



ARRAY OF MAGNETIC RESONANCE IMAGING FINDINGS IN POST-COVID MUCORMYCOSIS.

Radio-Diagnosis

Dr. Civilee Nanda	Resident, Department of Radiodiagnosis, Institute- Atal Bihari Vajpayee Institute of Medical Sciences and Dr Ram Manohar Lohia Hospital, New Delhi, India.
Dr Namrita Sachdev*	Professor, Department of Radiodiagnosis. Institute- Atal Bihari Vajpayee Institute of Medical Sciences and Dr Ram Manohar Lohia Hospital, New Delhi, India *Corresponding Author
Dr Sudhanshu Kathpalia	Resident, Department of Radiodiagnosis. Institute- Atal Bihari Vajpayee Institute of Medical Sciences and Dr Ram Manohar Lohia Hospital, New Delhi, India
Dr Shardul Tyagi	Resident, Department of Radiodiagnosis. Institute- Atal Bihari Vajpayee Institute of Medical Sciences and Dr Ram Manohar Lohia Hospital, New Delhi, India

ABSTRACT

Background: ROCM is a rare but extremely fatal fungal infection targeting immunocompromised individuals. There was a surge in cases in the past 2 years amongst the patients recovered from moderate to severe COVID-19 infection. Imaging is essential for early clinical recognition of this potentially fatal disease so that timely management can be done. **Methods:** We conducted a cross-sectional observational study with 30 COVID 19 patients suspected of having ROCM for a period of 2 months. MRI evaluation was done using conventional sequences, TOF MR Angiography and follow up imaging was done whenever possible. **Results:** The infection was predominantly bilateral in 22 patients (74%) with unilateral involvement seen in 8 cases (26%). Staging was done in preoperative patients (15 patients) with Stage 1 disease seen in 2 cases (10%), Stage 2 disease seen in 5 cases (25%) and stage 3 disease seen in 8 cases (40%). Cavernous sinus thrombosis was seen in 8 cases (26%), ICA thrombosis in 3 cases (10%), CCA thrombosis in 2 cases (10%), Optic neuritis in 8 cases (26%), ICA infarct in 5 cases (10%), involvement of pituitary gland in 1 case (3%), intracranial focal cerebritis in 5 cases (16%) and pachymeningitis in 5 cases (16%). Black turbinate and guitar pick signs were observed. Patients underwent endoscopic or open debridement under GA, with Orbital exenteration, ethmoidectomy and medial maxillectomy. **Conclusion:** ROCM is thus an emerging rapidly disseminating fungal infection afflicting the COVID recovered population. Aggressive debridement, systemic antifungal therapy, and control of underlying co-morbid factors is the mainstay of therapy. Radiologists play a significant role in its early diagnosis, evaluation of extent, thus aiding in better and faster management.

KEYWORDS

Rhino-orbital-cerebral mucormycosis, post-COVID mucormycosis.

INTRODUCTION:

Mucormycosis is a life threatening infection caused by fungi of the family Mucoraceae^[1] which is seen exclusively in the immunocompromised patients. The disease can present in two common forms: the rhino-orbital-cerebral form (ROCM) and as pulmonary infections. ROCM carries high overall mortality^[2] and poses a diagnostic and therapeutic challenge. There has been a surge of such cases in patients recovering from Covid 19 especially those with underlying diabetes mellitus, prior respiratory infections, use of immunosuppressive therapy in the form of steroids and broad-spectrum antibiotics. The systemic immune alterations occurring in COVID-19 infection itself has also led to the propensity to develop this secondary infection. Early clinical recognition of this fatal disease followed by aggressive debridement, systemic antifungal therapy, and control of underlying co-morbid factors are the mainstay of therapy^[3].

The patients generally present with fever, headache, facial pain, nasal discharge, nasal obstruction and crusting. The disease progresses rapidly within a period of a few hours to days leading to cranial nerve palsies and features of CNS involvement^[4]. Early imaging is crucial in assessing the extent of involvement and complications. MRI with its superior soft tissue resolution and multiplanar capability is the modality of choice to evaluate such patients. The objective of this study is to describe the imaging findings in patients who presented at various stages of the disease, as well as to describe the imaging findings of those patients who reported for follow up after treatment.

