MEDICINE PLUS SURGERY TREATS AN UNUSUAL CASE OF FUNGAL ENDOPHTHALMITIS

Careful attention to the patient’s history and persistent follow-up made for a positive result.

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Extreme morning sickness, or hyperemesis gravidarum, is a complication of pregnancy characterized by severe nausea and vomiting, weight loss, and even dehydration. Whereas mild cases of hyperemesis gravidarum can be treated with dietary changes, rest, and antacids, more severe cases can require hospitalization and intravenous nutrition. The following case report describes a young pregnant woman with fungal endophthalmitis in the setting of candidemia from fungal endocarditis after receiving total parenteral nutrition (TPN).

CASE REPORT

A 31-year-old black woman, at 24 weeks gestational age, was admitted to the San Antonio Military Medical Center for hyperemesis gravidarum requiring TPN. She returned 2 weeks later with complaints of blurry vision in her right eye (OD).

The patient had no previous ocular history or history of intravenous drug use. HIV test performed earlier in the pregnancy was negative. On presentation, visual acuity (VA) was 20/70 OD and 20/20 in her left eye (OS). Her intraocular pressure (IOP) was 19 mm Hg OD and 20 mm Hg OS, and there was no relative afferent pupillary defect. The external examination was unremarkable. Anterior chamber examination exhibited 1+ cell OD.

AT A GLANCE

- Ophthalmologic findings of C. albicans endophthalmitis have a strong association with disseminated candidiasis, especially in the setting of predisposing factors.
- In this case report, prompt vitrectomy and intravitreal injection of amphotericin led to rapid visual recovery.

Figure 1. Fundus photo OD. A superior juxtafoveal lesion is visible, and optic disc edema is apparent.
Funduscopic examination OD revealed a solitary fluffy white juxtafoveal lesion that measured 1 disc diameter with slight elevation. Overlying vitritis with small intraretinal hemorrhage was seen adjacent to the lesion (Figure 1). On scleral depression, numerous snowballs were present in the inferior vitreous.

Ocular coherence tomography (OCT) of the macula revealed vitreomacular adhesion (VMA) with a hyperreflective lesion superior to the fovea. Central fundus thickness (CFT) was 552 μm (Figure 2).

A systemic evaluation was performed, including echocardiogram, which revealed vegetation on the patient’s tricuspid valve. Initial blood cultures were negative for bacterial or fungal microorganisms, but Fungitell assay (Beacon Diagnostics Laboratory) was positive for the presence of fungus. The patient had no previous cardiac history, but she did have a remote history of bacteremia from a central line infection. Noncontrast magnetic resonance imaging of the brain and orbits was normal.

The patient was treated with intravenous liposomal amphotericin B and daptomycin, in consultation with infectious disease specialists, due to concern for concurrent native-valve endocarditis and the previous history of a central line infection. Extensive lab workup was unremarkable for rapid plasma reagin, cytomegalovirus (CMV), toxoplasmosis, immunoglobulin M and G antibodies, Brucella, histoplasmosis, Cryptococcus, and Coxiella antigen.

The next day, the patient’s VA had worsened to 20/200 OD. Examination revealed worsening papillary optic disc edema and vitritis. B-scan demonstrated worsening vitritis (Figure 3). Due to the extent of the vitritis and the location of the retinitis, the patient underwent pars plana vitrectomy with removal of the hyaloid. Intravitreal amphotericin B 5 μg was administered after vitrectomy. The results of vitreous biopsy were positive for Candida albicans.

On postoperative day 5, the patient’s VA was 20/100 OD, and OCT revealed interval clearance of the VMA, resolving intraretinal edema, and CFT of 392 μm (Figure 4). At 3 weeks postoperative, the patient’s VA had improved to 20/40 OD, and funduscopic examination revealed macular plaque, interval clearance of white clumps, and improved vitritis (Figure 5). Repeat blood cultures and biopsy from transesophageal echocardiogram revealed C. albicans.

The patient underwent 6 weeks of antibiotic therapy and surgical resection of vegetation with annuloplasty of her tricuspid valve to address the endocarditis. At postoperative month 5, she had returned to her baseline VA of 20/20 OD with a stable superior macular plaque.

