

Case Report

Survival of a Rhino-Orbital-Cerebral Mucormycosis Patient after Localized Combination Liposomal Amphotericin B Medications: A Case Report

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Keywords

Rhino-orbital-cerebral mucormycosis · Nasogastric tube · Liposomal amphotericin B · Orbital exenteration · Case report

Abstract

Introduction: The aim of this study was to report a case of ROCM related to nasogastric intubation who was survived by liposomal amphotericin B (LAmB) combination therapy in situ without orbital exenteration. **Case Presentation:** A 44-year-old woman presented with a 1-week history of rapidly enlarging swelling on the right nose, cheek, and lower eyelid after underwent gastrointestinal decompression. The lesions were derived from the nasal area where the nasogastric tube had been placed. Based on the biopsy results and clinical manifestations, ROCM was diagnosed. Immediate combination therapy with intravenous LAmB and micafungin and multisection debridement of the right facial region were applied. Postoperative treatment included cleaning, irrigating, and local dressing of the wound area using LAmB. LAmB was also used daily as binocular eye drops against deep infection on the eyeballs. The patient recovered well 4 months later and remained free of disease after 40 months of follow-up. **Conclusion:** This case adds to our knowledge on the potential risk of nasogastric intubation for mucormycosis infection. Nasogastric tube may be the source of infection associated with ROCM. This report evaluates the beneficial effect of LAmB combination therapy in situ for cleaning, irrigating, local wound dressing, and eye drops on lesion areas. The combination of LAmB as cleaning, irrigating, local dressing solution, and eye drops to control intraocular and intraorbital ROCM infection has not been previously reported to our knowledge. These methods provide multiple choices to substitute for orbital exenteration on the survival of ROCM patients.

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Introduction

In recent years, the epidemiology of mucormycosis has shown an alarming trend, especially during the outbreak of COVID-19 infection. Mucormycosis has rapidly become a healthcare-associated infection in immunocompromised patients. Adhesive bandages or tapes, catheters, wooden tongue depressors, and water circuitry damage were all identified as the source of healthcare-associated mucormycosis (HCM) [1]. HCM related to nasogastric intubation is an extremely rare disease and very few cases were reported [2–4]. Rhino-orbital-cerebral mucormycosis (ROCM) is the most common type of HCM. Even with treatment, the mortality rate of ROCM patients is more than 60% [5]. The underlying pathogenesis of ROCM patients is endothelial cell damage leading to vascular thrombosis, which limited intravenous antifungal drugs to reach effective concentration and prevent rapid progression. When progressive orbital disease appears, exenteration may be recommended. However, exenteration always has a dilemma of being potentially life-saving as well as causing significant complications including blindness, cosmetic disfigurement, and psychosocial trauma [6]. Here, we present an ROCM patient who was survived by an effective treatment strategy with liposomal amphotericin B (LAmB) combination therapy in situ without orbital exenteration.