METHODS

We evaluated the imaging and clinical data of 30 patients (18 males and 12 females), ranging from 26 to 75 years old, with suspected ROCM who presented to the Department of Radiodiagnosis ABVIMS & Dr Ram Manohar Lohia Hospital from 1st May 2021 to 30 June 2021 (2 months). All the patients had history of moderate-severe COVID infection in the last one month and had been administered steroids. Clinical details regarding presentation, management and evolution of disease were obtained in all cases.

Histopathological Evaluation

Histopathological examination showed fungal elements on KOH mount. Biopsy taken from turbinates demonstrated fungal granulomatous inflammation with broad aseptate fungal hyphae on PAS staining suggesting Mucor species.

Radiological Evaluation

All patients underwent MR imaging in a Siemens 3-T system using T1 weighted, T2 weighted sequences, Diffusion Weighted Imaging and post contrast imaging after administration of gadopentetate dimeglumine (0.1 mmol/kg). Magnetic resonance Angiography (TOF MRA) of Circle of Willis and Carotids was done in patients with suspected thrombosis. Of the 30 patients, 15 patients were evaluated preoperatively, 10 cases underwent post intervention MRI evaluation and 5 cases had both preoperative and postoperative MRI study. 8 patients additionally had undergone contrast enhanced CT scan on 256 slice scanner.

Preoperative MRI Images were evaluated for morphological characteristics such as signal intensity on pre and post contrast images as well as for presence of unilateral or bilateral involvement, extent of disease, presence of any complications and for typical signs observed in mucormycosis. Staging of Preoperative MRI findings was done into

- Stage 1 - Involvement of nose & paranasal sinuses,
- Stage 2 - Involvement of orbit, palate and oral cavity and
- Stage 3 - Involvement of periorbital region, preaural region, parapharyngeal space, brain and cavernous sinus.

Post intervention MRI on follow up was used to assess for presence of residual infection and complications.

RESULTS

Clinical features

All the patients presented with headache, facial swelling and sinusitis. Nasal discharge and epistaxis was seen in 10 patients (33%). Ophthalmological symptoms of reduced visual acuity was seen in 15 patients (50%) and exophthalmos in 8 cases (26%). Six patients (20%) had clinical symptoms of cavernous sinus involvement including diplopia/ophthalmoplegia and facial numbness. Fever with meningism were seen in 3 patients (10%) and 2 patients presented with stroke like features (10%).

Pattern of involvement

Bilateral involvement was more commonly seen, in 22 cases (74%) while unilateral involvement was seen in only 8 cases (26%). Staging was done in the 15 preoperative patients with Stage 1 disease seen in 2 cases (10%), Stage 2 disease seen in 5 cases (25%) and stage 3 disease was seen in 8 cases (40%).



Fig 1: Grading of mucormycosis a) Postcontrast T1 axial Grade 1 involvement of nasal cavity b) Post contrast T1 coronal Grade 2 involvement of ethmoids and orbits c) Postcontrast T1 Axial Grade 3 involvement of nasal cavity, orbits with Rt ICA & Cavernous sinus thrombosis

Extension of disease

A pattern of contiguous anatomic involvement affecting the nasal cavity, maxillary sinus and ethmoid sinus was consistently observed with a evidence of pansinusitis in 12 cases. Orbital involvement was seen in the form of involvement of superior orbital fissure in 18 cases (60%) and orbital apex in 3 cases (10%). Involvement of the retroantral fat pad was seen in 5 cases (16%), infratemporal fossa in 8 cases (26%), pterygopalatine fossa in 9 cases (30%), masticator space in 3 cases (10%), anterior cranial fossa via cribriform plate in 5 patients (16%) and leptomeningeal spread in 5 cases (16%).

Table 1: Involvement of extrasinus sites in patients of mucormycosis.

