[Correspondence – Case Report]

Fungal endophthalmitis in a case of rhino–orbital–cerebral mucormycosis treated with 0.02% intravitreal liposomal amphotericin B injection - a case report

Sangwon Jung, MD, M.S.P¹, Min Seok Kim, MD, MSc ²

¹Department of Ophthalmology, Seoul National University College of Medicine, Seoul National University Hospital, Seoul, Korea

²Department of Ophthalmology, Seoul National University Bundang Hospital, Seongnam, Korea

Address for Correspondence:
Min Seok Kim, MD, MSc
Department of Ophthalmology, Seoul National University Bundang Hospital, 173-82 Gumi-ro, Bundang-gu, Seongnam-si, Gyeonggi-do, 13620, South Korea
Tel: +82-31-787-7388, Fax: +82-31-787-8887, E-mail: 66217@snubh.org

IRB No: B-2303-815-701
Dear editor

Rhino-orbital-cerebral mucormycosis (ROCM) is one of the major clinical forms of mucormycosis, and diabetes mellitus is its common risk factor [1]. There have been several reports of ocular involvement following ROCM [2]. Although empirical intravitreal injection of liposomal amphotericin B (L-AMB) at a dose of 5-10 μg/mL is used for fungal endophthalmitis, a standard guideline for fungal chorioretinitis or endophthalmitis secondary to ROCM has not been established [2, 3]. We report a case of unilateral ROCM with contralateral endogenous chorioretinitis and endophthalmitis that improved after intensive intravitreal L-AMB injections.

A 48-year-old man with diabetes was referred to the emergency room in our tertiary hospital for acute loss of vision in his left eye for 1 day. He also complained of fever, ptosis, swelling of the left eyelid, headache, and facial pain with hypoesthesia in the left half of the face. He had undergone extraction of the left maxillary molar 3 days prior. At the initial presentation, the uncorrected visual acuity was 20/20 in the right eye and no light perception with mid-dilated and fixed pupil in the left eye. While the right eye showed a normal fundus (Fig. 1A), a generalized pale retina and a cherry-red spot were revealed in the left eye, suggestive of central retinal artery occlusion (CRAO) (Fig. 1B). Glycated hemoglobin level was 18.2%. Magnetic resonance imaging of the brain revealed invasive fungal sinusitis with left optic neuropathy, orbital cellulitis, and cerebritis (Fig. 1C). Since ROCM was suspected, 3 g of ampicillin-sulbactam combination every 6 h and 5 mg/kg of L-AMB every 24 h were administered intravenously, and endoscopic sinus surgery with debridement of the sinuses was performed (Fig. 1D). Mucormycosis was confirmed histopathologically in multiple para sinuses specimens (Fig. 1E-G). On the 13th day of hospitalization, visual acuity in the right eye suddenly decreased to 20/32, and ocular pain developed. Fundus examination revealed multiple yellowish retinal infiltrates without vitritis in the right eye and multifocal chorioretinitis with vitritis accompanied by anterior chamber cells in the left eye, suggesting progression of ROCM to right fungal chorioretinitis (Fig. 1H) and left fungal endophthalmitis, respectively. Intravitreal injection of L-AMB (0.01%, 10 μg of L-AMB in 0.1 mL of 5% dextrose water) was initiated in both eyes. Intravitreal injection in the left eye was discontinued after three doses because
the left eye already had severe visual loss due to CRAO, and retrobulbar injection of L-AMB was performed consistently for left orbital cellulitis. Despite five intravitreal injections of L-AMB (10 μg of L-AMB in 0.1 mL) twice a week in the right eye, inflammatory cells were observed in the anterior chamber and vitreous, and the number of yellowish lesions in the retina further increased. Additionally, retinal edema was developed in spectral domain optical coherence tomography (SD-OCT) images (Fig. 1I). Since progression to fungal endophthalmitis was suspected, we doubled the concentration to 20 μg of L-AMB in 0.1mL (0.02%) for intravitreal injection. After five subsequent injections of doubled concentration at the same intervals, the yellowish lesions and macular edema almost disappeared.

After eight additional intravitreal injections of L-AMB (20 μg of L-AMB in 0.1 mL) twice a week, the macular edema and yellowish retinal lesions disappeared completely; however, the vitreous opacities remained without active inflammation (Fig. 1J). During the 3-month follow-up after the last injection, the retina was stable with stationary vitreous opacities, and the visual acuity was 20/100 in the right eye.

The incidence of endophthalmitis complicated with ROCM is reportedly 1~2% [1]. If only chorioretinitis is present, it is generally treated with systemic antifungal treatment, whereas intravitreal antifungal injection is considered for endophthalmitis [4]. In some studies, it is known that complications such as toxic uveitis and retinal toxicity are less with L-AMB than with AMB deoxycholate (D-AMB) injection when administered intravitreally [5]. Furthermore, L-AMB has a long half-life in the vitreous and fungicidal activity, which is advantageous when compared to other antifungal drugs such as voriconazole, which has fungistatic activity [3].

In conclusion, if mucormycosis chorioretinitis progresses despite treatment with systemic antifungal agents and intravitreal injection of L-AMB (10 μg in 0.1 mL), the higher dose of L-AMB (20 μg in 0.1mL) twice weekly regimen could be considered for an effective and tolerable treatment option.

**Funding:** None.

**Conflict of Interest:** None.
REFERENCES


Figure Legends

Figure. 1. (A) At the initial presentation, clinical images showing non-specific finding in the right eye. (B) Wide fundus photography shows pale retina and a cherry-red spot, suggesting central retinal artery occlusion in the left eye at initial presentation. (C) Magnetic resonance imaging (T2-weighted-fluid-attenuated inversion recovery) shows invasive fungal sinusitis (white arrows) and optic neuropathy (red arrow). (D) Black eschar (white arrow) is seen in the left nasal sinus during endoscopic sinus surgery. The red arrows indicate positive findings for fungal hyphae with irregular thickness and length and scant septation, suggesting mucormycosis with (E) Grocott’s methenamine silver stain (20x), (F) Periodic acid-Schiff stain (20x), and (G) Hematoxylin-eosin stain (20x). (H) Fungal chorioretinitis occurs after 2 weeks of systemic liposomal amphotericin B (L-AMB) administration. (I) Fungal chorioretinitis was aggravated despite five intravitreal injections of L-AMB (10 μg in 0.1 mL) twice a week schedule. (J) After 13 intravitreal injections of L-AMB (20 μg in 0.1 mL) twice a week, macula edema and yellowish retinal lesions disappeared completely, though some vitreous opacities remained. The green arrow indicates the direction of the Spectral domain optical coherence tomography (SD-OCT) scans.