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Case Report

Rhino-Orbital Cerebral Mucormycosis (ROCM): Effective Management with Liposomal Amphotericin B

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ABSTRACT

Rhino-Orbital Cerebral Mucormycosis (ROCM) is a serious and often life-threatening fungal infection. The fungi class called zygomycetes are responsible for causing rhino-orbital mucormycosis which usually affects diabetic or immunocompromised patients. Infections of the nasal mucosa and paranasal sinuses occur in Stage I of ROCM, orbital involvement occurs in Stage II, and brain involvement occurs in Stage III, which mostly affects individuals with immunological or metabolic problems. Face discomfort and paraesthesia, headaches, enlarged orbits and nostrils, inflammation, drooping eyelids, proptosis, external and internal ophthalmoplegia, vision loss, and blackish necrosis of the palate and nasal mucosa are all symptoms of rhino-orbito-cerebral mucormycosis. Here we report a case of Rhino orbital cerebral mucormycosis in a 49-year-old male presented to an otorhinolaryngology department with at least 10days of retro-orbital pain and headache for, bilateral nasal obstruction, right sided facial pain and swelling and drooping of right eyelids and loss of vision in right eye from 5 days. The patient was diagnosed with invasive fungal sinusitis and underwent skull base surgery a week before admission for liposomal amphotericin-B infusion. The patient had medical history of type II diabetes mellitus and hypertension for 8 years, acute ischemic stroke recently. The patient had a history of covid 19 and was hospitalised for 25 days. The standard treatment for mucormycosis was initiated with Liposomal Amphotericin B (50 mg) Intravenous infusion-5 doses were given along with nasal packing every alternate day. Total cumulative dose of Amphotericin B-1500 mg was given. Early treatment and prompt treatment with Amphotericin B is necessary for avoiding devastating consequences.

Keywords: Rhino-Orbital Cerebral Mucormycosis, Liposomal amphotericin-B, Diabetes mellitus, Black mucus.

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INTRODUCTION

Rhino-orbital, which includes *Rhizopus* spp., *Mucor* spp., *Rhizomucor* spp., *Syncephalastrum* spp., *Cunninghamella, Bertholletia, Apophysomyces* spp., and *Lichtheimia* (formerly *Absidia*) spp., is responsible for causing rhino-orbital mucormycosis, which usually affects diabetic or immunocompromised patients.[1] It can spread into the mucor of the skull base and damage the paranasal sinuses, eroding the orbital contents. Many conditions, including hypoxia, hyperglycemia, metabolic acidosis, diabetic ketoacidosis, elevated free iron levels, and immunosuppressed leukocytes, oxidative and non-oxidative fungicidal mechanisms, promote the growth of Mucor spores.[2] Infections of the nasal mucosa and paranasal sinuses occur in Stage I of ROCM, orbital involvement occurs in Stage II, and brain involvement occurs in Stage III, which mostly affects individuals with immunological or metabolic problems. Facial discomfort and paresthesia, headaches, enlarged orbits and nostrils, inflammation, drooping eyelids, proptosis, external and internal ophthalmoplegia, vision loss, and blackish necrosis of the palate and nasal mucosa are all symptoms of rhino-orbital cerebral mucormycosis. However, survival in cases with fungal brain illness is uncommon, and extra-nasal involvement raises mortality rates.[3] The development of ROCM is facilitated by post-COVID-19 immunosuppression, hypoxia, metabolic acidosis, and elevated serum ferritin. One established risk factor for ROCM is diabetes mellitus. One possible cause of contracting ROCM is the COVID-19 virus's destruction of pancreatic islet cells, which results in new-onset hyperglycemia and aggravation of pre-existing diabetes mellitus or diabetic ketoacidosis.[4] Endothelial cell invasion is encouraged by elevated glucose and iron levels, which also upregulate Glucose-Regulated Protein 78 (GRP78). Mucormycosis is characterized by angioinvasion, which results in necrosis with bone degradation, tissue ischemia, arteritis, and vascular thrombosis. The organism can also spread to other organs by angioinvasion, and ischemic

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necrosis makes it more difficult for antifungal medications to reach their intended targets.[5] Lipid-based amphotericin B, which destroys the cell wall of the fungus, is the first-line medical treatment for mucormycosis and should be initiated as soon as the diagnosis is suspected. Posaconazole, a triazole that inhibits the growth of the fungus, has been proposed as a promising adjunctive or alternative treatment for mucormycosis. Further studies are needed to better understand the role of posaconazole in the primary treatment of mucormycosis. The FDA approved isavuconazole as a primary therapy for Invasive Aspergillosis (IA) and Mucormycosis (IM). The chance of survival can be raised with prompt medical attention and surgical debridement of the mucor-affected area.[6]

CASE DISCUSSION

A 49-year-old male presented to an otorhinolaryngology department with at least 10 days of retro-orbital pain and headache, bilateral nasal obstruction, right-sided facial pain, swelling, drooping of right eyelids, and loss of vision in the right eye for 5 days. The patient was diagnosed with invasive fungal sinusitis and underwent skull base surgery a week before admission for liposomal amphotericin B infusion. The patient had a medical history of type II diabetes mellitus and hypertension for 8 years and an acute ischemic stroke recently. The patient had a history of COVID-19 and was hospitalized for 25 days.

