2 Clinical Presentation of Cases with Rhino-Orbito-Cerebral Mucormycosis

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Rhino-Orbito-Cerebral mucormycosis (ROCM) is an angioinvasive mycosis that carries high morbidity and mortality risks. With the current pandemic's growing patterns, the grave clinical and pathogenetic complex has been brought into sharper light. During the second wave of the COVID-19 pandemic, a surge of rhino-orbito-cerebral mucormycosis was noted in patients a few weeks after recovery [1, 2].

Despite other nations have documented COVID-associated mucormycosis, India has the highest number of cases due to its reputation as the world's diabetic capital [2, 3]. ROCM is the commonest type of mucormycosis, and it includes the entire spectrum of mucormycosis from sino-nasal disease to rhino-orbital disease that may progress to rhino-orbital-cerebral disease [2, 4, 5]. A high rate of mortality is associated with ROCM [1, 6].

2.1 Background

Mucormycosis, has long been regarded as a dreaded clinical diagnosis and a disease of the immunocompromised. The comorbidities usually associated with both increased incidence and poorer outcomes are diabetes Mellitus, hematological malignancies, chemotherapy, organ transplant, and severe injuries [7]. Mucormycosis is caused by the Mucorales group of fungi. These fungi are present in the environment and on inhalation in an immune-competent host; Mucor is rejected from the surface by the mucosal barrier itself. It is in the immune-compromised host that the fungus can cross this immune barrier and invade the tissues due to uncontrolled diabetes mellitus, steroids intake, or those on immunosuppressants [1, 8].

The patients with hematological malignancies are more prone to pulmonary mycoses, while diabetic acidotic patients more commonly suffer from progressive and unrelenting rhino-orbito-cerebral disease. The interaction between the spore coat protein CotH3 and the Glucose Related Protein 78 (GRP78) on nasal epithelial cells may be the fundamental pathogenetic event in diabetics. Expression of both proteins is significantly increased by diabetic ketoacidosis chemistry, increased blood glucose, and increased circulating ketones. It facilitates invasion of the epithelium and cascades into often lethal rhino-orbito-cerebral disease [7].

The COVID-19 Pandemic has resulted in an explosion of cases of ROCM, referred to as COVID-Associated Mucormycosis (CAM). Nearly 50,000 cases were reported from India in 3 months of the second wave of the pandemic, ending July 2021 [9]. The sudden surge of cases was probably due to the immune disabling nature of COVID-19 and the use of steroids that

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precipitated diabetes in COVID-19 patients. These patients rarely develop pulmonary mucormycosis, which involves different receptors and fungal ligands (CotH7 and Integrin β1) [7].

2.2 Clinical Features

ROCM begins in the nasal passages and sinuses, spreads to the orbit and eye, and eventually reaches the brain. Angioinvasion and spreading ischemia are a hallmark of the disease. In the 1950s, Smith and Krichner established criteria for clinical diagnosis of Mucormycosis [10]: These include black necrotic turbinates, blood-tinged nasal discharge with or without ipsilateral facial pain, soft peri-orbital or peri-nasal swelling/discoloration or induration (Figs. 2.1 and 2.2), ptosis with drooping of eyelid lid edema, proptosis (Figs. 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 2.10, and 2.11), and ophthalmoplegia (Fig. 2.12). There may be associated multiple cranial nerve palsies unrelated to documented lesions [7].

Fig. 2.1 Clinical photograph of a patient showing edema of the paranasal area involving cheek skin

Fig. 2.2 Clinical photograph showing facial edema on the left side

Fig. 2.3 Clinical photograph showing ptosis with partial proptosis left (Photo Courtesy: Dr. Manisha Singh, RML Delhi)

Fig. 2.4 Clinical photograph showing left ptosis

Fig. 2.5 Clinical photograph showing left lid edema and proptosis

Fig. 2.6 Clinical photograph showing left lid edema

Fig. 2.7 Clinical photograph showing left periorbital cellulitis

Fig. 2.8 Clinical photograph showing right lid edema (Photo Courtesy: Dr. Bibhu Pradhan TDMC Kathmandu)

Fig. 2.9 Clinical photograph showing left ptosis (Photo Courtesy: Dr. Bibhu Pradhan TDMC Kathmandu)

Palatal lesions (Figs. 2.13, 2.14, and 2.15), loosened teeth, fistulae in the region of cheek and palpebral area, blackened areas of eschar, and necrosis developing and extending on the skin of the face are also common clinical presentations (Figs. 2.16, 2.17, and 2.18).