SITE OF INVOLVEMENT	NO. OF PATIENTS	PERCENTAGE OF PATIENTS
Orbital involvement	21	70%
Retroantral fat pad	5	16.67%
Infratemporal fossa	8	26.67%
Pterygopalatine fossa	9	30%
Masticator space	3	10%
Anterior cranial fossa	5	16.67%
Leptomeningeal spread	5	16.67%

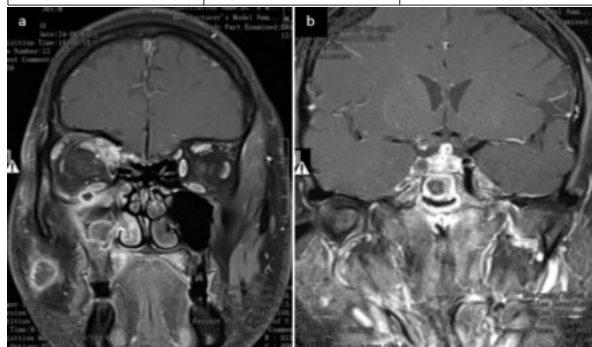


Fig 2: 42 year old postcovid ROCM patient a) Postcontrast T1 Coronal shows extensive Grade 3 Involvement with extension into right pterygoid space with abscess formation b) postcontrast T1 Coronal in same patient shows involvement of pituitary with enhancement of sella

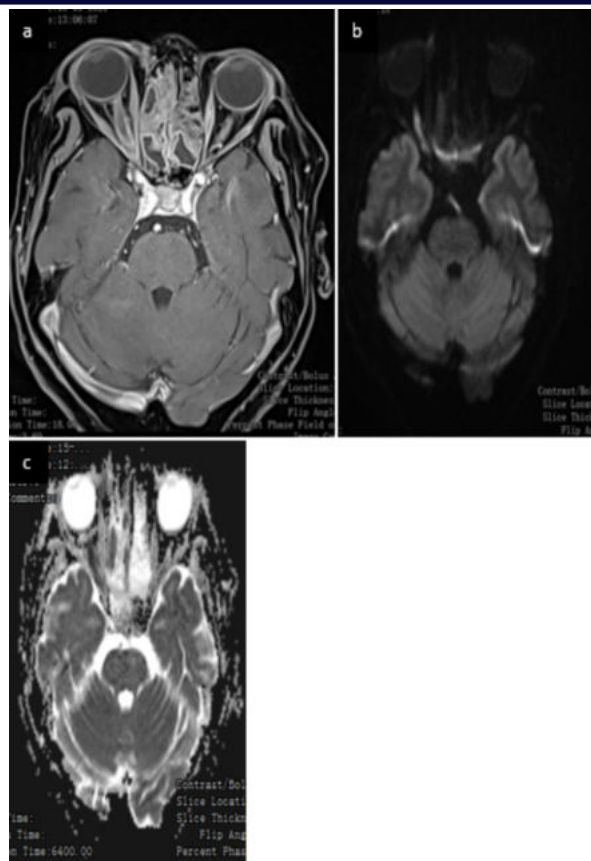


Fig 3: 32 year old patient of ROCM with sudden loss of vision in Rt eye a) Postcontrast T1 Axial shows enhancement of bilateral nasal cavity and ethmoid sinuses with thickening and peripheral enhancement of right optic nerve B) & c) DWI & ADC show diffusion restriction suggestive of Optic Nerve Infarction.

