



PATHOLOGICAL AND RADIOLOGICAL ASPECT OF RHINO ORBITAL CEREBRAL-MUCORMYCOSIS IN POST COVID PATIENTS: A CASE SERIES

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Abstract

A strong correlation was observed between extent of radiological findings and severity of clinical symptoms. Early diagnosis and aggressive surgical debridement along with antifungal therapy were critical in improving patient outcomes. Severe infection may cause sepsis and if not taken care of well, may cause death. Rhino-orbital cerebral mucormycosis in post covid-19 patients presents distinct pathological and radiological features that require heightened clinical awareness for prompt diagnosis and management.

Categories: Pathology, Ophthalmology, Radiology

Keywords: Immunocompromised, ROCM- rhino-orbital cerebral mucormycosis, post-covid-19,MRI,CT

Introduction

Mucormycosis is caused by fungi belonging to mucorale order and the mucoraceae family. [1] Pathophysiology consist of inhalation of spore through the nose or mouth or even through skin lacerations. Inhalation of sporangiospore from the atmosphere is the most common route for rhino orbito cerebral infection. [2] Mucormycosis in post covid patients is attributed to different causes. It is a life threatening fungal infection in low immunity host. Tissue invasion by the hyphae of mucormycosis must be seen microscopically to establish the diagnosis, along with Periodic Acid Schiff (PAS) and Grocott Methenamine Silver (GMS) stain. If patient is not treated promptly and properly mortality rate can go upto 94%. [3] India bears the highest burden of mucormycosis in the world. [4] Rhino-orbito cerebral mucormycosis invade vessles, soft tissue, nerve, bone and cartilage. The fungus invades arterial walls causing thrombosis, which leads to ischaemia and tissue necrosis. [5] The Rhizopus Oryzae is most common type and responsible for nearly 60% of mucormycosis cases in human and accounts for 90% of the rhino-orbital cerebral (ROCM) form. Covid 19 infection leads to immune dysregulation via decreasing T lymphocyte CD4+ T cells and CD8+ T cells. The

infection can directly spread into the paranasal sinuses and then invade into orbital via nasolacrimal duct or via cribriform plate. [6] In diabetics, the fungus moves from nasal sinus to orbit and brain causing rhino-orbital cerebral mucormycosis. [6] The pathogen can transform into hyphae form in individuals with predisposing factors such as uncontrolled diabetes mellitus, malignancy, renal failure, organ transplantation, advanced rheumatologic disorders using immunosuppressive agents, AIDS, extensive burn, and chronic sinusitis.

Fresh tissue preparation using 20% potassium hydroxide shows broad hyaline hyphae with wide angle branching. Hematoxylin and Eosin, Grocott - Methanamine Silver and Periodic Acid Schiff stains are commonly used to visualize the fungus. Without early diagnosis and treatment, there may be rapid progression of the disease, with reported high mortality rates from intra-orbital and intracranial complications. Even with prompt diagnosis, treatment of underlying diseases, and aggressive medical and surgical intervention, the management is often not effective, leading to an extension of the infection and ultimately death. A complex interplay of factors that include diabetes mellitus, any previous respiratory pathology, immunosuppressive therapy, nosocomial infection sources and systemic immune alterations of Covid-19 infection itself may lead to secondary infections and are increasingly being recognised in view of their impact on morbidity and mortality. Histopathologic examinations disclose relatively broad non-septate hyphae with right angle branches, necrotizing granulomatous inflammation, and vasculitis together with the presence of mucor hyphae within the vascular wall and lumen. Critically ill patients, especially in intensive care units and those who required mechanical ventilation, or who had a longer duration of hospital stays, even as long as 50 days, were more likely to develop fungal co-infections. Older patients (>65 years) along with other morbidity and ARDS are at increased risk of death. [7] Early diagnosis and treatment are essential to prevent further end organ damage. [8]

Case Presentation

Case 1: 40 year old female covid RT-PCR negative admitted in ENT department with complains of right nasal blockage and nasal discharge since 1 week and mild facial edema, numbness and mild fever since 4 days.