Fig. 2.10 Clinical photograph showing right ptosis (Photo Courtesy: Dr. Aparna; Fortis Faridabad)

Fig. 2.11 Clinical photograph showing left lid edema (Photo courtesy; Dr. Manisha Singh, RML Delhi)

Loss of vision, eye pain, and altered sensation in the infraorbital area are common and ominous as this indicates invasion of the infraorbital nerve. Involvement of the anterior parts of the eye, including cornea and conjunctiva, indicates orbital exenteration (Figs. 2.19, 2.20, 2.21, and 2.22). If the anterior structures are preserved, globe sparing orbital exenteration or an endoscopic orbital debridement can be performed based on the extent of the disease. Early symptoms of stuffiness and nasal discharge, sometimes blood stained, maybe missed. In late cases, a nasal endoscopy may demonstrate the presence of eschar or slough (Figs. 2.23, 2.24, and 2.25). These may rapidly evolve into the orbital and intracranial compartment symptoms of severe pain in the eyes and head.

All the progressive symptoms and signs are the result of extending thrombosis and associated ischemia and tissue necrosis. The sudden blindness seen in complicated ROCM can be due to several pathogenetic mechanisms like central retinal artery

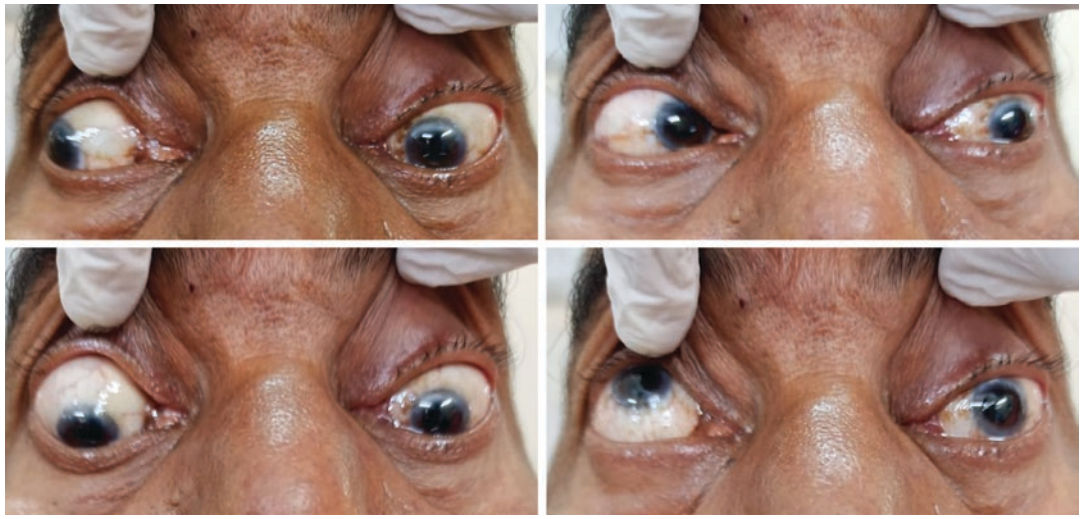

Fig. 2.12 Clinical photograph showing Ophthalmoplegia, restricted eye movements

Fig. 2.13 Clinical photograph showing palatal necrosis (Photo Courtesy: Dr. Rajeev Pachauri Agra)

Fig. 2.14 Clinical photograph showing palatal bogginess (Photo Courtesy: Dr. Rajeev Pachauri Agra)

occlusion, thrombosis of the posterior ciliary artery, optic nerve infarction in the intraorbital course, direct fungal invasion of the optic nerve in the intracranial part or even optic chiasm [11].

2.3 When to Suspect COVID-Associated Mucormycosis

A patient presenting with the symptoms of ROCM described above and the history of COVID with deterioration of vision, unrelenting sharp head-

Fig. 2.15 Clinical photograph showing palatal necrosis (Photo Courtesy: Dr. Rajeev Pachauri Agra)

ache, and facial pain/numbness. There may be an associated history of nose block/blood-stained nasal discharge with or without symptoms of central nervous system involvement, focal neurological signs, and encephalopathy indicate a grave prognosis. Signs of intracranial invasion, periorbital necrosis, and cavernous sinus involvement are poor prognosticating factors.