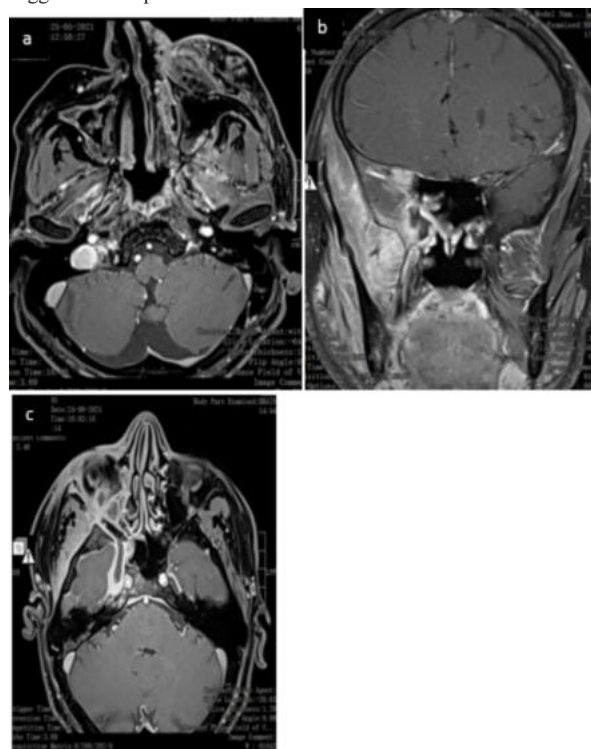


Fig 4: Extension of Disease a) Post contrast Axial involvement of Right premaxillary and retroantral region b) Postcontrast T1 coronal involvement of Masticator space c) Postcontrast T1 Axial extension of disease to meckel's cave and pterygopalatine fossa.



Fig 5: Involvement orbital apex a) Postcontrast T1 axial Enhancement and involvement of left orbital apex b) postcontrast T1 coronal image showing similar finding

Complications:

Cavernous sinus thrombosis, Internal and common carotid artery (ICA and CCA) thromboses, optic neuritis, pituitary gland involvement, focal cerebritis, pachymeningitis were seen in patients with complicated infection.

Cavernous sinus thrombosis was found in 8 cases (26%), ICA thrombosis was seen in 3 cases (10%) and CCA thrombosis in 2 cases (10%), Optic neuritis was seen in 8 cases (26%), involvement of pituitary gland 1 case (3 %), focal cerebritis in 5 cases (16%) and pachymeningitis in 5 cases (16%).

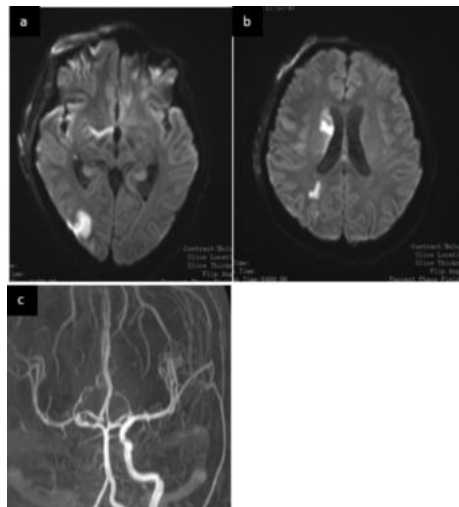


Fig 6: 26 year old patient of ROCM with RT MCA infarct a) b) Diffusion restriction on DWI c) TOF MRA non visualization of RT MCA suggestive of thrombosis

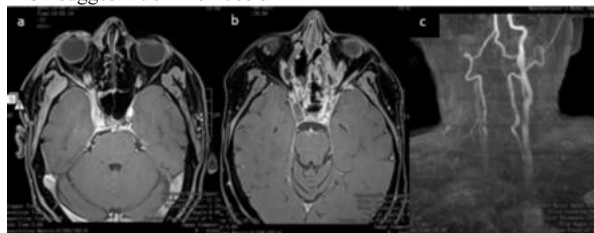


Fig 7: 41 year old case of ROCM a) b) postcontrast T1 axial with lack of enhancement of RT ICA suggestive of thrombosis c) TOF MRA of neck in same patient shows complete occlusion of ICA

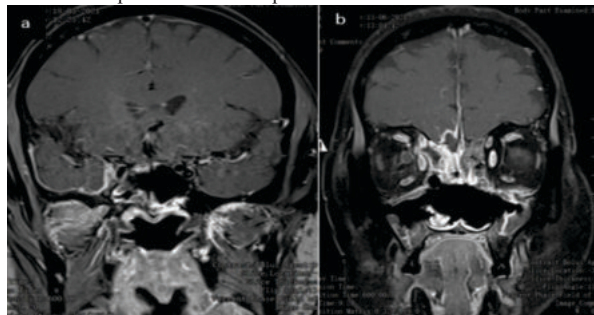


Fig 8: Intracranial Complications of ROCM Postcontrast T1 coronal

scan with a) dural involvement with enhancement of medial temporal b) Another patient of ROCM with evidence of focal cerebritis in right basifrontal region

