

Rhino-Orbital Mucormycosis as a Complication of COVID-19 Pneumonia Treatment

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ABSTRACT

Our aim was to discuss rhino-orbital mucormycosis developing after coronavirus disease-2019 pneumonia treatment. A 45-year-old man presented with visual loss, headache, and numbness in the palate and the left mid-face. The patient had been administered methylprednisolone for coronavirus disease-2019 disease at another hospital. The head and neck examination revealed ophthalmoplegia and chemosis in the left eye and hypoesthesia in the site under the left orbit. Endoscopic nasal examination revealed a black eschar tissue on the left inferior turbinate and the middle meatus. Liposomal amphotericin B was promptly administered with a dose of 5 mg/kg with a preliminary diagnosis of mucormycosis. Urgent endoscopic medial maxillectomy and orbital decompression were performed. Once total visual loss was seen in the patient in the follow-up period, orbital exenteration was performed. The diagnosis of mucormycosis was made based on the histopathological examination, which revealed non-septate hyphae causing invasion in the tissues and the blood vessels. There was no growth of specific fungal microorganisms in the tissue cultures. The patient has been alive during the 2 months follow-up periods and no complications were observed. Patients with coronavirus disease-2019 should be closely monitored in terms of the underlying disease and mucormycosis. Corticosteroids should be administered carefully in coronavirus disease-2019 patients.

Keywords: *Mucor*, mucormycosis, coronavirus disease-2019

Introduction

Mucormycosis is a fulminant disease developing in patients with uncontrolled diabetes mellitus or immunosuppression. In order to establish the diagnosis of mucormycosis, it is important to identify the fungi on tissue culture or histopathological examination. Early diagnosis and prompt treatment are mandatory for patients' survival.¹

Coronavirus disease-2019 (COVID-19) results from SARS-CoV-2, which has caused a pandemic from Wuhan, China. When the virus infects the lungs, an inflammation begins in the alveolar epithelial-interstitial-endothelial area. Cytokine storm starts with the release of cytokines from the inflamed tissue.² Corticosteroids (CS), which may cause immunosuppression, can be used to reduce the immune response to cytokine storm in COVID-19.

In this case report, we present rhino-orbital mucormycosis, which developed after the treatment for COVID-19 pneumonia, and which was medically and surgically managed. We have

emphasized the cautious use of CSs during the COVID-19 pandemic in order to prevent steroid-related mucormycosis.

Case Presentation

A 45-year-old man presented with visual loss, headache, and numbness in the palate and the left mid-face. The patient did not have a known disease. Before admission, the patient had been administered methylprednisolone 40 mg intravenously per day for 16 days and favipiravir 1200 mg oral daily dose for 10 days for COVID-19 pneumonia at another hospital.

Head and neck examination revealed ophthalmoplegia and chemosis in the left eye (Figures 1 and 2) and hypoesthesia in the site under the left orbit. Endoscopic nasal examination revealed a black eschar tissue on the left inferior turbinate and the middle meatus (Figure 3). Ophthalmoplegia and a decrease of 70% in visual acuity in the left eye were documented by the ophthalmologist. The serum glucose level (SGL) was 380 mg/dL, hemoglobin A1c was 10.6%, C-reactive protein was 178.84 mg/L, and erythrocyte sedimentation rate was 39 mm/h. Computed

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Figure 1. The left orbital edema and the paralyzed upper eyelid.

tomography revealed an increased density in the left ethmoid and maxillary sinus, as well as retrobulbar heterogeneity in the left orbit, and magnetic resonance imaging (MRI) revealed signal heterogeneity in the left retrobulbar area.

Liposomal amphotericin B was promptly administered at a dose of 5 mg/kg after the Infectious Diseases Department consultation with a preliminary diagnosis of mucormycosis. Subsequently, urgent endoscopic medial maxillectomy and orbital decompression were performed under general anesthesia. Aggressive debridement was applied, and necrotic tissues were removed until the bleeding mucosa was seen. The surgical samples were



Figure 2. The view of the severe chemosis and ophthalmoplegia in the left eye. The dilated and fixed left pupil and the fixed left eye at center while the right eye looks outward.

Main Points

- Corticosteroids should be carefully used for cytokine storm in coronavirus disease-2019.
- Hyperglycemia, ophthalmological signs, and the side effects of corticosteroids may be overlooked due to severe coronavirus disease-2019 symptoms.
- Mucormycosis should be kept in mind in the setting of hyperglycemia, corticosteroid use, and coronavirus disease-2019 treatment.