Fig. 2.16 Clinical photograph showing skin necrosis near the right medial canthus (Photo courtesy: Dr. Manisha Singh, RML Delhi)

Fig. 2.17 Clinical photograph showing necrosis of the left eye-lid skin extending up to the medial canthus (Photo courtesy: Dr. Manisha Singh, RML Delhi)

Fig. 2.18 Clinical photograph showing extensive skin necrosis (Photo Courtesy: Dr. Satish Jain Jaipur)

Fig. 2.19 Clinical photograph showing conjunctival chemosis

Fig. 2.20 Clinical photograph showing involvement of the anterior structures of the left eye

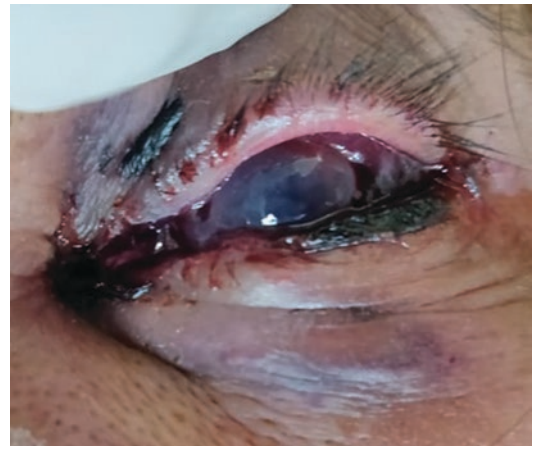

Fig. 2.21 A melting cornea with bluish discoloration of the conjunctiva (Photo courtesy: Dr. Manisha Singh, RML Delhi)

Fig. 2.22 Severe conjunctival congestion and chemosis

2.4 ROCM Pre-COVID and During COVID Pandemic

COVID-associated mucormycosis presents unique problems and can be alarming in the context of the ongoing pandemic. The COVID-Associated Mucormycosis has some distinctive features. It is more common in men, older patients, and patients who have had a complicated course of COVID-19. The latter includes the need for steroids, hypoxia, and hospitalization and new or preexisting diabetes mellitus [6].

These patients must undergo urgent diagnostic nasal endoscopy and fresh KOH preparation/ Fungal culture and biopsy, be sent from the

Fig. 2.23 Endoscopic view of the left nasal cavity demonstrating necrotic tissue with discharge (Photo Courtesy: Dr. Aparna, Fortis Faridabad)

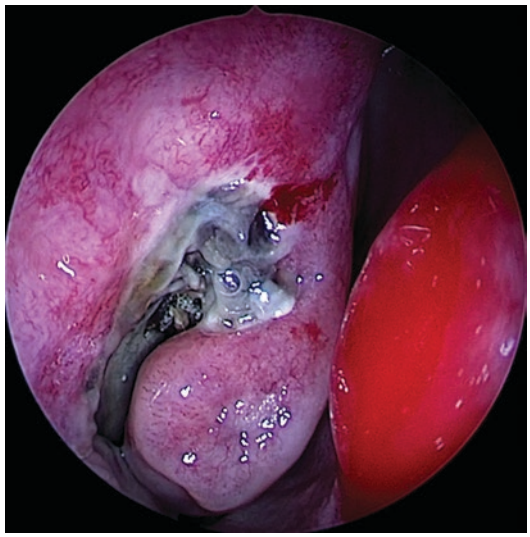

Fig. 2.24 Endoscopic view of the right nasal cavity showing characteristic eschar

affected areas involving the healthy margins adjoining the necrotic areas. Further workup of these patients in the form of radiological diagnosis has been mentioned in the subsequent chapter. The surgical debridement is planned based on disease mapping on MRI, and the steps of each procedure have been described in the chapters on surgical management of ROCM.

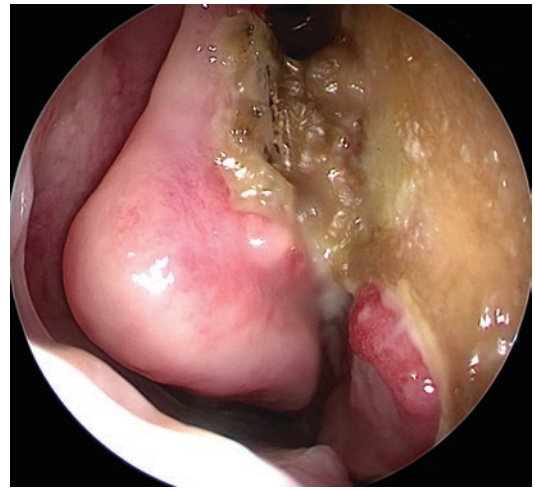

Fig. 2.25 Endoscopic view of the right nasal cavity showing necrosis of the right turbinate and septum

2.5 Conclusion

Acute ocular signs represent late presentation in COVID-associated ROCM. Despite our best efforts, the prognosis remains grim in these cases. This kind of presentation urges clinicians to keep a high degree of suspicion, educate patients about early signs and symptoms and perform a quick nasal endoscopy and imaging. Early institution of therapy leads to improved outcomes.

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