Patient developed sudden right eye vision loss with redness of eyes with lid edema and retro orbital pain for one day. There was a past history of treatment for covid with dexamethasone and oxygen therapy for 15 days and was discharged with no covid complains. There is no history of diabetes mellitus. On examination there was facial edema with numbness including crusting in right nose with black eschar formation. There was proptosis and ptosis of right eye with restricted movement in all gaze. Pupil was fixed and mildly dilated. Contrast MRI show enhancement of bilateral ethmoid sinuses and bilateral infratemporal fossa (pterygoid muscle) and lesion extending towards right orbit.(Figure 1)

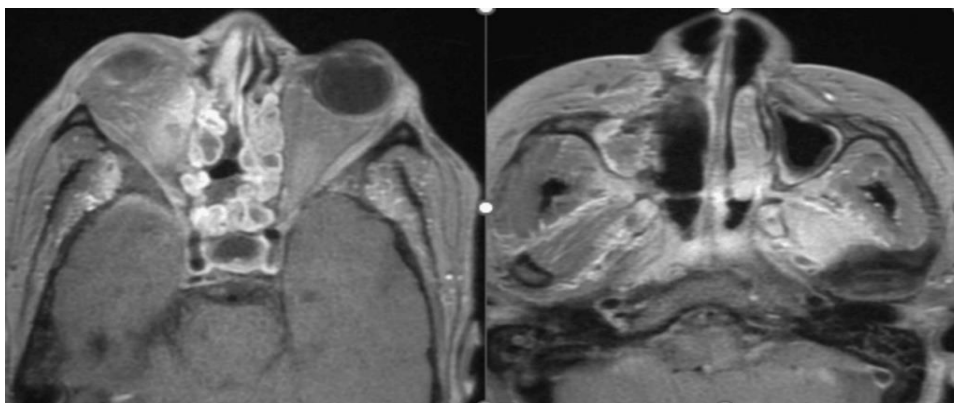


FIGURE 1. Contrast MRI show enhancement of bilateral ethmoid sinuses and bilateral infratemporal fossa (pterygoid muscle) and lesion also extends towards right orbit.

The histopathology section of pathology department received 3 separate containers -

Container 1:- labelled as brain tissue- received multiple grey white soft tissue pieces all together measuring 4cc.

Container 2:- labelled as nasal cavity- received multiple grey brown soft tissue pieces all together measuring 6cc.

Container 3:- labelled as right eye exenteration- received exenterated specimen of right eye with attached eye lid measuring 5x4x4 cm. cut surface unremarkable(Figure 2)



FIGURE 2: Received exenterated specimen of right eye with attached eye lid measuring 5x4x4 cm. cut surface is unremarkable.

On microscopic examination, extensive tissue necrosis noted with large non-septate fungal hyphae, having ribbon-like appearance, with budding and dichotomous branching.

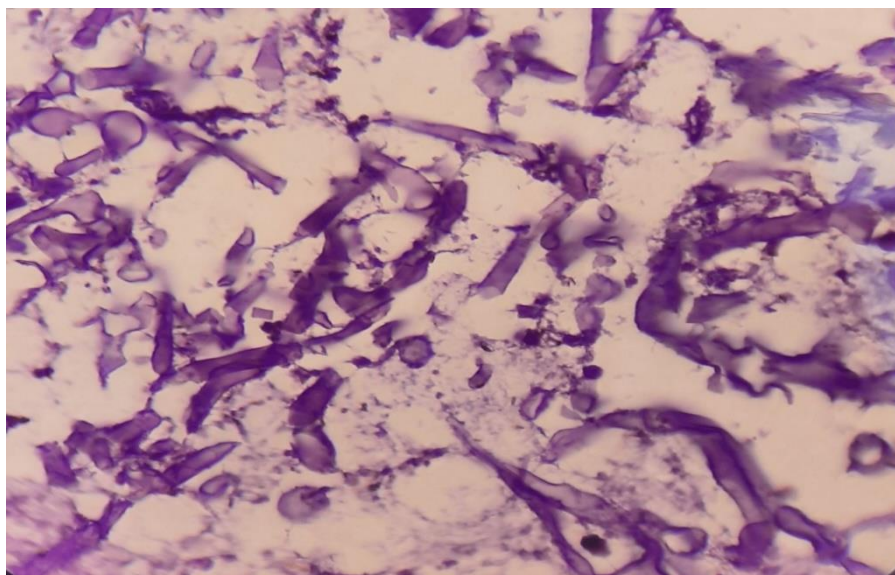


FIGURE 3: On microscopic examination ,figure shows extensive tissue necrosis noted with large non- septate fungal hyphae, having ribbon- like appearance, with budding and dichotomous branching seen.

