Rhino-Orbital Mucormycosis in a COVID-19 Patient: A Dreadful Challenge

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a pandemic disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2). COVID-19 infections may be associated with a wide range of bacterial and fungal co-infections. Recent studies are reporting invasive fungal infection associated with severe COVID-19. Herein, we report a case of COVID-19 rhino-orbital mucormycosis infection caused by Rhizopus sps in a 32 year old diabetic patient who was successfully managed with early aggressive debridement of infected tissue endoscopically with extended ethmoidectomy by modified Denker's approach along with orbital decompression and antifungal therapy with Liposomal Amphotericin B and Posaconazole. Serial diagnostic nasal endoscopy showed no evidence of progression of the infection. The patient was discharged on 21st day of hospitalization still on oral Posaconazole for a total of 3 months.

KEY WORDS

Amphotericin B, Covid-19, Mucormycosis, Surgical debridement

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a pandemic by the World health organization in March 2020. Rhino-orbital mucormycosis is an acute fulminant fungal infection caused by angioinvasive fungi of the family mucoraceae occurring mostly in immunocompromised hosts. However, in COVID-19 patients, the use of immunomodulatory drugs, concurrent use of glucocorticoid therapy and presence of comorbid conditions like diabetes mellitus predisposes to opportunistic fungal infection during the course of illness.[1]

The primary site of inoculation is the nose and paranasal sinuses but it can proliferate and spread to orbit and brain by direct route or through hematogenous spread causing life threatening rhino-orbital and rhino-cerebral mucormycosis.[2] Prompt management is critical in reducing mortality and morbidity.[3] The prognosis of mucormycosis is poor despite early aggressive combined surgical and medical therapy. We report the case of patient with COVID-19, who during the course of treatment, developed rhino-orbital mucormycosis.

CASE REPORT

A 32 year old male presented to Dhulikhel Hospital, Kathmandu University Hospital, Emergency Department with complains of left sided headache since five days, which was sudden in onset, insidious, dull aching, gradually progressive in nature. He also gave history of left retro orbital pain with protrusion of left eyeball which was associated with sudden blurring of vision since five days. There was occasional history of passage of blood mixed discharge from the left side of nose associated with nasal blockage on the same side. He was tested positive for COVID-19 by real-time PCR (nasal and oropharyngeal swab) 17 days back prior to presentation to our hospital and was hospitalized for 6 days in one of the local hospitals. The patient was also not vaccinated against COVID-19.

On clinical examination, the patient was afebrile on presentation. Pulse was 120 beats per minute, blood pressure was 110/70 mmHg and oxygen saturation was 91% in ambient air. Systemic examination was unremarkable, and there was no clinical evidence of diabetic ketoacidosis.

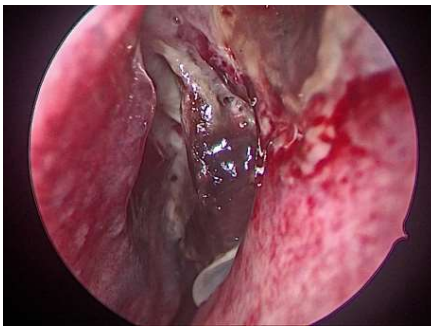

Figure 1. Diagnostic nasal endoscopy showing black turbinate and sloughing of nasal mucosa

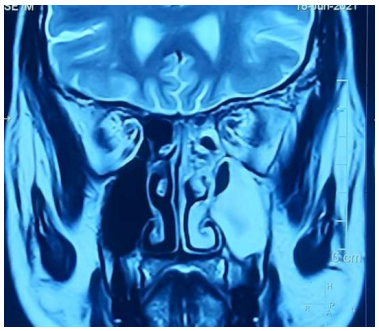

Figure 2. Coronal Computed tomography scan of the nose and paranasal sinuses with brain showed hyperdense content in left sphenoid, ethmoidal and maxillary sinuses without obvious bony erosion or remodelling indicating sinusitis with inspissated collection possilbly due to fungal rhinosinusitis

