CASE Series

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Story of The Black and White Devils- Mucormycosis and Aspergillosis: A Distinct Entity with Rising Clinical Presentation in COVID Era

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Abstract

Background: Background: Fungal rhino-sinusitis is a rare, rapidly progressing, life-threatening opportunistic infection, primarily affecting immunocompromised patients, such as those with diabetes and lung diseases, recently observed in post-COVID pneumonia cases. Clinically, it presents with partial neurological dysfunction and progressive necrosis secondary to blood vessel invasion and thrombosis, potentially involving the cranium, increasing morbidity and mortality. First-line treatment includes antifungal therapy, followed by surgical intervention.

Aim: To emphasize the significance of timely diagnosis and treatment strategies for Rhino-orbital-cerebral Mucormycosis and Aspergillosis.

Methods: Since the coronavirus outbreak in India, our hospital has treated thousands of patients, including nine confirmed cases of invasive fungal rhino-sinusitis from April to July 2021. We collected data from electronic records to ensure accuracy, with diagnoses based on clinical presentation, nasal endoscopy, imaging, KOH mount, fungal culture, and histopathology. Our team provided tailored medical and surgical management to meet each patient's needs, demonstrating our commitment to high-quality care during this challenging time.

Results: Five out of nine patients survived our treatment; the mortality rate was reported as 37.5%, with one patient lost to follow-up.

Conclusion: Timely surgical intervention, effective debridement, and appropriate antifungal therapy can significantly reduce mortality and morbidity in patients with Rhino-orbital-cerebral Mucormycosis and Aspergillosis.

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Introduction

The COVID-19 pandemic posed a significant health crisis globally, with symptoms ranging from mild to severe, including life-threatening pneumonia (1). Amid the pandemic in India, there was an alarming rise in systemic fungal infections, particularly invasive molds (2). Acute invasive fungal rhinosinusitis primarily affects immunocompromised individuals, such as those with uncontrolled diabetes or hematological malignancies (3). A surge in cases was noted during the second wave, linked to factors like corticosteroid use, non-sterile humidifiers, and the interplay of COVID-19 with pre-existing conditions (4). In healthy individuals, immune cells combat Mucorales infections. Still, in neutropenic patients or post-COVID individuals with lymphopenia, the risk of fungal infections rises due to impaired phagocytosis and inflammatory responses (5). Steroids, while reducing the need for invasive ventilation, can lead to neutrophilic leukocytosis and lymphopenia, increasing vulnerability to opportunistic infections (6). Overall, the incidence of fungal rhinosinusitis during COVID-19 was low, with a mean age of

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21-33 years, primarily affecting males from lower socio-economic backgrounds. In past outbreaks, such as SARS-CoV, fungal infections accounted for a significant percentage of mortality (7). Mucormycosis is a rare and aggressive fungal infection caused by Mucorales, primarily Rhizopus oryzae, characterized by black eschar formation. Aspergillosis is mainly caused by fungi such as Aspergillus, Bipolaris, Curvularia, and Alternaria, marked by thick, peanut butter-like mucus that may appear whitish-yellow or brown (3).

Case Series

Since the coronavirus outbreak in India, our hospital has cared for thousands of patients, including nine clinically confirmed invasive fungal rhino sinusitis cases from April to July 2021. Relevant data were retrospectively collected from electronic records. The diagnosis was based on clinical presentation, nasal endoscopy, imaging findings, positive KOH mount, fungal culture, and histopathology. Patients received combined medical and surgical management as needed. Institutional ethics and scientific committee approval were obtained, with patient consent for analysis and publication. The study received no external funding. Data was recorded on Microsoft Excel 2019 and analyzed via SPSS v21.0, with categorical variables presented in frequency and percentages.

Patients presented with symptoms including stuffy nose, blood-stained nasal discharge, facial pain, and headache. Additional sinus-related complaints involved dental pain, palatal discoloration, orbital pain, edema, restricted eye movements, and sometimes vision loss. Intracranial symptoms included altered sensorium and loss of consciousness, while cutaneous signs featured facial discoloration and numbness. Figures 1-3.3 illustrate the various clinical presentations.





