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ORIGINAL ARTICLE

ACUTE ISCHAEMIC STROKE ASSOCIATED SECONDARY INFECTION WITH RHINO-ORBITAL CEREBRAL MUCORMYCOSIS ASSOCIATED WITH COVID-19 WITH BETA THALASSAEMIA TRAIT

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ABSTRACT

Coronavirus disease 2019 (COVID-19) 1st emerged in Wuhan, China in December 2019, and since then the frequency of bacterial and fungal coinfections has been continuously rising. While invasive pulmonary aspergillosis is increasingly being recognized in association with COVID-19, there is limited information with regards to COVID-19 associated mucormycosis. During the current pandemic of COVID-19, a myriad of manifestations and complications has emerged and are being reported on. We are discovering patients with COVID-19 are at increased risk of acute cardiac injury, arrythmias, thromboembolic complications (pulmonary embolism and acute stroke), and secondary infection to name a few. In this article we describe a novel case of COVID-19 in a who presented for altered mental status and proptosis. She was ultimately diagnosed with mucormycosis and orbital compartment syndrome, in addition to COVID-19. Early identification of these high morbidity conditions is key to allow for optimal treatment and improved outcomes.due to facial swelling and numbness,and a diagnosis of COVID-19 associated rhinosinusitis mucormycosis due to Rhizopusoryzae was conrmed with PCR and DNA sequencing. This report aims to address the importance of short-term follow-up in COVID-19 patients who have received systemic corticosteroids, particularly those with predisposing conditions, as early detection and prompt, aggressive treatment is essential for the management of invasive fungal infections.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a new disease entity caused by a novel coronavirus (SARS-CoV-2) first documented in China in December 2019 and subsequently causing a worldwide pandemic. While the pathophysiology of the virus is still under investigation, new symptomatic manifestations and complications of the disease continue to be identified and described in medical literature. Mucormycosis and orbital compartment syndrome are rare, time sensitive conditions that must be recognized and treated promptly to avoid mortality and morbidity. Herein I present a case of rhino-orbital-cerebral mucormycosis in a patient who presented to the Emergency Department with altered mental status, proptosis, and COVID-19 infection. Emerging evidence suggests that patients infected with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) may develop bacterial and fungal secondary infections [1]. While invasive pulmonary aspergillosis (IPA) is increasingly being recognized in association with coronavirus disease 2019 (COVID19), especially in critically ill patients hospitalized in the intensive care unit, [2] there are only a few cases of COVID-19 associated mucormycosis (CAM) available in the literature [3]. Mucormycosis is a rare, opportunistic, highly fatal fungal infection that typically occurs in individuals with underlying compromising conditions, such as diabetes mellitus, corticosteroid use, hematologic malignancies, neutropenia, solid organ/allogeneic stem cell transplant, primary immunodeciency, and treatment with immunosuppressants. Nevertheless, such infections can be seen in apparently immunocompetent patients on extremely rare occasions [4].

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Rhino-orbito-cerebral mucormycosis is considered as the most common manifestation of mucormycosis that is thought to be acquired via the inhalation of fungal spores into the paranasal sinuses. Here, we describe a patient with uncontrolled diabetes who received dexamethasone and remdesevir for COVID-19 treatment, but was readmitted after discharge with a diagnosis of rhinocerebralmucormycosis.

Department	Neurology
Patient Name	MD. SHAHJAHAN
Patient ID	1000516703
Age	65 years
Gender	Male
Bed	555-H

Date of Admission:	17.04.2021 at 4.00 PM	Date of Discharge:	24.04.2021 at 11.30 AM	Brief History:

Md. Shahjahan, a 65-year-old diabetic, normotensive gentleman was admitted to internal medicine department on 17.04.2021 as a case of COVID-19 infection (RT PCR positive on 27.03.21) with generalized weakness associated with slurring of speech & swelling of right eye for 7 days. Next day, on 18.4.2021, patient was taken over by Neuromedicine as repeat COVID-19 RT PCR came out negative & CT brain (done outside) findings showed acute infarct in the right cerebellum. On MRI of brain with MRA and MRV on 19.04.21 showed acute infarct in cerebellum including vermis & brain stem on the right side with inflammatory change involving right frontal, ethmoidal, maxillary & sphenoidal sinuses including supero-medial wall of the orbit & right cavernous sinus; dural enhancing of right temporal fossa with unremarkable MRA & MRV.On arrival to Neuromedicine department, his pulse: 88 beats/min; blood pressure-130/70 mmHg, SpO2: 97% in room air and Temp-980 F, RBS: 14.2 mmol/L. On neurological examination: patient was drowsy, however able to follow simple commands slowly, oriented. GCS: 15/15. Right pupil: 3 mm, non reacting to light, there was chemosis, protrusion of right eyeball with complete ophtalmoplegia; there was no perception of light on the right eye. Left eye examination was normal. Patient was moving all 4 limbs. Plantar response was bilaterally flexor. Cardiovascular system examination revealed normal 1st and 2nd heart sound. Respiratory system, abdominal system and other systemic examinations were unremarkable. Now he is being discharged on request andtransfer under care of Ophthalmologist for further management with following medications & advice.