Case 2: A 69 year old female patient covid RT-PCR negative admitted in ENT department with complains of headache, fever since ten days; trismus and diplopia since four days; sudden right eye vision loss with redness and lid edema along with severe headache and retro orbital pain since one day. There was a past history of treatment of covid with dexamethasone and oxygen therapy for 3 weeks .The patient was discharged with no covid complains. The patient have type 2 diabetes mellitus and was in renal failure. On examination there was facial edema. Proptosis and ptosis of right eye with restricted movement in all gaze and fixed pupil of right eye with moderate dilatation were also found. Contrast enhanced MRI showed moderate enhancement of wall of bilateral maxillary sinus, ethmoid sinus and lesion extends intracranially (intracranial abscess)(Figure 4).

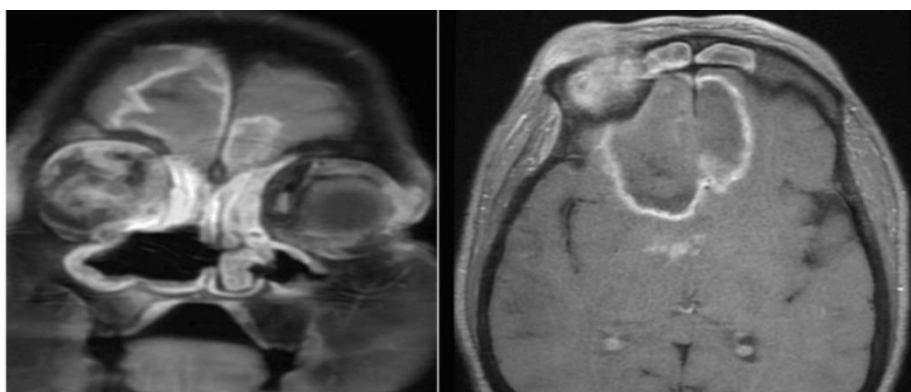


FIGURE 4: . Contrast enhanced MRI show moderate enhancement of wall of bilateral maxillary sinus, ethmoid sinus and lesion extends intracranially (intracranial abscess)

Surgery was done and dead and infected tissue removed and sent to pathology department. Histopathology of Hematoxylin and Eosin stained slide showed angioinvasion by fungal hyphae.(Figure 5). Angioinvasion highlighted by PAS stain and Grocott methanamine silver stain. (Figure 6 and 7)

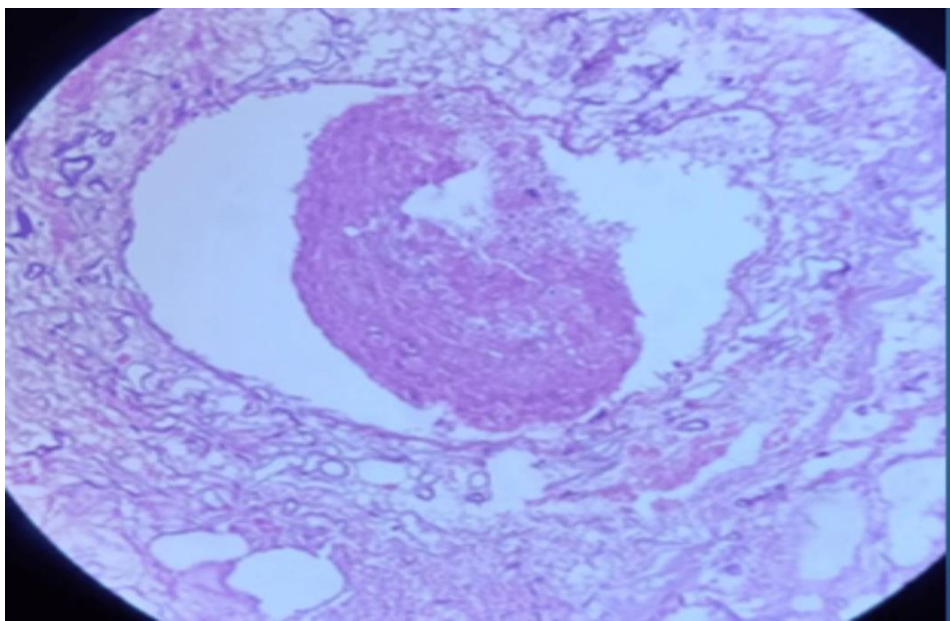


FIGURE 5. Histopathology of Hematoxylin and Eosin stained slideshows angioinvasion by fungal hyphae.