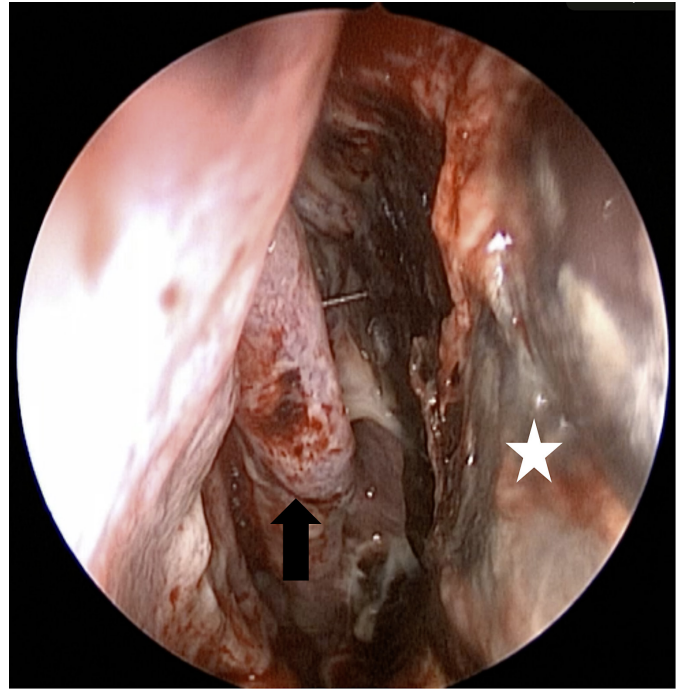


Figure 3. Endoscopic view of the nasal cavity. Black arrow: the left middle turbinate, white asterisk: a black eschar on the left inferior turbinate and the middle meatus.

sent for tissue culture and histopathological examination. The patient was closely followed up regarding the regulation of SGL, hypotassemia, renal functions, and the clinical course of the disease. Histopathological examination revealed non-septate hyphae within the tissues and the blood vessels. Fungal growth was not observed in the tissue cultures. Orbital exenteration was performed 13 days after the admission due to the total visual loss during the follow-up and signs of the retrobulbar infection in the control orbital MRI. Enoxaparine sodium was applied subcutaneously at a dose of 4000 IU twice a day since MRI also revealed a contrast enhancement in the left cavernous sinus. The patient has been alive during the 2 months follow-up period and no complications have been observed. Written informed consent was obtained from the patient.

Discussion

Mucormycosis results from the inhalation of fungi of the family called Mucoraceae, members of which include *Absidia*, *Rhizopus*, and *Mucor*. Fungal reproduction and tissue invasion are mostly facilitated by hyperglycemic and acidotic media, prolonged CS use, hematological malignancies, chemotherapy, solid organ, or bone marrow transplantation.¹ The fungal organism colonizes on nasal mucosa and can invade the surrounding tissues and the blood vessels. Thrombus formation within the blood vessels can cause ischemia and infarction. Mucormycosis can affect the nasal cavity, the paranasal sinuses, the palate, the face skin, and the brain.³ Symptoms may include fever, nasal obstruction, facial pain, visual loss, diplopia, and an altered mental status. The diagnosis is made by the medical history, the clinical manifestations, imaging methods, and culture or histopathological examination. Mucormycosis exhibits a 40-80% mortality rate; thus, early diagnosis and intervention are essential for the patients' survival.³ Treatment necessitates

the reversal of the underlying disease, early amphotericin B administration, and aggressive surgical debridement.

Normal human SGL inhibits the mucor growth while high SGL promotes mucor reproduction. The ketone reductase enzyme produced by the fungi also enables it to live in the setting of ketoacidosis. Corticosteroids can suppress the immune system and cause hyperglycemia. Consequently, diabetic ketoacidosis and CS use can provide a suitable medium for mucormycosis.⁴ If the patient has the afore-mentioned predisposing factors with the symptoms of nasal obstruction, fever, facial pain, headache, facial swelling, impaired vision, and ophthalmoplegia, the physician should take into consideration mucormycosis and should promptly administer treatment.^{3,5}