Diagnosis

Acute ischaemic stroke (cerebellum including vermis and brain stem on the right side) Right eye proptosis with ophthalmoplegia-? Orbito rhinocerebral mucormycosiswithcavernous sinus syndrome ?Idiopathic orbital inflammatory disease (Right) Diabetes mellitus H/O COVID- 19 pneumonia Beta thalassaemia trait (known case)

Hospital Course

His hospital course was uneventful. He was managed with conservative approach. ENT consultation was sought and advised to do FESS for both therapeutic & diagnostic purposes. But family declined FESS procedure. Ophthalmology consultation sought who diagnosed the case as idiopathic orbital inflammatory disease & recommended topical dexamethasone & antibiotic eye drops along with high dose I/V steroid-Solupred 1 gm for 3 consecutive days followed by prednisolone for 14 days. As the family declined FESS, biopsy could not be taken for establishing the diagnosis of rhinocerebralmucormycosis. On denial of patient's son to go for any further intervention regarding right eye,advised to transfer patient under care of Ophthalmologist for further management. During his hospital stay, Infectious disease consultation was also sought. Professional Speech therapist assessed for swallowing reflex and found intolerance to liquid diet orally and advised to go for semisolid diet.

Investigations

All the investigation reports are supplied to the patient's attendant. Important investigations are:

CT scan of brain: Acute infarct in cerebellum including vermis and brain stem on the right side; inflammatory changes involving right side of para-nasal sinuses including supero-medial wall of the orbit. MRI of brain with MRA and MRV: Acute infarct in cerebellum including vermis and brain stem on the right side; inflammatory change involving right side of para-nasal sinuses including supero-medial wall of the orbit and cavernous sinus; dural enhancing of right temporal fossa; unremarkable MRA and MRV study of brain. HRCT scan of chest: Focal ground glass densities in all lobes of both lungs- sequelae of Covid- 19; focal emphysematous change in left upper lobe; minimal pericardial effusion.
Peripheral Blood film study:

RBCs: Anisochromic, anisocytic and microcytic with target cells
WBCs: Mature. Neutrophils are increased.
Platelets: Normal
Comment: suggestive of congenital hemolytic anaemia with neutrophilia.
APTT: APTT of sample 23.80 seconds; APTT of normal control : 28.50 seconds;
PT with INR: PT of sample 13.80 seconds; PT of normal control: 13.80 seconds; INR :1.00
Iron profile:
Serum Iron: 47 µg/dl
TIBC: 167 µg/dl
Ferritin: 1790 µg/L
Transferrin Saturation: 28.14 %
Serum Electrolytes : Sodium :133.0 mmol/l
Potassium : 4.57 mmol/l
Renal Function Test: Serum Creatinine : 0.70 mg/dl
e-GFR : > 60 ml/min/1.73 m²
S. Urea: 24 mg/dl
S. Uric Acid: 1.60 mg/dl
CBC: Hb 8.7 gm/dl , WBC 7.9 $x10^3$ /µl, Platelets 173 $x10^3$ /µl, ESR 57 mm in 1st Hour
CRP: 62.0 mg/L
D-Dimer: 1290 µg/L FEU
Ferritin: 1970 µg/L
Liver function test:
S. Bilirubin: 0.60 mg/dl
SGPT: 50 U/L
SGOT: 19 U/L
Alkaline Phosphatase: 65 U/L
Lipid Profile: Cholesterol: 133 mg/dl; HDL: 38 mg/dl; LDL: 92 mg/dl; TG: 69 mg/dl
HbA1c: 10.80 %
RT PCR for COVID 19 virus: negative.
hsTnI : 4.80 pg/ml
S. NT-pro BNP: 180 pg/ml
Urine R/E: Albumin nil, sugar 3+, Pus cell 1/HPF, RBC nil/HPF, Epithelial cell 1/HPF
Blood for C/S: Aerobic and anaerobic –no growth.
Urine for C/S: No growth (aerobic).