1 2 3.1 3.2 3.3

Figure 1. 51-year-old female with left orbital swelling, pain, and black eschar; history of COVID pneumonia 2 months ago.

Figure 2. A 56-year-old male presents with confusion, right nasal cavity blood-stained discharge, facial weakness, headache, dental pain, and right orbital swelling; history of COVID-19 infection 6 months ago.

Figure 3.1-3.3. A 78-year-old female patient with left orbital swelling and chemosis progression over 48 hours of presentation to the hospital; facial numbness, brownish nasal discharge, restricted eye movement with loss of vision noted; history of COVID-19 pneumonia 2 weeks ago.

Management and Outcomes

Nasal endoscopy was performed on all patients with the mentioned complaints. Common findings included dark nasal crusting, mucopurulent discharge, destruction of turbinates and mucosa, widening of the nasal cavity, and palatal involvement. (Figure 4.1) Swab samples were collected for histopathological analysis using Grocott-Gomori methenamine silver (GMS) fungal stain and cultures in Sabouraud dextrose agar (SDA) to confirm the diagnosis. (Fig:5.1-.2) Contrast-enhanced MRI brain, orbit, and PNS with CT correlation were ordered for every patient for a better understanding of the extent of the disease and management (Figures 6.1-.2).

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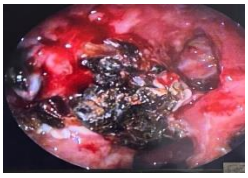
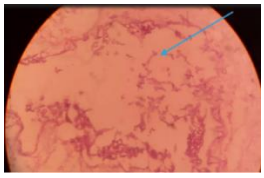
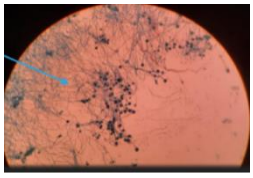
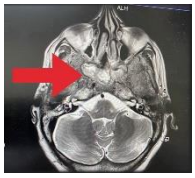
After confirming the diagnosis through endoscopy, imaging, and histopathology, all patients with invasive fungal rhino-sinusitis received immediate treatment. Liposomal amphotericin B (5-10 mg/kg/day) was administered for 3 weeks. Patients with mucormycosis were prescribed posaconazole (200 mg orally, four times daily for 10 weeks), while those with aspergillosis received voriconazole (200 mg orally, twice daily for 10 weeks), with close monitoring of renal, blood sugar, cardiac, and liver functions (8).

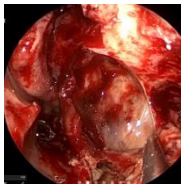
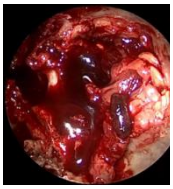
Emergency functional endoscopic sinus surgery with surgical debridement was performed after obtaining patient consent and consulting with neurosurgery, internal medicine, and ophthalmology departments. Intra-operative images documented the surgical approach. (Figures 7.1-7.3) A clinical-based endoscopy was performed every 48 hours post-surgery to clear slough and debris from the sinus cavity and assess tissue viability. Insensitive or pale tissues were debrided and sent for repeat fungal culture and HPE. (Figure 8.0) Lipid-based amphotericin B gel applied locally in the nasal cavity, and sinuses significantly improved nasal mucosa health and reduced disease recurrence. Patients were advised to perform nasal douching with Ringer's lactate three times daily. (Figure 9.0).



4.1 **5.1** **5.2** **6.1** **6.2**

Figure 4.1. Nasal endoscopy shows Black eschar formation in the right nasal cavity with mucosal destruction. **Figure 5.1.** Broad, aseptate, hyaline fungal hyphae with right angle branching suggest mucormycetes. **Fig: 5.2** Septate hyphae with acute angle branching suggestive of aspergillum. **Figure 6.1**. The coronal cut of the CT scan shows complete opacification of the left maxillary sinus with areas of hyperattenuation, which is suggestive of fungal concretions. **Figure 6.2**. Saggital cut a MRI scan showing fungal concretions in the bilateral posterior ethmoids and sphenoid sinus.