Laboratory details showed the patient had a previous HbA1c value of 10.5%, a current haemoglobin of 12.5 g/dL, and a red blood count of 4.1 million/cu.mm. Total leucocyte count-Neutrophils-84%, Lymphocytes-9%, C-reactive protein-54.90 mg/L, PPBS-211 mg/dL, Fasting blood sugar: 156 mg/dL, serum magnesium: 1.67 mg/dL.

Revision Functional endoscopic sinus surgery was done on the patient in a supine position by inducing a general anesthetic. Under zero-degree endoscopic visual evaluation, synechia was noted between the right inferior turbinate and septum, which was separated. The right maxillary sinus medial wall moved, and the nasolacrimal ducts were trimmed. Polypoidal tissue was noted in the right nasal cavity and removed; black unhealthy mucosa was noted in the posterosuperior part of the lateral wall as shown in Figure 2 and was removed similarly in the left nasal cavity; polypoidal tissue was noted in the anterior ethmoids, removed, and sent for histopathological examination. Hemostasis achieved.

A contrast Magnetic Resonance Imaging (MRI) of the brain demonstrates features suggestive of rhino-orbital cerebral mucormycosis with perineural spread of the right trigeminal nerve along with the cavernous sinus, Meckel's cave, cisternal segment, root entry zone, pterygopalatine fossa, and foramen ovale and showed an impression of long segment diffusion restriction in the right optic nerve and trigeminal nerve, likely ischemic neuropathy. Pachymeningitis along the right medial temporal dura and subacute hemorrhagic infarcts in the right cerebellar hemisphere, anterior lobe of the cerebellum, superior and middle peduncles, superior colliculus of the midbrain, and pons, which is demonstrated in Figure 1.

Treatment includes the opinions of endocrinologists and nephrologists. By considering the raised blood sugars, the patient was prescribed Inj. Actrapid of 10-10-6 units and Insulatard 10-0-6 units and immediately started Inj. Liposomal Amphotericin B with regular monitoring. A dermatologist's opinion was taken for irritant contact dermatitis, and the patient was advised to take levocetirizine tablets and topical framycetin ointment. The advice was taken on low magnesium levels, which were corrected by the administration of Magnesium Sulfate ($MgSO_4$), prescribed as a loading dose and maintained by ultramag 200 mg. Liposomal Amphotericin B (50 mg) IV infusion-5 doses was given along with nasal packing every alternate day. A total cumulative dose of amphotericin B-1500 mg-was given. The patient was treated with other antifungal agents like clotrimazole 1% along with neomycin 0.5%, beclomethasone 0.025% ear drops, and first-line antibiotics.