Status on Discharge

Please take medications regularly. Please continue limb physiotherapy regularly as demonstrated. Please check blood sugar routinely and keep records. Please change NG tube &catheter on 07.05.2021.

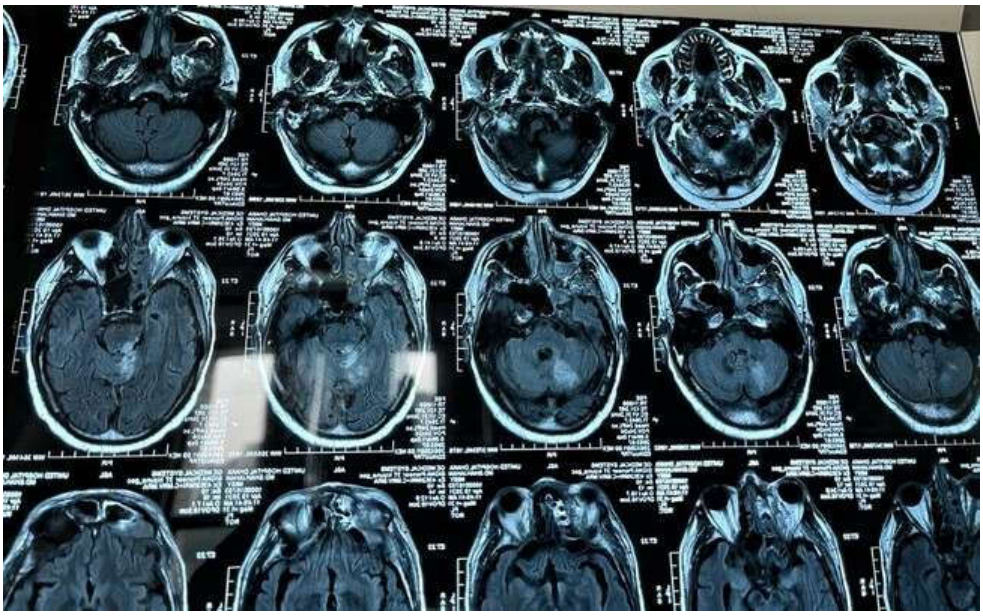
Diet

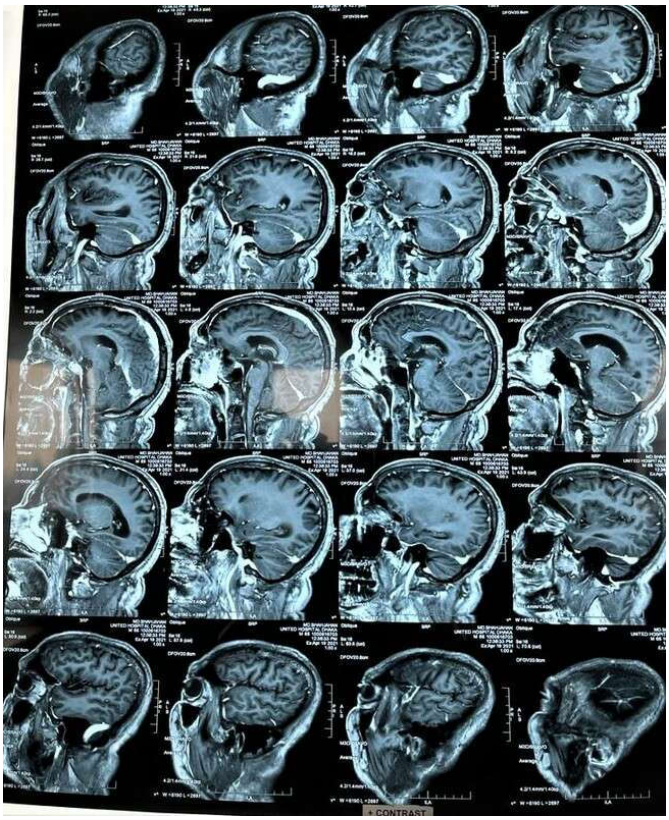
Diabetic-NG feeding: 150 ml every 2 hourly for total 10 feeds daily.