The lung cells infected by COVID-19 may produce cytokines such as TNF- α , IL-1, and IL-6. These cytokines may cause cytokine storm causing vascular inflammation, disseminated intravascular coagulation, hypotension/shock, acute respiratory distress syndrome, and death. Corticosteroid may decrease the production of IL-1, IL-2, IL-6, IL-8, IFN- γ and TNF- α and prevent the cytokine-related severe immune response.⁶ On the other hand, CS may lead to immunosuppression and hyperglycemia with reduction in insulin sensitivity.⁷ Hyperglycemia with immunosuppression depending on CS may cause an increased risk for infections.⁸ Thus, care should be taken with regard to mucormycosis depending on CS use for COVID-19.^{4,9,10}

Endoscopic debridement can be sufficient for disease limited to the nasal cavity or the paranasal sinuses, but open radical approaches including orbital exenteration, maxillectomy, removal of the palate or facial resection are needed for the extensive diseases. Additionally, intracranial spread of mucormycosis is associated with a poor prognosis and intracranial spread of mucormycosis can occur through both the optic canal and the superior orbital fissure.¹¹ Early surgical intervention can help prevent the intracranial spread. Thus, early orbital exenteration can increase the overall survival if the orbit is affected by the disease. A few reports in the English literature have demonstrated rhino-orbital mucormycosis with high mortality rates associated with COVID-19.^{4,5,9,12,13}

In conclusion, mucormycosis is still very rare and endemic in COVID-19 pandemic. The rationale of the use of immunosuppressants such as CS is the inhibition of the cytokine storm during the follow-up of COVID-19. However, the physician should keep in mind that indiscriminate administration of these medications may cause hazardous complications such as invasive rhino-orbital fungal infections that may result in orbital exenteration and death.

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

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References

1. Gen R, Horasan EŞ, Vaysoğlu Y, Arpacı RB, Ersöz G, Özcan C. Rhino-Orbito-Cerebral mucormycosis in patients with diabetic ketoacidosis. *J Craniofac Surg.* 2013;24(2):e144-e147. [\[CrossRef\]](#)
2. Singh AK, Majumdar S, Singh R, Misra A. Role of corticosteroid in the management of COVID-19: a systemic review and a Clinician's perspective. *Diabetes Metab Syndr.* 2020;14(5):971-978. [\[CrossRef\]](#)
3. Süslü AE, Öğretmenoğlu O, Süslü N, Yücel OT, Önerci TM. Acute invasive fungal rhinosinusitis: our experience with 19 patients. *Eur Arch Otorhinolaryngol.* 2009;266(1):77-82. [\[CrossRef\]](#)
4. Mekonnen ZK, Ashraf DC, Jankowski T, et al. Acute invasive rhino-orbital mucormycosis in a patient with COVID-19-associated acute respiratory distress syndrome. *Ophthal Plast Reconstr Surg.* 2021;37(2):e40-e80. [\[CrossRef\]](#)
5. Baskar HC, Chandran A, Reddy CS, Singh S. Rhino-orbital mucormycosis in a COVID-19 patient. *BMJ Case Rep.* 2021;14(6):e244232. [\[CrossRef\]](#)
6. Frieri M. Corticosteroid effects on cytokines and chemokines. *Allergy Asthma Proc.* 1999;20(3):147-159. [\[CrossRef\]](#)
7. Clore JN, Thurby-Hay L. Glucocorticoid-induced hyperglycemia. *Endocr Pract.* 2009;15(5):469-474. [\[CrossRef\]](#)
8. Buchman AL. Side effects of corticosteroid therapy. *J Clin Gastroenterol.* 2001;33(4):289-294. [\[CrossRef\]](#)
9. Alekseyev K, Didenko L, Chaudhry B. Rhinocerebral mucormycosis and COVID-19 pneumonia. *J Med Cases.* 2021;12(3):85-89. [\[CrossRef\]](#)
10. Nehara HR, Puri I, Singhal V, Ith S, Bishnoi BR, Sirohi P. Rhinocerebral mucormycosis in COVID-19 patient with diabetes a deadly trio: Case series from the north-western part of India. *Indian J Med Microbiol.* 2021;39(3):380-383.
11. Arndt S, Aschendorff A, Echternach M, Daemmrich TD, Maier W. Rhino-orbital-cerebral mucormycosis and aspergillosis: differential diagnosis and treatment. *Eur Arch Otorhinolaryngol.* 2009;266(1):71-76. [\[CrossRef\]](#)
12. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. *Cureus.* 2020;12(9):e10726. [\[CrossRef\]](#)
13. Werthman-Ehrenreich A. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. *Am J Emerg Med.* 2021;42:264.e5-264.e8. [\[CrossRef\]](#)