Case Presentation

A 44-year-old female presented with a 1-week history of rapidly enlarging swelling on right nose, cheek, and lower eyelid. Her previous medical history included a 2-year history of diabetes mellitus. She took daily oral medication regularly and the fasting blood glucose was controlled at 8–10 mmol/L. One week ago, she underwent gastrointestinal decompression after pancreatitis in another hospital. Laboratory tests showed random blood sugar 9.6 mmol/L, lactic acid 0.8 mmol/L, pCO₂ 35.2 mm Hg, pO₂ 74 mm Hg, serum kalium 3.1 mmol/L, urine sugar +, blood urea nitrogen 1.65 mmol/L, and creatinine 41.4 μmol/L. Later, she developed swelling, ache, and necrosis from her right nose. The lesions were derived from the nasal area where the nasogastric tube had been placed. Then the swelling and ache spread rapidly to right cheek and eyelids. When admitting to our hospital, this patient was observed that her right facial skin swelled with dark in color. The right nasal passage was partly blocked by a black scab. The right eyelids swelled severely, leading to ptosis, hypophthalmos, and limited ocular movement. Further examination showed the right eye – exophthalmos, mild bulbar conjunctival hyperemia, high edema, small amount of white, thin secretions in the conjunctiva sac, cornea still transparent, no pus found in the anterior chamber, pupil dilated about 6 mm, direct and indirect response to light disappeared, and fundus optic disc pale and the left eye – only mild ectropia, cornea clear, pupil about 4 mm, slow response to direct light, and fundus optic disc color slightly light. The visual acuity of the right eye was light perception, while the left eye was 6/60. Fundoscopy revealed bilateral neuropapillitis in Figure 1a, b. Laboratory tests results showed leucocyte $18.22 \times 10^9/L$, random blood sugar 15.5 mmol/L, postprandial blood sugar 20.3 mmol/L, urine sugar +++, urine ketone body +, blood urea nitrogen 1.50 mmol/L, and creatinine 59.8 μmol/L. Nasal sinuses computed tomography images showed swollen subcutaneous tissues in the right cheek and lower eyelid, bilateral maxillary sinusitis, ethmoiditis, and right prosopansitis. Orbital magnetic resonance images showed widespread necrosis infiltrated into right sinus cavity, orbit, and zygoma in Figure 2.

Immediate treatment including intravenous insulin, fluid infusion, and correction of ketoacidosis were performed. Surgical debridement of facial lesions was performed after obtaining the patient's consent. A large amount of necrotic tissue was extracted along the edge

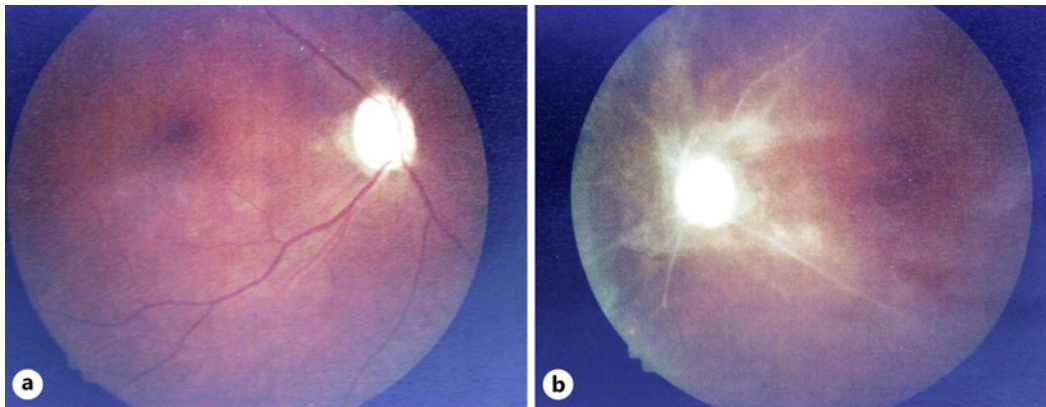


Fig. 1. Fundoscopy on the right eye (a) showing a pale swelling optic disc with blurred margin and central retinal arteries occlusion; on the left eye (b) showing a light-colored retina, pale optic disc, and retinal vascular occlusion.

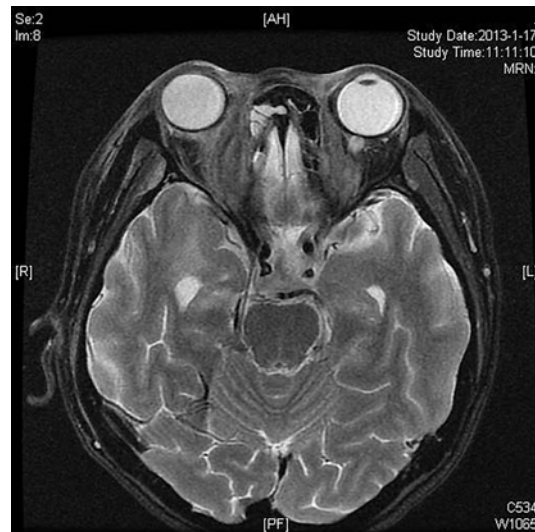


Fig. 2. Orbital magnetic resonance images showing widespread necrosis infiltrated into right sinus cavity, orbit, and even zygoma.

of the lesions and sent for bacterial and fungal evaluation. Fungal masses and hyphal elements were extracted from the biopsy tissue. KOH wet mount showed broad, transparent, and nonseptate hyphae with right-angle branching and characteristic of mucormycosis. Based on the biopsy results and clinical manifestations, ROCM was diagnosed and combination antifungal medications were administered.