7.1 **7.2** **7.3** **8** **8** **9**

Figure 7.1-7.3. intra-op FESS with surgical debridement of fungal debris. **Figure 8.0**. pre-op and post-op nasal endoscopy findings of a single case indicating healthy mucosa post-op. **Figure 9.0.** post-op local application of amphotericin B ointment.

Results

A total of 9 cases were distributed as follows: 6 cases of mucormycosis and 3 cases of aspergillosis. Among the patients, there were seven males and two females. Notably, 8 out of the nine patients (89%) had a known history of type 2 diabetes mellitus, and 5 out of 9 patients had additional co-morbidities such as hypertension and hypothyroidism. All patients had a history of COVID-19. The severity of their COVID-19 illness, as determined by the CT severity score, revealed that two patients experienced mild disease, 6 had moderate disease, and 1 had severe disease. Five out of the nine patients received remdesivir, and all nine patients were treated with corticosteroids for COVID-19. Six patients underwent oxygen therapy, while information regarding drug and oxygen therapy was unavailable for one patient. All patients presented with nasal symptoms.

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Additionally, seven patients exhibited orbital symptoms, 4 had cutaneous symptoms, 2 reported oral complaints, and 1 had intracranial disease extension. Cranial nerve involvement was noted in 6 out of the nine patients with mucormycosis, with cranial nerves 5, 6, and 7 affected in 2 patients and the optic nerve in 1 patient.

In the cases of aspergillosis, cranial nerves 4, 6, and 7 were involved in 1 patient. During follow-up, out of the 6 cases of mucormycosis, three patients recovered, and one was lost to follow-up. Among the 3 cases of aspergillosis, two patients recovered. Mortality occurred in 2 cases of mucormycosis and 1 case of aspergillosis, resulting in an overall mortality rate of 37.5%. Table 1 represents patient characteristics, medical and surgical interventions, and outcomes.

Table 1. Patient characteristics, medical and surgical interventions, and outcomes.

Serial no.	1	2	3	4	5	6	7	8	9
Age (years)	38	77	73	51	37	43	56	78	56
Sex	Male	Male	Male	Female	Male	Male	Male	Female	Male
Comorbidities	DM2	DM2	DM2/HTN/ IHD	DM2/ Hypothyroid	NIL	DM2/CLD	CKD/DM 2	DM2/HTN	DM2
Severity	Mild	Moderate	Mild	Moderate	Severe	Moderate	Moderate	Moderate	Mild
Steroids	No	No	No	Yes	Yes	Yes	Yes	Yes	No
Remdesivir	No	Yes	No	Yes	Yes	Yes	Yes	-	No
O2 requirement	No	No	No	Yes	Yes	Yes	No	-	No
Cranial nerve involvement	IV,VI	II,V,VII	IV,VI	V,VII	VII	1V,VI	-	VII	IV,VI
Presentation	Rt Eye Pain, Chemosis	Rt Eye Chemosis, Loss of Vision	Epistaxis	Lt Side Facial Pain, Nose Block	Pain, Gum Bleed	Epistaxis, Nasal Crusting	Rt Eye Swelling	Headache, Facial Pain	Rt Eye Pain, Decreased Vision
HPE and fungal smear- Aseptate/ septate	Broad aseptate hyphae	Broad aseptate hyphae	Broad aseptate hyphae	Septate hyphae	Septate hyphae	Broad aseptate hyphae	Broad aseptate hyphae	Septate hyphae	Broad aseptate hyphae
Treatment	B/L FESS, Lamb	B/L FESS, Lamb, posaconazole	FESS, Lamb, posaconazole	FESS, Lamb, voriconazole	B/L FESS, Lamb, voriconazole	Caldwel luc, Lamb, posaconazole	B/L FESS, Lamb, posaconazole	B/L FESS, Lamb, voriconazole	FESS, Lamb, posaconazole
Radiological evidence	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Clinical outcome	Death	Recovered	Death	Recovered	Recovered	Recovered	Recovered	Death	Lost to follow up