**DISCUSSION**

Fungal endophthalmitis from Candida infections primarily develops from an endogenous source via hematogenous spread to the choroid. Long-term indwelling central venous catheters increase the risk for bacteremia, particularly Staphylococcus aureus. Increased parenteral caloric intake is another independent risk factor for bloodstream infections, particularly those resulting from C. albicans. The differential diagnosis for fungal endophthalmitis includes endogenous or exogenous bacterial endophthalmitis, toxoplasma retinochoroiditis, primary intraocular lymphoma, and CMV retinitis. Posterior uveitis from other inflammatory and infectious conditions such as sarcoidosis, syphilis, tuberculosis, Lyme disease, and Brucellosis may also be considered.

The diagnosis of fungal endophthalmitis is based on ophthalmologic appearance and high suspicion for fungemia in the setting of predisposing factors. Fungal endophthalmitis is
associated with fluffy white chorioretinal lesions and vitritis that is manifested by small, white, snowball-like opacities. A positive vitreous culture is the gold standard for diagnosis; however, vitreous tap has a sensitivity of approximately 44%, whereas vitrectomy offers an increased diagnostic yield, ranging from 75% to 92%.4–6

Fungal bacteremia may be initially missed on routine blood cultures,9 as was the case with our patient. Various other serologic procedures have been employed to quickly identify a fungus source. In this case, the Fungitell assay was used, which detects the (1→3)-β-D-glucan cell wall constituent and has reported a sensitivity of 93.3% and specificity of 77.2%.10

Treatment of fungal endophthalmitis represents a unique challenge, given the presence of the blood-ocular barrier, which can prevent the adequate concentration of antifungal agents within the vitreous cavity. Due to the highly vascular nature of the choroid and retina, chorioretinitis without vitritis can be successfully treated with systemic therapy alone with either fluconazole and voriconazole or liposomal amphotericin B with or without flucytosine. Furthermore, patients with a concern for S. aureus bacteremia due to indwelling central lines can be treated with intravenous daptomycin, which has good intravitreal penetration.11 Vitreous involvement requires intravitreal injection with either amphotericin B deoxycholate (5–10 µg/0.1 mL) or voriconazole (100 µg/0.1 mL). The administration of intravitreal antifungal agents, whether only through tap and inject or combined with vitrectomy, is evolving.

Historically, involvement of the posterior pole and vitreous has been treated with vitrectomy, with or without intravitreal amphotericin B (5–10 µg/0.1 mL) in an effort to decrease infectious load and provide immediate delivery of drug.12,13 Recently, small case series have advocated for early complete vitrectomy in addition to intravitreal antifungal agents, with demonstration of favorable outcomes. A retrospective review of 44 eyes found that Candida endophthalmitis was associated with poor visual outcome, especially in patients with poor presenting VA and posterior pole involvement (relative risk, 5.01; P < .05). Vitrectomy helped to significantly reduce the risk of retinal detachment (P = .02).14

A recent 7-year retrospective review of 40 eyes with fungal endophthalmitis demonstrated that 71% of patients treated with vitrectomy plus an intravitreal antifungal agent have more than 2 lines of VA recovery, compared with 25% of patients treated with intravitreal antifungal injection alone (P = .034).15 A prospective analysis in a subset of patients with fungal endophthalmitis who underwent early, complete vitrectomy with either amphotericin B or voriconazole (n = 6) had statistically significant vision improvement as compared with diagnostic vitrectomy with antifungal agents.16

CONCLUSION

In the patient described here, vitrectomy was performed and intravitreal amphotericin was administered due to worsening VA, severe vitritis, and posterior pole involvement. The rapid effectiveness of vitrectomy was highlighted by improved VA, and postoperative OCT demonstrated dramatic resolution of intraretinal edema and clearance of the VMA.

Severe inflammation from endophthalmitis and VMA are independent risk factors that can lead to retinal detachment, but vitrectomy performed within 1 week of presentation is associated with a lower risk of retinal detachment.5,17 This case illustrates that ophthalmologic findings of C. albicans endophthalmitis have a strong association with disseminated candidiasis, especially in the setting of predisposing factors. Furthermore, early surgical treatment with vitrectomy and intravitreal antifungal therapy in eyes with posterior pole and vitreous involvement can lead to rapid visual recovery.

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