Figure 3. Wet mount showing nonseptate hyphae suggestive of mucormycosis

On examination of nose and paranasal sinuses, there was deviation of septum to left with nasal secretions and crusting (fig. 1). Maxillary sinus was tender on left side. His opthalmological findings in the left eye showed ptosis. Visual acuity was limited to finger counting at 3 meters and extraocular movements were restricted. All the findings were normal in the right eye. An urgent Computed tomography scan of the nose and paranasal sinuses with brain showed hyperdense content in left sphenoid, ethmoidal and maxillary sinuses without obvious bony erosion or remodelling indicating sinusitis with inspissated collection possibly due to fungal rhinosinusitis. Mild thickening and hyperdensity of left optic nerve with minimal left proptosis was also noted (fig. 2). MRI Brain, paranasal sinuses and optic nerve was promptly done which revealed altered signal intensity with at sphenoid, left ethmoid, and maxillary sinuses with few air pockets and enhancement of mucosa. Thickening of medial and inferior rectus muscle with enhancement on left side was also noted along with mild intraconal fat strading with mildly bulky left optic nerve.

Prompt reversal of diabetic ketosis was done with insulin infusion. Antifungal therapy with Liposomal Amphotericin B was reinforced at a dose of 5 mg/kg/day for a total of 18 days. Early aggressive debridement of infected tissue along was done endoscopically with extended ethmoidectomy by modified Denker's approach along with orbital decompression on the left side and functional endoscopic sinus surgery was done on the right side on the second day of admisssion. Blackish unhealthy mass was noted in the posterior part of septum, posterior and medial wall of maxillary sinus in left and minimal growth in posterior ethmoidal sinus in right. Retroorbital Amphotericin B injection was given thrice. However, visual prognosis remained poor. Diagnostic nasal endoscopy was done on alternate day which showed only crusting with no any fungal debris. Nasal irrigation was done with Liposomal Amphotericin B for a total of four times during his admission period. Histopathological analysis of the biopsy sample from maxillary sinus showed fungal colonies of broad aseptate hyphae at an obtuse angle with periodic acid–Schiff stain, which was consistent with mucormycosis (fig. 3). Fungal culture of the sample obtained after sinus debridement also confirmed mucormycosis (Rhizopus species). However, serological fungal markers and fungal culture sensitivity were not tested. Patient was admitted for a total of 21 days. Oral Posaconazole 300 mg BD was added on the 19th day of hospitalization and dose was changed to OD on 20th day and continued for 3 months. After surgery, the patient was stabilized. Since resolution of symptoms and complete clinical and radiological recovery was noticed on the 21st day of admission, the patient was discharged from hospital. No clinical evidence of relapse was observed during the subsequent follow-up.

DISCUSSION

Mucormycosis is a severe but uncommon opportunistic systemic mycosis caused by a number of 'mucoraceous' moulds, most commonly Aspergillus fumigatus, Lichtheimia ramosa, Rhizomucor spp., Mucor spp and R. arrhizus .The fungi invade the blood vessels resulting in rapid vascular thrombosis leading to ischaemia and tissue necrosis, which is almost always fatal if left untreated. Definitive diagnosis is by culture, but histopathological confirmation is required as the fungi may be environmental contaminants.

Multiple predisposing factors such as diabetes mellitus, use of immunosuppressive therapy, neoplasias, chronic renal failure, hematopoietic stem cell transplantation (HSCT), trauma, burns, iron overload, antineoplastic agents, corticosteroid use, protein-calorie malnutrition, organ and bone marrow transplantation and AIDS form the etiology of mucormycosis.[3-5] Recently, higher levels of inflammatory cytokines observed among cases of severe COVID-19 infection has also been recognized as an important predisposing factor which potentiates the net state of immunosuppression predisposing the patient to opportunistic fungal infection during the course of illness.

The immune dysregulation associated with COVID-19, with reduced numbers of T lymphocytes, CD4+T, and CD8+T cells, may alter innate immunity.[6]

Previous studies have reported the highest occurrence of rhinorbital mucormycosis is in patients with uncontrolled diabetes mellitus.[7] Our patient also had recovered from COVID-19 was newly diagnosed diabetic with high level of glycosylated haemoglobin (HbA1C). Recent bodies of literature on mucormycosis in COVID-19 recovered patients have identified Amphotericin B as a drug of choice and suggest that a multimodal approach with aggressive surgical debridement, antifungal therapy, and reversal of underlying risk factors such as neutropenia and immunosuppression are found to have favourable outcomes.[8-19]

A successful outcome in this patient could probably be due to timely initiation of antifungal therapy with aggressive surgical debridement under good glycaemic control.