Discussion

Fulminant invasive fungal rhinosinusitis is an acute, angio-invasive fungal infection affecting the paranasal sinuses and brain (9). This condition is considered an opportunistic infection, typically occurring in patients with compromised immune systems due to poorly controlled diabetes mellitus, underlying malignancies, neutropenia, or the use of immunosuppressive agents (10). Serial debridement often becomes necessary to control the infection (11,12).

The clinical presentation can vary widely. Most patients present with signs of advanced disease that have already spread beyond the paranasal sinuses, commonly involving the orbit and palate. Rarely are extensions seen intracranially (13). Recent evidence suggests that COVID-19 creates a pro-coagulable state, leading to increased thrombotic events. This state promotes the angioinvasion of Mucor species due to vessel thrombosis, resulting in

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disseminated infections (9). A study published by Song et al. investigated 99 patients with fungal infections post-COVID-19 in China and found that about 5% of these infections were caused by Aspergillus and a significant percentage by Mucor species (5). In our case series, 8 out of 9 patients had type 2 diabetes mellitus and were on insulin treatment. Similar case series by Nezafati et al. and Kolekar et al. reported that 90% and 80% of their patients had underlying diabetes, respectively (13,14). The severity of COVID-19, the use of oxygen therapy, and the potential sharing of humidifiers in hospital settings during treatment are important factors to consider when collecting patient histories and understanding their contribution to developing this disease (15).

The most commonly reported signs in the literature include blood-stained nasal discharge, facial swelling, palatal ulceration or necrosis, and black necrotic eschar in the nasal cavities. Ocular signs can consist of ophthalmoplegia, proptosis, loss of vision, and chemosis. Intracranial infection may occur through spread within the vasculature or due to invasion through the cribriform plate (16). Regarding patient demographics, previous case series, similar to our report, found the average age to be approximately 62 years (13,14). A concerning sign of cranial nerve palsy is a facial weakness with eye involvement in diabetic patients (17).

In our case series, we observed a similar pattern of presenting features; however, most patients presented with advanced disease that had already spread beyond the paranasal sinuses, primarily affecting the orbit and palate (6). Rare intracranial extensions were noted in one case, which caused left internal carotid artery thrombosis, and another case presented with a parapharyngeal space abscess (mucormycosis), confirmed by imaging and KOH mount analysis.

Conclusion

Due to immune dysregulation, COVID-19 can lead to higher rates of secondary infections, mainly fungal infections like mucormycosis and aspergillosis. These infections predominantly affect individuals with diabetes or compromised immune systems. Diagnosis typically involves histopathological analysis, nasal endoscopy, and CT imaging to evaluate disease severity. Although initial occurrences are rare, patients may already exhibit extensive disease with orbital or intracranial complications. Without early diagnosis and treatment, these infections can be fatal, especially when cerebral involvement is present. Our case series underscores the critical need for prompt identification and urgent management in high-risk groups. Mycologist Paul Stamets notes, "fungi are the interface organisms between life and death." Timely surgical intervention, effective debridement, and appropriate antifungal therapy can reduce mortality and morbidity significantly.

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Conflicts of Interest

The authors declare no conflicts of interest.

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Ethics

Institutional ethics committee and scientific committee approval was obtained from the Institute, and the study was carried out after patient consent was obtained for study and publication.

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Authors Contributions

Gautam Kumar Arora conceived work, acquired and analyzed data, drafted content, approved publication version, and agreed to accountability. Alok Kumar, Abhijit Kumar, and Deepali Singh analyzed and interpreted data, drafted content, approved the publication version, and agreed to accountability.