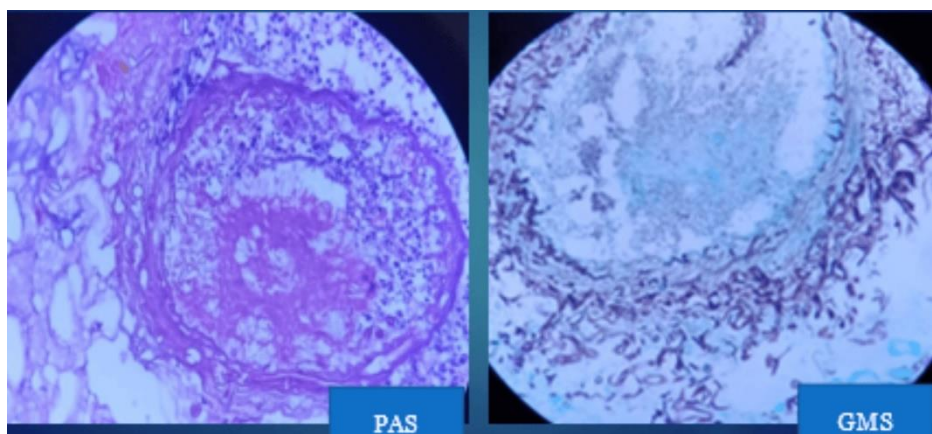


FIGURE 6. Angioinvasion highlighted by PAS stain and Grocott methanamine silver stain.

Case 3 : A 52 year old diabetic male patient covid RT-PCR negative admitted in ENT department with complains of facial swelling, fever and headache for 9 days; blurring of vision for 7 days and sudden loss of vision for one day. There was a past history of treatment of covid with dexamethasone and oxygen therapy for 1 months. The patient developed uncontrolled sugar level while on treatment but later on controlled by regular insulin therapy. MRI was done which showed cerebral infarct with sinusitis (Figure 7). Surgery was done and dead and infected tissue was removed and sent for histopathological examination.

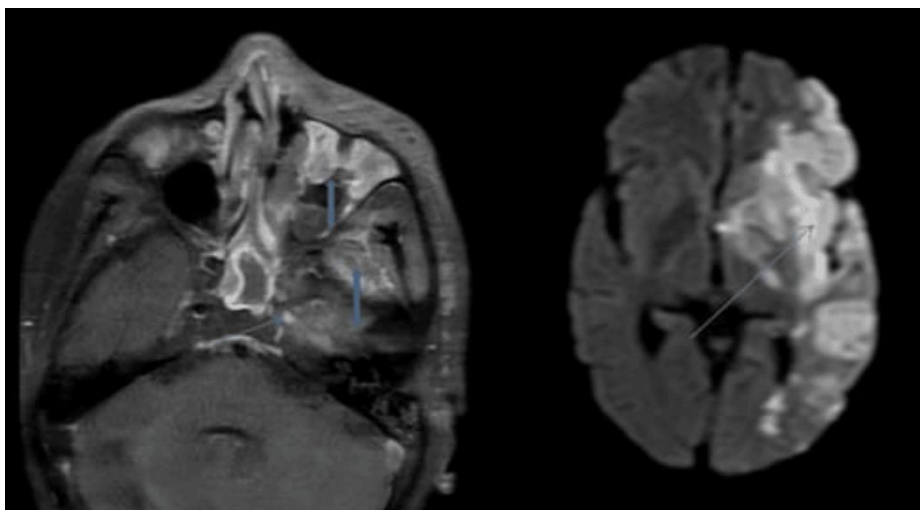


FIGURE 7. MRI was done which showed cerebral infarct with sinusitis

Received maxillectomy specimen with sinuses and Hematoxylin and Eosin stained slide showed fungal hyphae which was highlighted by Grocott -Gomori methanamine silver stains (Figure 8).