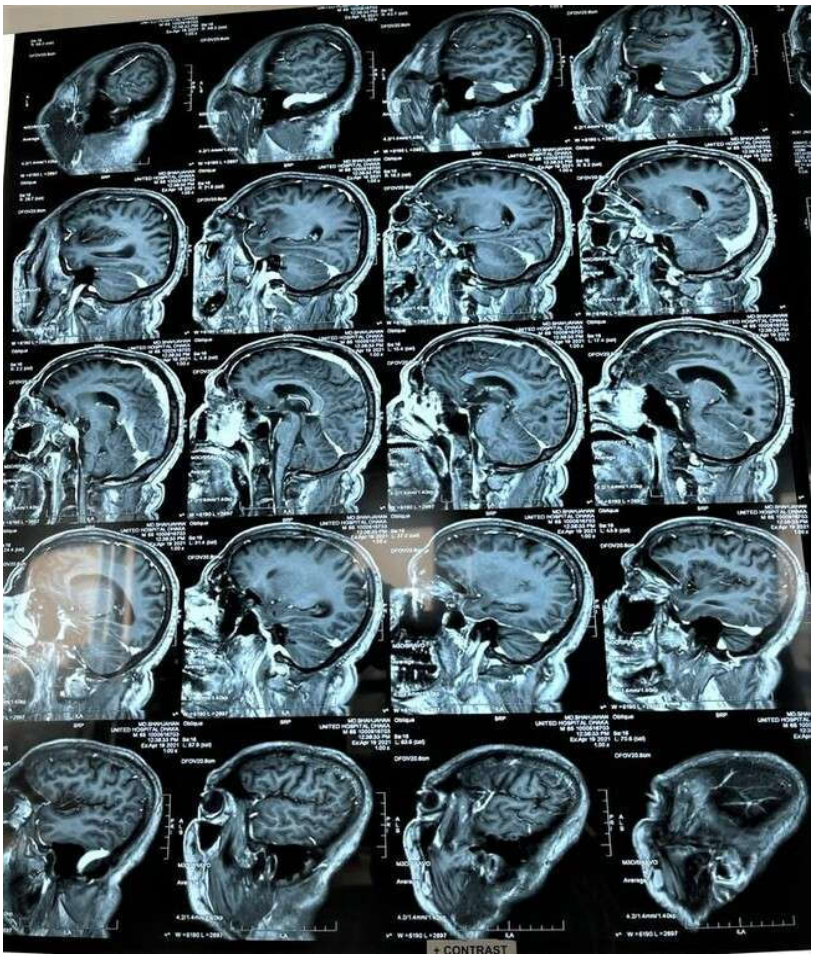
Ongoing medications

Name of Medicines	Doses	Special Instructions	Duration
Tab. Clopid AS	0+1+0	After meal	Continue
Tab. Rosuva 10 mg	0+0+1	Before meal	Continue
Optimox Eye Drop	1 drop in right eye; 2 hourly		Continue
Optimox Eye ointment	Apply in both eyes at bed time		Continue
Sonexa Eye Drop	1 drop in right eye; 4 hourly		Continue
Lubric Eye Drop	1 drop in both eyes; 2 hourly		Continue
Tab. Pantonix 20 mg	1+0+1	Before meal	1 month
Inj. Carbanem 1 gm	I/V; 8 hourly	Start from: 18.04.2021	Upto 27.04.2021
Inj. Levoxin 500 mg	I/V; once daily	Start from: 18.04.2021	Upto 27.04.2021
Inj. Mixtard 30/70 U -100	26+0+20, subcutaneously	15 minutes before meal	Continue
Tab. Pase 1 mg	0+0+1		If sleeplessness

Follow-up visit: Chief Consultant with prior appointment at OPD-2 after 1 month.