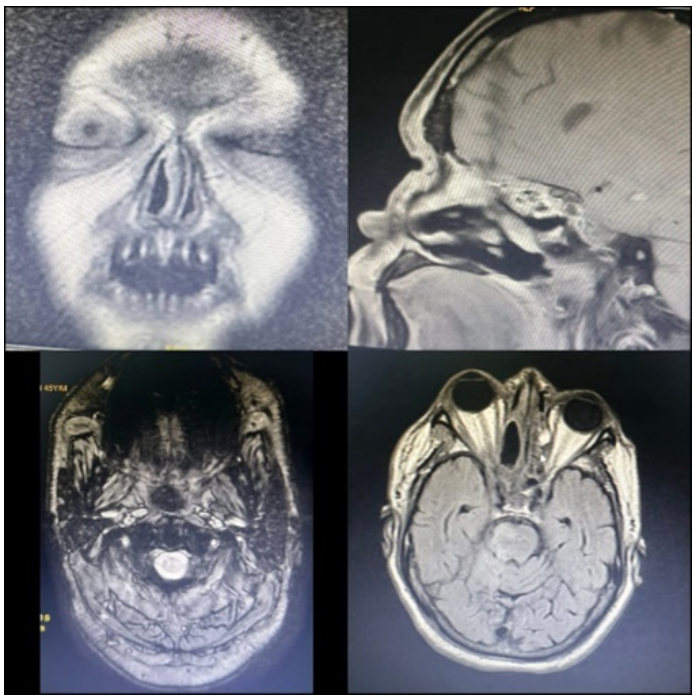

Figure 1: MRI brain in T1,T2W1 view suggesting Subacute infarcts in the right cerebellar hemisphere, anterior cerebellum, peduncles, midbrain, and pons, diffusion restriction and enhancement of the right trigeminal nerve (Meckel's cave to foramen ovale), pachymeningeal enhancement along medial temporal dura, chronic small vessel ischemic changes in periventricular and fronto-parietal regions, extensive mucosal thickening in paranasal sinuses with extension to infratemporal and pterygopalatine fossae, right orbital apex syndrome with optic nerve and peri-orbital involvement, post-surgical changes from prior sinus surgeries like maxillectomy, ethmoidectomy, sphenoidotomy and right middle turbinectomy.

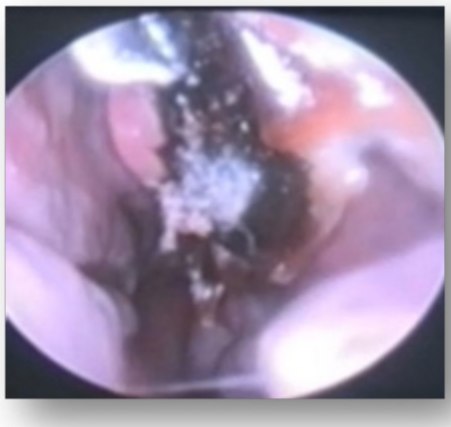

Figure 2: Demonstrating Black unhealthy mucosa noted in post superior part of the lateral wall.

DISCUSSION

This case emphasizes how crucial it is to comprehend ROCM risk elements and the necessity of prompt assessment and treatment. The Mucormycosis are opportunistic infections that belong to the Mucorales order. Rhizopus, Lichtheimia, and Mucor are the genera that contain the most commonly reported species. Saprophytic fungi, which decompose food and waste, are frequently found in soil. The primary cause of human infection is spore inhalation; traumatic inoculation and contaminated food consumption are rare ways of transmission. Mucormycosis infection is characterized by angioinvasion that results in systemic dissemination, extensive tissue necrosis, and vascular thrombosis.[3]

Asexual spore production is the cause of mucormycosis infection and the microscopic Spores travel through the air and land on human noses and oral mucosa. A phagocytic reaction will restrict these spores in the majority of immunologically competent hosts. If this reaction is unsuccessful, hyphae will grow and germination will occur. In immunocompromised people, the infection becomes entrenched because polymorphonuclear leukocytes are less efficient in eliminating hyphae. As the hyphae start to infiltrate arteries, they spread throughout the artery walls and lumens, resulting in thrombosis, ischemia, and infarction along with dry gangrene of the afflicted tissues. Sepsis can result from hematogenous spread to other organs, such as the brain, lung, and so forth.[7]

Diabetes is the leading risk factor for ROCM worldwide. In our case, the medical history of type II diabetes mellitus for 8 years, acute ischemic stroke recently, and history of COVID-19 are predisposing risk factors that called for early diagnosis of ROCM. The cornerstones of first treatment in ROCM are antifungal drugs and managing the underlying illness. It has been demonstrated that liposomal amphotericin B (50 mg) IV infusion-5 doses were given along with nasal packing every alternate day, and a total cumulative dose of amphotericin B-1500 AL mg was given efficiently to treat mucormycosis.

According to a recent investigation of a sizable dataset of more than 2000 ROCM cases linked to COVID-19, orbital exenteration was linked to a mortality decrease in ROCM stage 4 disease with intracranial extension from 52% to 39%. The aggressiveness of presentation, the nature of the underlying disease process, and the responsiveness to first therapy are the factors that determine globe survival.[8]

CONCLUSION

Rhino-orbital-cerebral Mucormycosis is a critical and potentially fatal condition that must be considered in patients at risk who have a medical history of type II diabetes mellitus, acute ischemic stroke recently, and a history of COVID 19, who exhibit sinus-related symptoms and pain. Early recognition and timely treatment are essential to improving patient outcomes. Organizing logistics should be increased to guarantee a sufficient supply of liposomal amphotericin B which will save the lives of these individuals.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ROCM: Rhino-Orbital Cerebral Mucormycosis; **GRP78:** Glucose-regulated protein 78; **IA:** Invasive Aspergillosis; **MRI:** Magnetic resonance imaging.

DECLARATION OF PATIENT CONSENT

The authors declare that the patient's consent was taken for the publication.

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