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References

1. Zhou F, Yu T, DuR, et al.: Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020,395:1054-62. 10.1016/S0140-6736(20)30566-3

2. MishraN,Mutya VSS, Thomas A, RaiG, ReddyB, MohananAA, et al. A case series of invasive mucormycosis in patients with COVID-19 infection. Int J Otorhinolaryngol Head Neck Surg 2021;7:867-70.

3. Scott brown's otorhinolaryngology head and neck surgery; vol1; ch96; page 1047-1057

4. Zeinab Mehrabi, Maryam Salimi, Kianoush Niknam, Farzaneh Mohammadi, Hesan Jelodari Mamaghani, Mohammad Reza Sasani, Mohammad Javad Ashraf, Amir hossein Salimi, Mohammad Hassan Zahed roozegar, Zohreh Erfani, "Sino orbital Mucormycosis Associated with Corticosteroid Therapy in COVID-19 Infection", Case Reports in Ophthalmological Medicine, vol. 2021, ArticleID9745701, 7 pages, 2021.

5. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. Mycopathologia. 2020;185: 599-26.

6. Singh Y, Ganesh V, Kumar S, et al. (July03,2021) Coronavirus Disease-Associated Mucormycosis from a Tertiary Care Hospital in India: A Case Series. Cureus 13(7):e16152. doi:10.7759/cureus.16152 Balai E, Mummadi S, Jolly K, et al. (November 29, 2020) Rhino cerebral Mucormycosis: A Ten-Year Single Centre Case Series. Cureus12(11):e11776. doi:10.7759/cureus.11776

7. Patel D J, Patel P G, Patel P P, Sapariya B, Parmar M B, Diwanji N S. Case series of mucormycosis occurring in patients of COVID-19. IntJ Res Med Sci 2021;9:1746-50.

8. Spellberg B, Walsh TJ, Kontoyiannis DP, Edwards J Jr, Ibrahim AS. Recent advances in the management of mucormycosis: from bench to bedside. Clin Infect Dis. 2009; 48(12):1743-1751. doi: 10.1086/599

9. Balai E, Mummadi S, Jolly K, et al. (November 29, 2020) RhinocerebralMucormycosis: A Ten-Year Single Centre Case Series.Cureus12(11):e11776. doi:10.7759/cureus.11776

10. Roden M M, Zaoutis T E, Buchanan W L, et al.: Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis. 2005, 41:634-53.10.1086/432579

11. Onyango J F, Kayima J K, Owen WO: Rhino cerebral mucormycosis: case report. EastAfrMedJ.2002,79:390-393.10.4314/eamj.v79i7.8845

12. Petrikkos G, Skiada A, Lortholary O, et al.: Epidemiology and clinical manifestations of mucormycosis. Clin Infect Dis. 2012,54:23-34.10.1093/cid/cir866

13. Nezafati S, Kazemi A, Asgari K,et al.: Rhino cerebral mucormycosis, risk factors and the type of oral manifestations in patients referred to a University Hospital in Tabriz, Iran 2007-2017. Mycoses. 2018,61:764-769.10.1111/myc.12802

14. Kolekar JS: Rhino cerebral mucormycosis: a retrospective study. IndianJOtolaryngolHeadNeckSurg.2015,67:93-96.10.1007/s12070-014-0804-5

15. Singh AK, Singh R, Joshi SR, MisraA. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and inIndia. DiabetesMetabSyndr.2021; 15(4):102146.doi:10.1016/j.dsx.2021.05.019

16. Sharma S, Grover M, Bhargava S, Samdani S, Kataria T. Post corona virus disease mucormycosis: a deadly addition to the pandemic spectrum. J LaryngolOtol. 2021; 1-6.

17. Sachdeva K. Rhino-oculo Cerebral Mucormycosis with Multiple Cranial Nerve Palsy in Diabetic Patient: Review of SixCases. Indian J Otolaryngol Head Neck Surg.2013; 65(4):375-379.doi:10.1007/s12070-013-0659-1