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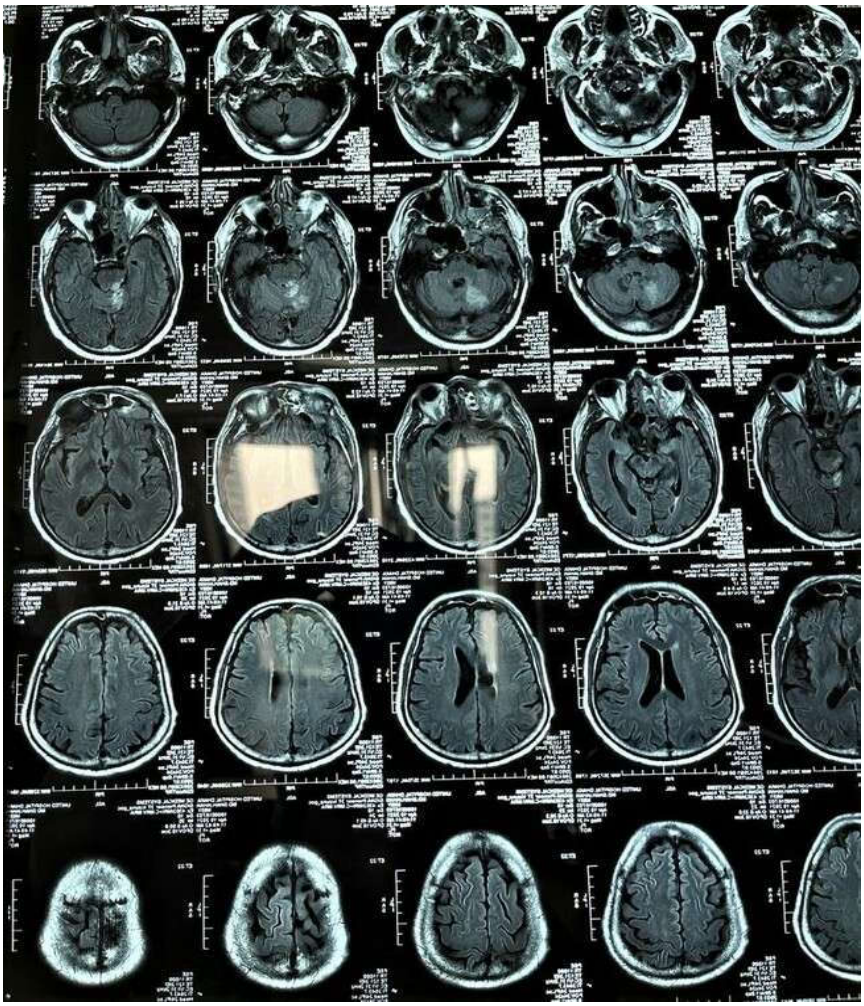