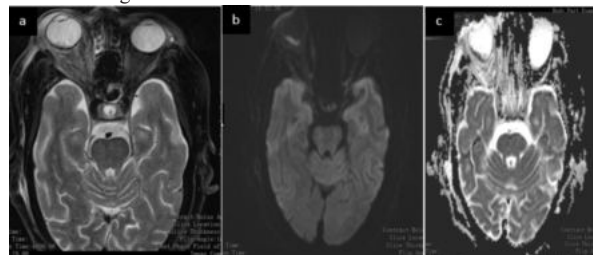


Fig 9: Complication of ROCM in a 52 year old patient with involvement of retinochoroid a) T2 axial shows extensive orbital involvement with subtle irregularity in globe on right side b) c) DWI shows diffusion restriction confirmed on ADC

Typical Signs for mycormycosis

Black turbinate sign caused due to devitalization of the sinonasal mucosa caused by mycotic vascular invasion in ROCM, was seen in contrast-enhanced sequence as focal lack of enhancement of the turbinate in contrast to the unaffected normally enhancing turbinates. This feature can aid in earlier detection of the disease^[5].

Guitar pick sign refers to the conical tenting and deformation of the posterior ocular globe suggesting increased intraocular pressure (orbital compartment syndrome) was seen associated with permanent visual loss and was associated with a poor prognosis.^[6]

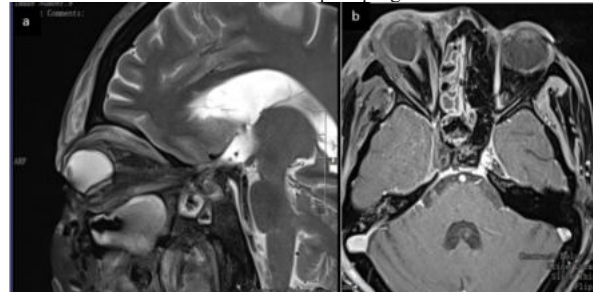


Fig 10: 26 year old diabetic & post covid patient with rhinocerebral mucormycosis a) T2 sagittal b) post contrast axial shows extensive orbital involvement with deformity of posterior globe with typical Guitar Pick Sign.

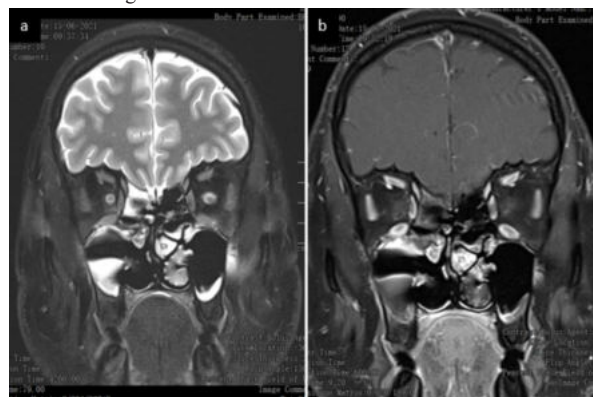


Fig 11: 32 year old post covid patient of angioinvasive mucormycosis a) coronal T2 b) postcontrast T1 shows non enhancement of left inferior turbinate suggestive of Black Turbinate sign : an early indicator of ROCM on MRI

MRI Signal Intensity and enhancement pattern

Most of the patients (80%) had isointense lesions relative to brain in T1-weighted images and hyperintense lesions in T2-weighted images. On Post contrast study, the lesions predominantly showed heterogeneous enhancement in 19 cases (63%) and rim enhancement with central nonenhancing areas was seen in 8 cases (26%). 2(6%) patients had mild enhancement and one case (5%) showed no enhancement. Dural enhancement was observed in three patients (10%) and intracranial enhancement suggestive of cerebritis was seen in another 3 patients (10%).

Surgical and medical management

Patients underwent endoscopic or open debridement under general anesthesia, with Orbital exenteration, ethmoidectomy and medial maxillectomy. More extensive debridement of necrotic tissue was performed as required according to surgical findings. All patients received amphotericin-B locally and parenterally along with systemic antibiotics.