Micafungin (150 mg/day) was administered intravenously immediately after ROCM was diagnosed as upfront therapy for 10 days. Then, LAmB was administered intravenously at an initial dose of 5 mg/day. Two weeks later, 50 mg/day was applied as the maintenance dose. Meanwhile, the patient underwent surgical debridement on the right facial region including the maxillary, cellulae ethmoidales and frontal sinus. After 2 months, the overall general condition of the patient was improving the usage of antifungal medicine terminated. Later, the patient underwent surgical debridement, and the ethmoid sinuses, frontal sinuses, and maxillary sinuses were fully opened and drained. After conventional irrigation of the operative cavity during each debridement, the local area was rinsed with LAmB-diluted solution (25 mg LAmB + 500 mL water for injection). Postoperative treatment included cleaning, irrigating, and local dressing of operative cavity using LAmB-diluted solution each day. LAmB



Fig. 3. Photograph of the patient at 40 months after treatment.

was used daily as binocular eye drops (5 mg/mL, 4 times a day) against deep infection on eyeballs. Postoperative eyes conditions in both eyes showed that conjunctiva sacs were clean without secretion, corneas were transparent anterior chamber, and aqueous humor was clear. The dilated pupil diameter is 6 mm in the right eye and 4 mm in the left eye consistent with those preoperatively. The visual acuity of right eye remained almost the same level of light perception as that when the patient admitted to the hospital, while the left eye went down to FC/20 cm. The patient recovered well and was discharged 4 months later. She remained free of disease after 40 months of follow-up shown in Figure 3.

Discussion

HCM has been associated with iatrogenic immunosuppression, or a variety of procedures or devices used in hospitals, including contaminated wound dressings, transdermal nitrate patches, intravenous catheters, tongue depressors, and even allopurinol pills [7]. For our case, she developed infectious signs from the right distal nasal cavity where the nasogastric tube had been placed. The infection spread from nasal mucosa to the skin of ala nasi even the whole right facial region. Nasogastric tube is sterilized medical equipment, which could be used only in an aseptic process. That is probably the reason why the reports of HCM caused by contaminated nasogastric tube are very rare. Till now, there have been only four reported cases including our case. The comprehensive systemic and topical therapy contributed to the good prognosis of our case, while the other three mucormycosis cases related to nasogastric incubation were not survived with or without orbital exenteration. Yet the exact relation between the nasogastric tube and ROCM as well as the infection portal of entry on the nasogastric tube in our case was not clear. However, cases of invasive mycosis following nasogastric tube have been reported, raising concern regarding the possibility of an association between the two. Meanwhile, mucormycosis infection occurs commonly in patients with poorly controlled diabetes mellitus, hematologic malignancies, immunosuppressive and chemotherapy agents, hematopoietic stem cell or solid organ transplantation, and some other factors like the coronavirus disease 2019. Diabetes mellitus is the most common predisposing condition. The state of diabetic ketoacidosis would exacerbate this risk. In the present case, her previous medical history only included a 2-year history of diabetes mellitus with daily FBG controlled at 8–10 mmol/L. Before gastrointestinal decompression, serious metabolic disorders even the accompanying state of diabetic ketoacidosis were not observed given the lab tests. Therefore, infection related to the nasogastric tube was thought to be the most important factors causing mucormycosis in this patient.