In patients with COVID-19 with comorbidities, it is important to have high index of suspicion for fungal co-infections. Simple tests like vision, pupil, ocular motility and sinus tenderness can be part of routine physical evaluation of a patient with COVID-19 hospitalised with comorbidities or those receiving systemic corticosteroids.[4]

Early diagnosis and treatment of mucormycosis that involve antifungal therapy and surgical debridement are necessary to reduce mortality and morbidity. Moreover use of immunosuppressants drugs in treatment of COVID-19 patients should be cautiously done and monitored thereafter.

REFERENCES

1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020 Feb 15;395(10223):507–13.
2. Gupta S, Goyal R, Kaore NM. Rhino-Orbital-Cerebral Mucormycosis: Battle with the Deadly Enemy. *Indian J Otolaryngol Head Neck Surg*. 2020 Mar;72(1):104–11.
3. Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. *Lancet Infect Dis*. 2019 Dec;19(12):e405–21.
4. Ferguson BJ. Mucormycosis of the nose and paranasal sinuses. *Otolaryngol Clin North Am.* 2000;33:349-65.
5. Andreani G, Fadda G, Gned D, Dragani M, Cavallo G, Monticone V, et al. Rhino-orbital-cerebral mucormycosis after allogeneic hematopoietic stem cell transplantation and isavuconazole therapeutic drug monitoring during intestinal graft versus host disease. *Mediterranean Journal of Hematology and Infectious Diseases*. 2019;11(1).:e2019061. Published 2019 Nov 1. doi:10.4084/MJHID.2019.061
6. Revannavar SM, Supriya PS, Samaga L, Vineeth V. COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world? *BMJ Case Reports*. 2021 Apr 1;14(4):e241663.
7. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clin Infect Dis.* 2005.
8. Prakash H, Ghosh AK, Rudramurthy SM, Singh P, Xess I, Savio J, et al. A prospective multicenter study on mucormycosis in India: epidemiology, diagnosis, and treatment. *Med Mycol*. 2019;57:395–402.
9. Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. *Lancet Infect Dis*. 2019;19:e405–21.
10. Sarkar S, Gokhale T, Choudhury S, Deb A. COVID-19 and orbital mucormycosis. *Indian J Ophthalmol.* 2021;69:1002–4. https://doi.org/10.4103/ijo.IJO_3763_20.
11. Sen M, Lahane S, Lahane TP, Parekh R, Honavar SG. Mucor in a viral land: a tale of two pathogens. *Indian J Ophthalmol.* 2021;69:244–52. https://doi.org/10.4103/ijo.IJO_3774_20.
12. Sharma S, Grover M, Bhargava S, Samdani S, Kataria T. Post coronavirus disease mucormycosis: a deadly addition to the pandemic spectrum. *J Laryngol Otol.* 2021.
13. Maini A, Tomar G, Khanna D, Kini Y, Mehta H, Bhagyasree V. Sino-orbital mucormycosis in a COVID-19 patient: a case report. *Int J Surg Case Rep*. 2021.
14. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. *Cureus.* 2020.
15. Rao R, Shetty AP, Nagesh CP. Orbital infarction syndrome secondary to rhino-orbital mucormycosis in a case of COVID-19: clinico-radiological features. *Indian J Ophthalmol*. 2021;69:1627–30.
16. Ravani SA, Agrawal GA, Leuva PA, Modi PH, Amin KD. Rise of the phoenix: Mucormycosis in COVID-19 times. *Indian J Ophthalmol*. 2021;69:1563–8.
17. Revannavar SM, Supriya P, Samaga L, Vineeth K. COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world? *BMJ Case Rep*. 2021
18. Saldanha M, Reddy R, Vincent MJ. Title of the article: paranasal mucormycosis in COVID-19 patient. *Indian J Otolaryngol Head Neck Surg.* 2021.
19. Rizk SS, Kraus DH, Gerresheim G, Mudan S. Aggressive combination treatment for invasive fungal sinusitis in immunocompromised patients. *Ear, Nose and Throat Journal*. 2000 Apr;79(4):278-85.