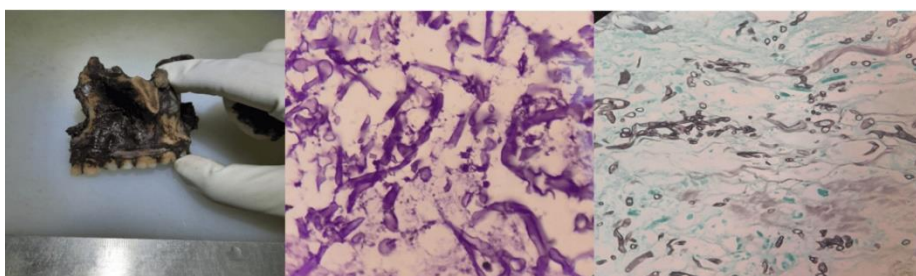


FIGURE 8. Gross specimen received by pathology department,along with Hematoxylin and Eosin stained slide and Grocott -Gomori methanamine silver stains were used to highlight the fungal hyphae

Case 4 : A 53 year old covid RT-PCR negative male patient admitted in ENT department with complains of facial swelling for one week and sudden loss of vision for 2 days. The patient had a past history of diabetes mellitus and myocardial infarction. The patient was covid RT-PCR positive 15 days back and was on oxygen support and taking dexamethasone and insulin. MRI showed ethmoid sinusitis with right orbit involvement. (Table 9).

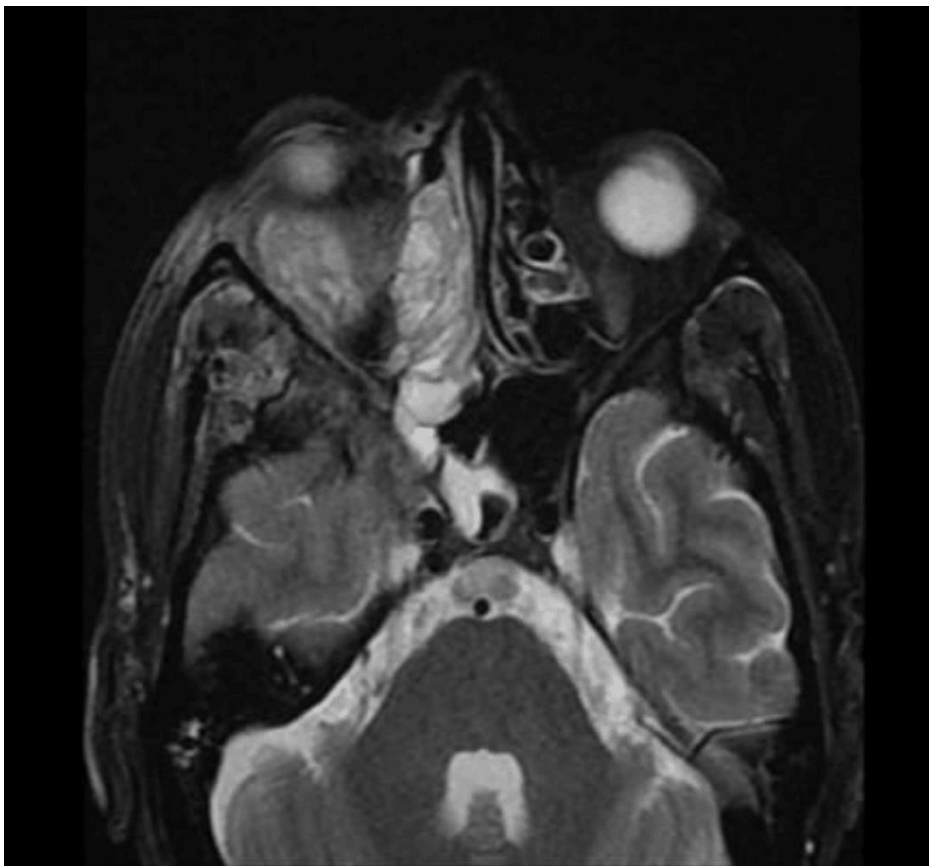


FIGURE 9. MRI shows ethmoid sinusitis with right orbit involved.