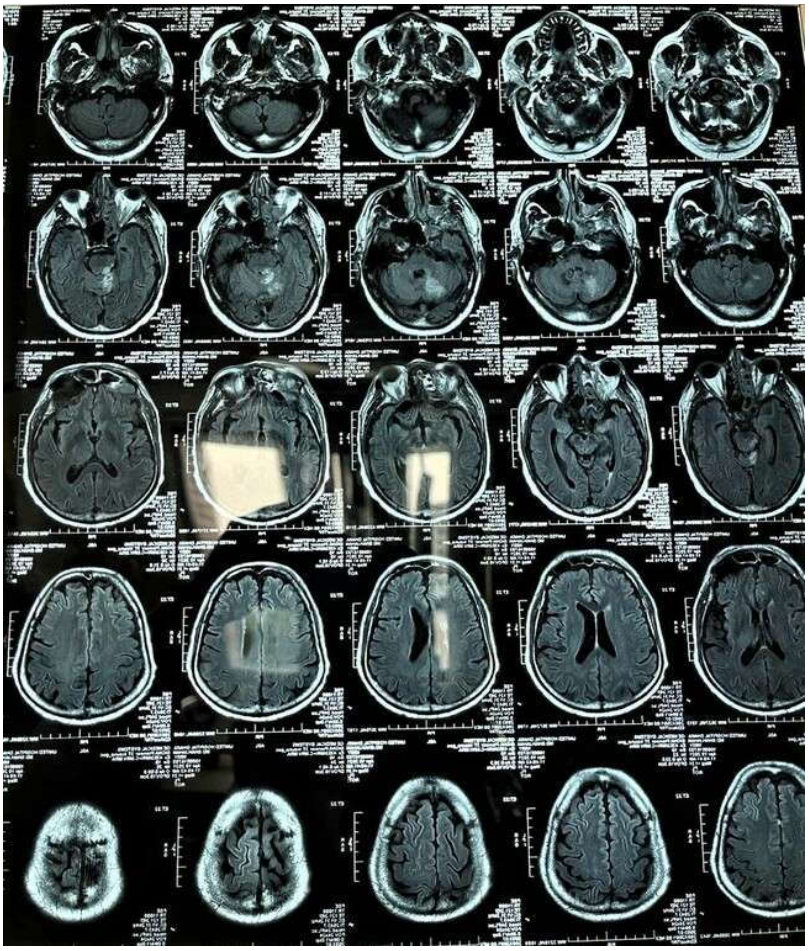

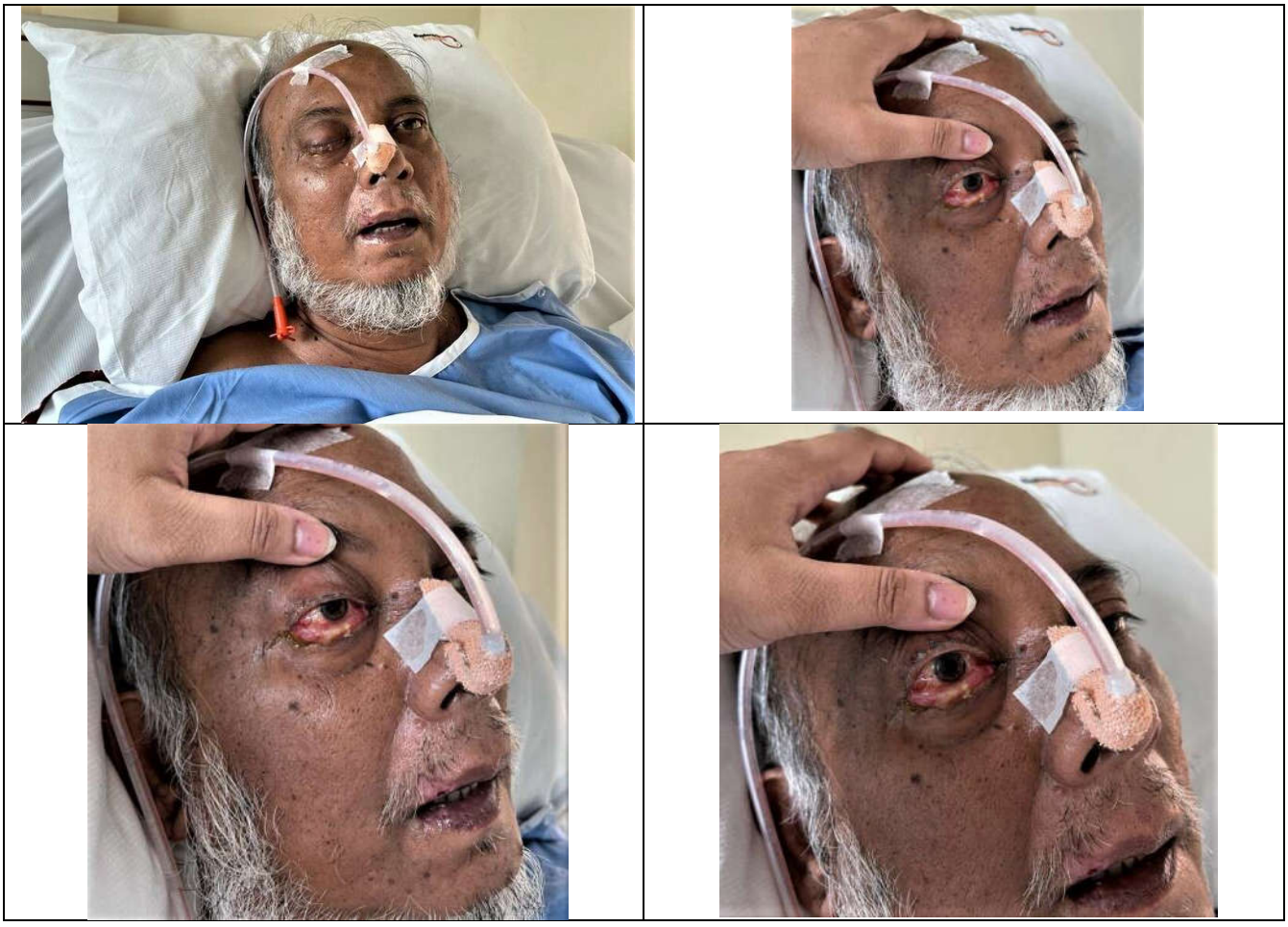

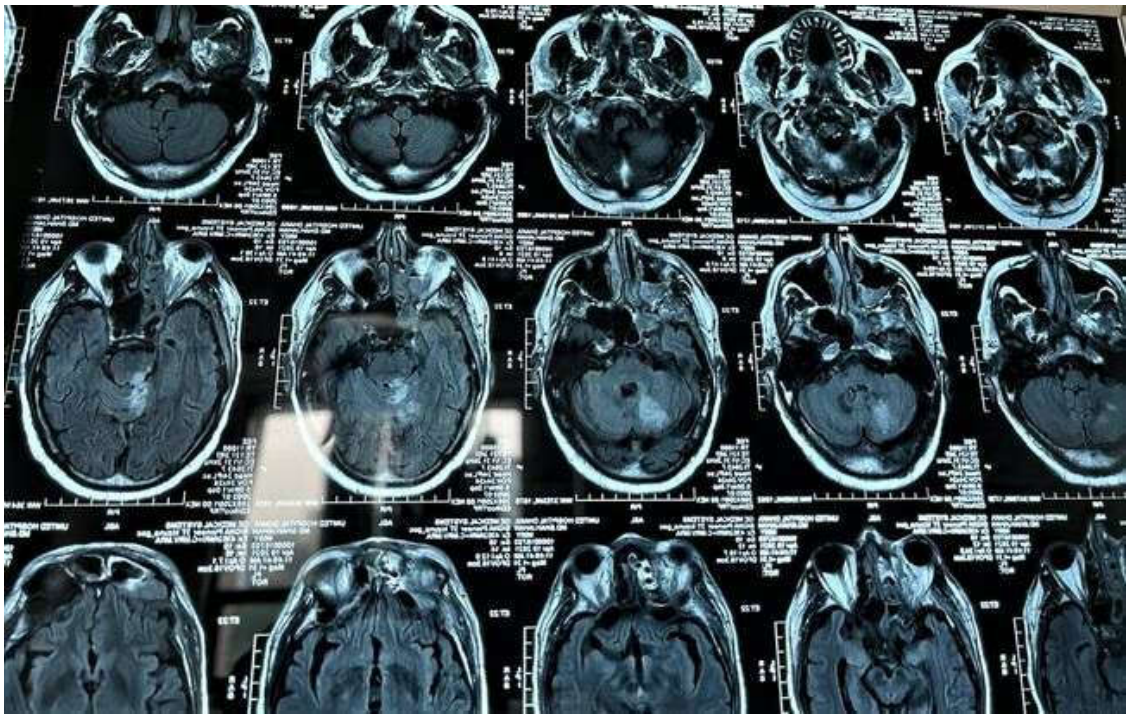

DISCUSSION

Fungal co-infection is increasingly identified as a cause of morbidity and mortality in COVID-19 patients. Aspergillosis and Candida have been reported as the main fungal pathogens for co-infection.1 Three prior cases of mucormycosis associated with COVID-19 have been reported.2–4 What remains unclear is the pathophysiology responsible.

It is well known that immunosuppression is a primary risk factor for the development of acute invasive fungal sinusitis. The use of dexamethasone to modulate immune-mediated organ damage is also well documented in the treatment of hospitalized patients with COVID-19.5 In addition to immunosuppression, corticosteroids have several other side effects, notably blunting the action of insulin and increasing blood glucose. This hyperglycemic effect is magnified in diabetic patients and can lead to ketoacidosis.

The enhanced ketoacidotic environment is particularly favorable for opportunistic mycotic organisms, as free serum iron is readily available.6 Thus, diabetic patients with COVID-19 receiving corticosteroids in particular require close monitoring of blood glucose as altogether these three factors increase susceptibility to opportunistic fungal infections. Careful co-management between critical care and endocrinology is essential to identify and reverse ketoacidosis when present. We postulate that additional shared risk factors for invasive fungal disease exist in COVID-19 patients including mechanical ventilation and Sars-CoV-2 induced immunosuppression, as suggested by the decreased absolute number of CD4+ and CD8 + T cells in COVID-19 patients.7 Moreover, two cases of Sars-Cov-2 positive immunocompetent adolescents were reported presenting with primary sinusitis, secondary orbital cellulitis, and intracranial angio-invasive spread.8 In both cases fungal cultures returned negative, suggesting that both true secondary invasive fungal disease and radiographic mimics can occur in COVID-19 patients.