DISCUSSION

Rhino-orbito-cerebral mucormycosis (ROCM) is a life threatening infection caused by phicomycetes class of fungi which commonly targets the immunocompromised patients. Patients presented with nonspecific symptoms of headache, low-grade fever, facial swelling and orbital or paranasal sinus syndrome. These patients developed symptoms commonly after 20 days of admission and management with steroids for moderate-severe COVID-19 which is considered as an aggravating factor in these cases. COVID-19 also leads to secondary infection by primarily causing immune dysregulation^[7]. Clinicians should be aware of secondary invasive fungal infections as a complication in this cohort of patients. ROCM arises from nasal and sinus mucosa and spreads rapidly to orbit and brain. Extensive angioinvasion is considered as the main cause leading to vascular thrombosis and tissue necrosis^[8]. Vascular involvement leading to vessel thrombosis and cerebral infarcts is the main reason behind the high morbidity and mortality attributed to mucormycosis. Fungal hyphae also tend to involve nerves and vessel wall leading to perineural spread and cavernous sinus invasion^[9]. Infiltration of the cavernous sinus and orbital apex causes reduction in visual acuity often leading to blindness. Intracranial involvement can cause narrowing of internal carotid artery leading to ischemic infarcts^[10], leptomenigitis and pachymenigitis. In cases with limited involvement of the paranasal sinuses, survival rates are between 50% and 80%^[11]. However, when cerebral involvement has occurred, mortality is greater than 80%. Because of its lethal nature, ROCM must be recognized early and treated aggressively.

Imaging helps in early diagnosis of ROCM and in evaluating the extent of disease. It thus plays a crucial role in timely intervention. CT scan demonstrates nodular mucosal thickening with absence of fluid levels, hyperdense content and erosion of bony sinus walls. MRI, however, is the modality of choice for evaluation of these patients as it provides better evaluation of intracranial and soft tissue involvement, skull base invasion, perineural spread and vascular obstruction. MRI demonstrates variable signal intensity depending on the sinus contents, due to iron and manganese in the fungal elements^[12]. Post contrast MRI shows extent of disease with spread to extrasinusoidal regions like involvement of orbit, infratemporal fossa, parapharyngeal region, masticator, buccal space, premaxillary and retroantral region. It thus guides the treating surgeon towards areas that need to be debrided.

Complications and vascular obstruction involving internal and common carotid arteries are seen well on TOF MRA, although slow flow on T2WI can suggest internal carotid artery invasion by the fungus^[10]. Evidence of leptomenigeal enhancement and involvement of brain parenchyma in the form of focal cerebritis can accurately be picked up by contrast MRI. Orbital complication like Optic neuritis is suggested by thickened and enhancing optic nerve. Cerebral infarctions are seen well on Diffusion weighted imaging which forms an essential sequence to be done in these patients. Cavernous sinus thrombosis as a complication of ROCM can be seen on plain MRI as loss of flow voids and on contrast scans as enhancement and bulging of the lateral wall of the sinus with intracavernous thrombosed ICA appearing as a filling defect.

Post operative MRI follow up scan is crucial to assess for evidence of residual disease and presence of complications.

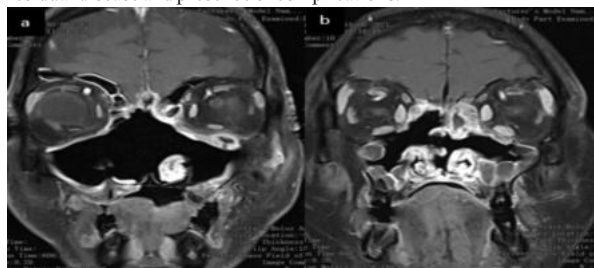


Fig 12: Post operative Follow up MRI postcontrast T1 coronal a)28

year old post operative case shows normal enhancing mucosa with no residual disease b) another patient on post op imaging reveals extensive residual disease with enhancing areas in both maxillary sinuses and orbits.

CONCLUSION

ROCM is thus an emerging rapidly disseminating fungal infection when associated with immunocompromised conditions and carry fatal prognosis with cavernous sinus involvement^[13]. Hence, radiologists play a crucial role to evaluate the extension and involvement of invasive fungal sinusitis which can lead to early diagnosis and timely management with antifungal agents. Preoperative MRI helps in providing a road map for surgical debridement so as to reduce morbidity and mortality. Follow up MRI assesses the residual disease load with monitoring of intracranial complications.

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