The patient was operated after proper control of blood sugar and all necrotic and infected material was removed. Hematoxylin and Eosin stained slide showed fungal hyphae resembling mucor species. which was highlighted by Grocott -Gomori methanamine silver stain (Fig-10)

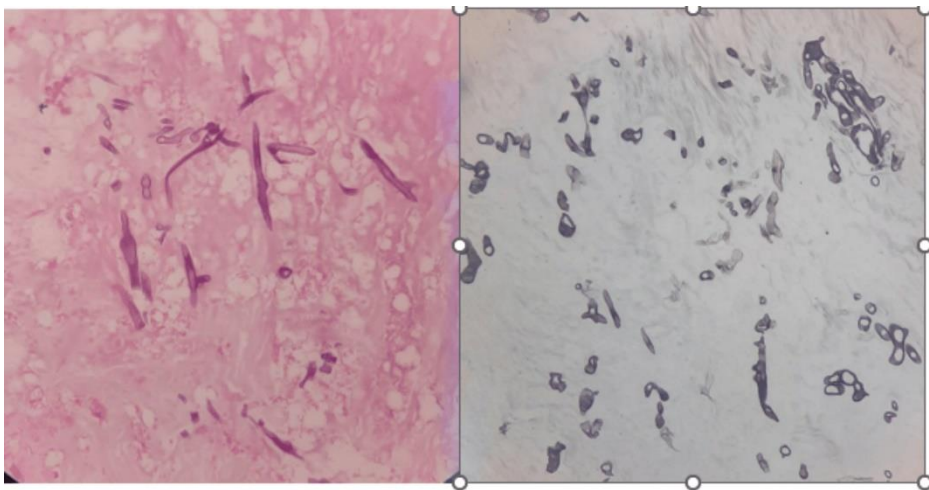


FIGURE 10. Histopathology of Hematoxylin and Eosin stained slide showed fungal hyphae resembling mucor species. Grocott -Gomori methanamine silver stain of the slide was done and showed fungal hyphae in black color.

Discussion

The COVID-19 pandemic has significantly altered the landscape of secondary infections, with ROCM presenting as a severe and life-threatening condition. Early recognition and prompt intervention are critical for improving outcomes. The pathological and radiological aspects of ROCM in post-COVID patients underscore the need for heightened vigilance and a multidisciplinary approach to management.

This study examines a series of four patients diagnosed with rhino-cerebro-orbital mucormycosis. The patients, aged between 35 and 70 years, presented with a nasal blockage and discharge, headache, facial pain and edema, mild fever, redness of eye, lid edema, proptosis, vision loss, and retro orbital pain. Diabetes mellitus tends to change the normal immunological response of body to any infection. Hyperglycemia stimulates fungal proliferation and also causes decrease in chemotaxis and phagocytic efficiency which cause innocuous organisms to thrive in acidic environment. CT and MRI scans were performed on all patients to assess the extent of fungal invasion. All patients exhibited complete opacification of the paranasal sinuses, with evidence of bone erosion. Proptosis and infiltration of the orbital fat were observed in three cases. One cases showed extraocular muscle involvement. As the infection spread to orbit and skull the patient may become confused and comatosed. [2] We report two unique cases of intracranial involvement of mucormycosis, one develops cerebral abscess in basi-frontal lobe and another develop cerebral infarct along left middle cerebral artery territory region.

Biopsy samples from affected organ of all patient were subjected to histopathological examination, revealing broad, non-septate hyphae with right-angle branching(characteristic of Mucorales) were identified in all samples. Extensive tissue necrosis and angioinvasion were prominent in all cases, contributing to the aggressive nature of the infection.

The correlation between radiological and pathological findings underscores the invasive nature of rhino- cerebral orbital mucormycosis. Radiological imaging is pivotal in delineating the extent of the disease, guiding biopsy, and surgical debridement. Pathological examination confirms the diagnosis and helps in identifying the specific fungal pathogen, which is crucial for targeted antifungal therapy.

Prompt diagnosis along with reversal of predisposing factor and aggressive surgical debridement remain conerstone for this deadly disease. [5] The integration of radiological imaging with pathological analysis provides a comprehensive approach to managing this life-threatening condition. Multidisciplinary collaboration among radiologists, pathologists, and clinicians is essential for timely and effective treatment.

Conclusions

ROCM in post-COVID patients is a severe and life-threatening condition characterized by distinct pathological and radiological features. Early recognition, comprehensive imaging, and a multidisciplinary treatment strategy are essential for improving patient outcomes. Ongoing research and documentation of such cases will enhance our understanding and management of this devastating complication in the context of the COVID-19 pandemic. This case series highlights the significance of radiological and pathological correlation in diagnosing and managing rhino-cerebral orbital mucormycosis. Prompt recognition and aggressive treatment are imperative to mitigate the high morbidity and mortality associated with this devastating infection.

Conflicts of interest :The author declare no conflict of interest.

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