Treatment of invasive fungal sinusitis includes systemic antifungals, surgical debridement of necrotic sinonasal tissue, and reversal of immunosuppression when possible.9 Debridement not only provides specimen for culture, but also reduces fungal load and potentially improves penetration of both antifungal therapy and the host immune response to adjacent, still viable tissues. However, endoscopic sinonasal surgery is an aerosol generating procedure with high-risk of Sars-CoV-2 exposure and spread when performed on positive patients. Suggested guidelines in the otolaryngology literature propose that endoscopic debridement of invasive fungal sinusitis constitutes “surgery that cannot be postponed” and should proceed with level 3 personal protective equipment (PAPR or N95 with surgical mask, gowns, double gloves, eye protection, and head cover including neck protection).10,11 However, in both our cases, debridement was deferred due to poor prognosis as a result of rapid intracranial spread at time of presentation to our institution. This raises into question the mortality/morbidity benefit of surgical debridement in cases of extensive rhino-orbital-cerebral involvement versus the risk of Sars-CoV-2 aerosolization. Altogether, we present these two cases to highlight the challenging diagnosis and management of rhino-orbital-cerebral mucormycosis associated with COVID-19 given shared risk factors and at times conflicting treatment. Clinicians should be keenly aware of ophthalmic signs of invasive fungal disease, particularly in this patient population, to allow prompt diagnosis and mitigation of spread where possible.

Disclosure statement: No conflicts of interest in regard to this report.

REFERENCES

Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest. 2020;130(5):2620–2629. doi:10.1172/JCI137244. PMID: 32217835. [Crossref], [PubMed], [Web of Science ®], [Google Scholar]

Couloigner V, Schmerber S, Nicollas R, Coste A, Barry B, Makeieff M, et al. COVID-19 and ENT surgery. Eur Ann Otorhinolaryngol Head Neck Dis. 2020;137(3):161–166. doi:10.1016/j.anorl.2020.04.012. PMID: 32362564. [Crossref], [PubMed], [Web of Science ®], [Google Scholar]

Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Lindell L, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021;384(8):693–704. doi:10.1056/NEJMoa2021436. PMID: 32678530. [Crossref], [PubMed], [Web of Science ®], [Google Scholar]

Kalin-Hajdu E, Hirabayashi KE, Vagefi MR, Kersten RC. Invasive fungal sinusitis: treatment of the orbit. CurrOpinOphthalmol. 2017;28(5):522–533. doi:10.1097/ICU.0000000000000394. PMID: 28505035. [Crossref], [PubMed], [Web of Science ®], [Google Scholar]

Lammers MJW, Lea J, Westerberg BD. Guidance for otolaryngology health care workers performing aerosol generating medical procedures during the COVID-19 pandemic. J Otolaryngol Head Neck Surg. 2020;49(1):36. doi:10.1186/s40463-020-00429-2. PMID: 32493489. [Crossref], [PubMed], [Web of Science ®], [Google Scholar]

Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. Cureus. 2020;12(9):e10726. doi:10.7759/cureus.10726. PMID: 33145132. [Crossref], [PubMed], [Web of Science ®], [Google Scholar]

Mekonnen ZK, Ashraf DC, Jankowski T, Grob SR, Vagefi MR, Kersten RC, et al. Acute invasive rhino-orbital mucormycosis in a patient with COVID-19-associated acute respiratory distress syndrome. Ophthalmic PlastReconstr Surg. 2020. doi:10.1097/IOP.0000000000001889. PMID: 33229953. [Crossref], [Google Scholar]

Petrikkos G, Tsioutis C. Recent advances in the pathogenesis of mucormycoses. ClinTher. 2018;40(6):894–902. doi:10.1016/j.clinthera.2018.03.009. PMID: 29631910. [Crossref], [PubMed], [Web of Science ®], [Google Scholar]

Song G, Liang G, Liu W. 2020. Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. Mycopathologia. 185(4):599–606. doi:10.1007/s11046-020-00462-9. PMID: 32737747. [Crossref], [PubMed], [Web of Science ®], [Google Scholar]

Turbin RE, Wawrzusin PJ, Sakla NM, Traba CM, Wong KG, Mirani N, et al. Orbital cellulitis, sinusitis and intracranial abnormalities in two adolescents with COVID-19. Orbit. 2020;39(4):305–310. doi:10.1080/01676830.2020.1768560. PMID: 32419568. [Taylor & Francis Online], [Google Scholar]

Werthman-Ehrenreich A. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. Am J Emerg Med. 2020;S0735-6757(20):30826. doi:10.1016/j.ajem.2020.09.032. PMID: 32972795. [Crossref], [Google Scholar]

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