Systematically, amphotericin B (AmB) and its liposomal formulation are the first antifungal agent licensed for primary therapy of mucormycosis and significantly improve the survival rate [8]. Combination therapy with LAmB and caspofungin is synergistic and may be more effective for ROCM. Here, we present successful treatment using combination therapy with LAmB and micafungin, an echinocandin, which was in accordance with previous reports on murine models and case studies [9]. In situ, surgical debridement includes extensive resection of infected and necrotic tissues as a part of source control and reduction of fungal load. The orbital involvement may need decompression or exenteration. The role of routine orbital exenteration or the timing of exenteration is currently unclear. Although exenteration is associated with longer survival in patients with refractory orbital impairment or invasion of the central nervous system, exenteration also causes significant complications including blindness, cosmetic disfigurement, and psychosocial trauma [6]. Given this procedure's unsatisfactory outcome, alternative methods of treatment should be considered.

The angioinvasive nature of mucormycosis limits the delivery of systemic antifungal medications. The mechanism of AmB is to form permeable channels in the cellular membrane of the pathogen, leading to cell death. Administration of AmB directly into the orbit region allows for high antifungal concentration and local control of infection. The use of local antifungal agents to treat ROCM was first described in 1969 [10]. Since then the treatment of ROCM with AmB using transcutaneous retrobulbar injections, surgical packing of the orbit with soaked gauze, orbital irrigation through a catheter, etc. were reported. Exenteration was necessary in only very few patients reported to have been treated with local AmB as a result [11–15]. Compared with free AmB, application of liposomal AmB results in greater corneal tissue concentration and less ocular toxicity [16]. For our case, after multisection surgical debridement, the medial tissue of the right orbit was absent, and the lateral wall of ethmoid sinus, the floor wall of frontal sinus, and the anterior wall of maxillary sinus were exposed. LAmB-diluted solution was able to be used directly to change dressings, and irrigate and drainage the operative cavities, which increased the drug concentration of LAmB in lesion areas and limited the progression of orbital fungal infections effectively.

LAmB used as eye drops has been reported in the treatment of fungal keratitis and corneal ulcer. LAmB can penetrate the blood-retinal barrier in the inflamed eyes. Upon repeated daily usage, LAmB can be detected in the cornea, aqueous humor, and vitreous [17]. For our case, when she admitted to the hospital, the only positive sign of infection in the right eye was a small amount of white secretion in the conjunctiva sac. The cornea was clear, no exact inflammation or lesion was found in the ocular anterior segment, while bilateral neuropapillitis caused by mucor invasion was detected in the fundus. Based on surgical debridement on the right facial region, LAmB was also used as binocular eye drops daily for postoperative treatment. As a result, the secretion in the conjunctiva sac disappeared and the ocular anterior segment was not involved by infection, and the visual acuity remained almost the same level of light perception on the right eye as that when the patient admitted to the hospital, while the left eye dropped to FC/20 cm. Despite multiple lesions in the naso-orbital tissues, the spread of infection was controlled without deep involvement of the eyeballs, which might benefit from a high dose of topical LAmB therapy. To our knowledge, the combination of LAmB as cleaning, irrigating, local dressing solution, and eye drops to control intraocular and intraorbital ROCM infection has not been previously reported. The present topical LAmB medications could be an alternative way in treating ROCM instead of orbital exenteration.

In conclusion, mucormycosis has a high mortality rate and the incidence has increased during the past decade. The present case adds to our knowledge on the potential risk of nasogastric intubation for mucormycosis infection. Nasogastric tube may be the risk source of infection associated with ROCM. Our case emphasizes the effect of LAmB used in situ for cleaning, irrigating, and local dressing of the wound area and for binocular eye drops. These

methods achieve higher doses of the drug at the site of infection, block the progression of mucor infection, and keep the disease from getting worse. As a result, the present individualized treatments bring patients to favorable prognosis and better cosmetic and psychological results and provide multiple choices to substitute for orbital exenteration on the survival of ROCM patients. Hence, there is also a need for more sensitive combination therapy and more related clinical trials for these infections. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see <https://doi.org/10.1159/000536185>).

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Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The author declares that there are no conflicts of interest related to this article.

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Author Contributions

Yang Zhou conceptualized the manuscript and was involved in the collection, analysis, interpretation of data, writing, and approval of the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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