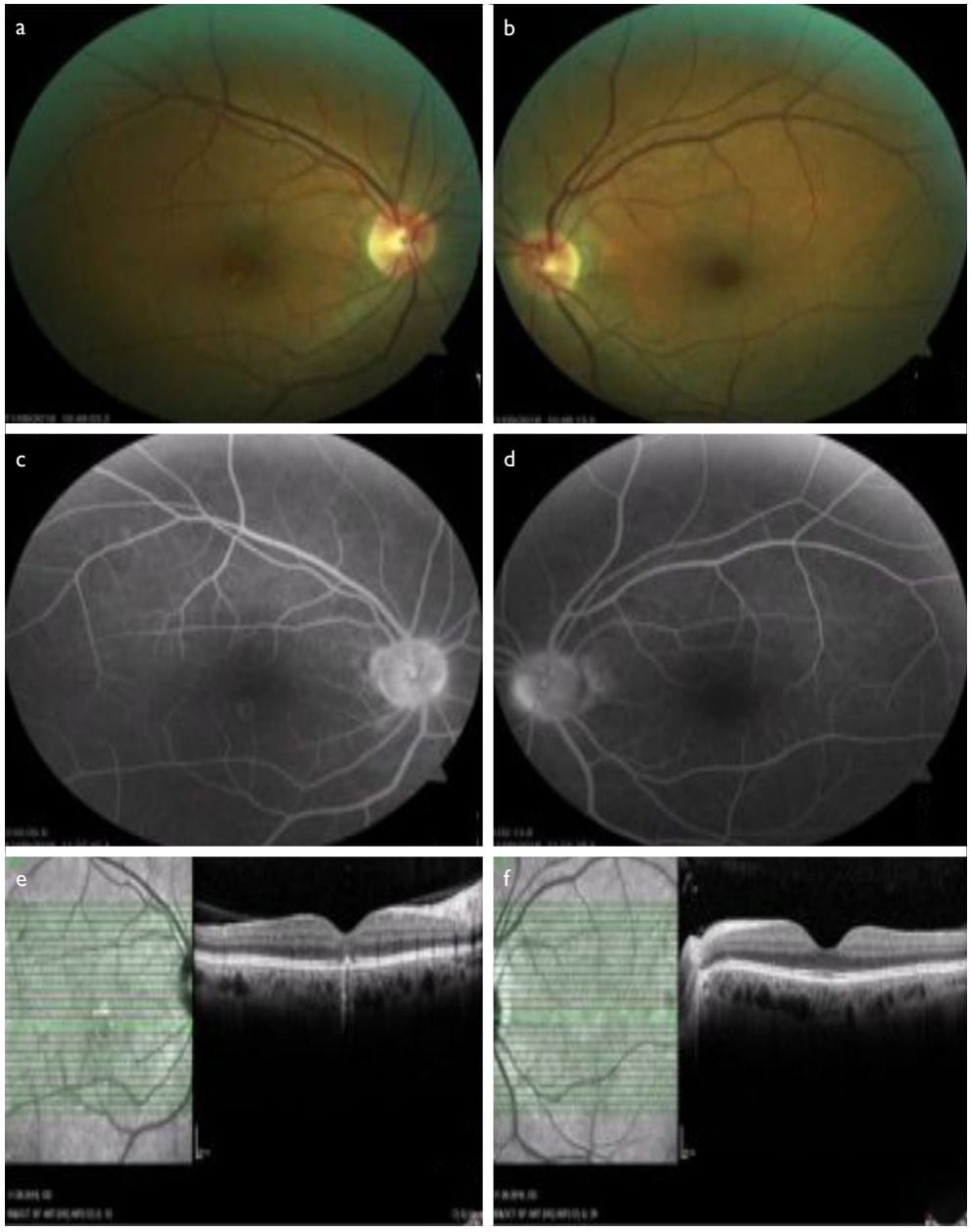

Figure 2. Fundus images at the first month. **(a, b)** Color fundus imaging showing pigment changes in the fovea of the right eye; **(c, d)** Fluorescein angiography imaging demonstrating a window defect in right eye; **(e, f)** Right spectral-domain optical coherence tomography imaging illustrating the retinal pigment epithelial layer and disruption of the inner segment/outer segment connection.

started treatment with IV voriconazole according to the recommendations of infectious diseases clinic. The absence of pathogens found in the cultures and the broad range of effects of voriconazole also recommended this preference. Reports have demonstrated less retinal toxicity and better safety with intravitreal voriconazole treatment compared with intravitreal AmB in fungal chorioretinitis (16,17). We did not pursue intravitreal treatment because of the regression seen in the chorioretinal lesions and no sign of intravitreal spread during follow-up.

In cases of endogenous fungal chorioretinitis, clinical findings can outweigh culture results in making the diagnosis. Patients with risk factors for fungemia who have a recurrent fever may be referred to an ophthalmologist. Though many clinical tests may have negative results, a careful fundoscopic examination can reveal signs of fungemia-related chorioretinitis. Voriconazole, the most recent antifungal agent, can be used as a first-line drug, as it has demonstrated a broad spectrum of action, adequate vitreous concentration in systemic use, and a low level of retinal toxicity (13,14,16,17).

Disclosures

Informed consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Involved in design and conduct of the study (FS); preparation and review of the study (FS, HK, KA); data collection (FS, HK).

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