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ORIGINAL RESEARCH

Observational Study of Imaging Findings in COVID -19 Related Rhino-Orbito-Cerebral Mucormycosis – A Tertiary Care Center Study

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Abstract

Background: There has been a tremendous increase in number of cases of rhino-orbito-cerebral involvement with mucor in the COVID era, as reported from India. It is well established that management of ROCM involves early clinical and radiological diagnosis, reversal of underlying risk factors, prompt antifungal therapy and surgical debridement when indicated.

Materials &Methods: Multiplanar MR imaging and CT scan were performed for brain, orbit and paranasal sinuses. All the cases were assessed for involvement of the paranasal sinuses, nasal cavities, orbits and brain.

Results: 25 cases with ROCM were identified over 8 months. The mean age of the cases was 56.1 years. 18 of the 25 cases had a positive RT-PCR test result at the time of diagnosis with ROCM. 20cases had poorly controlled diabetes mellitus, 2 had a hematological malignancy, 2 had chronic kidney disease and 1 had ischemic heart disease. There was involvement of the paranasal sinuses, nasal cavities, orbits and brain inclusing necrosis in most of the cases. The number of cases identified during the interval is much higher than the numbers presenting in the prior 2 years during equivalent intervals than those reported in the literature in different settings in the pre-pandemic era.

Conclusions: Rhino-orbito mucormycosis can have aggressive necrosis of the involved paranasal sinuses and orbits with or without cerebral extension. Hence, the correct diagnosis is imperative as prompt antifungal drugs and surgical debridement can significantly reduce mortality and morbidity.

Key words: COVID-19, ROCM, Mucormycosis, Black turbinate sign, Guitar pic sign.

Introduction

Rhino-orbital-cerebral mucormycosis (ROCM) is a rare life-threatening invasive fungal infection that often occurs in immunocompromised individuals, with around 70% of the cases complicating a diabetic ketoacidosis (DKA) event.[1,2] The condition originates in the nose and paranasal sinuses but is often suspected following orbital spread, explaining its poor

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prognosis.[3]The infiltrating fungus destroys the surrounding bone and soft tissue through vascular thrombosis and subsequent tissue infarction and may reach the brain with fatal complications.[2]

The incidence of mucormycosis is often underestimated.[4] This could be attributed to the rarity of the condition, declining autopsy rates, occasional unavailability of confirmatory tissue biopsy for diagnosis, and scarcity of population-based studies.[4] Furthermore, most epidemiological studies report the incidence of all forms of mucormycosis combined (0.43–1.7 cases per million population) with no subgrouping specific for ROCM incidence.[4,5]Nevertheless, emerging reports[6,7] have described a rising trend in mucormycosis in the latest decades, which is hypothesized to reflect the growing populations with diabetes mellitus (DM), hematological malignancy, and bone marrow transplants.

Reports on ocular manifestations in patients with the novel coronavirus disease 2019 (COVID-19) describe self-limiting conjunctivitis[8]and rare neuro-ophthalmic manifestations that include optic neuritis and ocular motor cranial neuropathies.[9]We have observed an increased rate of ROCM cases in our hospital during COVID- 19 pandemic. We set out to identify if this were a true increase and, should it be, review the COVID-19 status of the patients, other associated comorbidities, and clinical manifestations.

Objective

To describe the imaging findings in Covid-19 related Rhino-orbito-cerebral Mucormycosis

Materials and Methods

Research protocol was submitted to Human Ethical Committee, Medical College, Thiruvananthapuram. Study was initiated after getting clearance from both the Human Ethical Committee and Research committee.

Study Design

Retrospective study – case series

Study setting

Department of Radiodiagnosis, Government Medical college, Thiruvananthapuram

Conduct of Study

All patients with clinical diagnosis of ROCM in covid19 who were referred to the Department of Radio diagnosis, as part of their routine management,were assessed for involvement of the paranasal sinuses, nasal cavities, orbits and brain. CT and MR imaging were performed with contrast given wherever appropriate. CT scans were performed on multislice (128 slice) Siemens machine using a routine paranasal sinuses protocol with 120 kV and 150–180 mA tube current. Intravenous contrast (low osmolar, non-ionic, 300 mg/ml Iodine content) was used routinely.

Multiplanar MR imaging was performed on 1.5 T Siemens MRI machines for brain, orbit and paranasal sinuses. T1 weighted, T2 weighted, fluid-attenuated inversion recovery (FLAIR) and post-contrast T1 weighted images were obtained. Diffusion weighted images were also obtained. All the cases are assessed for involvement of the paranasal sinuses, nasal cavities, orbits and brain.

On CT, partial/ complete sinus opacification, inflammatory changes, enhancement patterns and bony erosions are evaluated. On MRI, signal alterations in the mucosa and patterns of enhancement after intravenous contrast agent are evaluated. Involvement of the peri antral soft tissues, orbits, brain parenchyma and adjacent bones are also assessed. The presence of any vascular complication are also noted and described. The imaging findings are broadly

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categorized into five groups based on the extent of regional involvement, namely sino-nasal, periantral, orbital, bony, intracranial and vascular involvement.

Study Duration
8 months – from May 2020 to December 2020

Study tools
Structured proforma
CT scan
MRI scan

Sample size
All the cases referred to department of Radiodiagnosis for imaging from May 2020 to December 2020 are included in the study. There are approximately 25 cases. So 25 cases are included in the study.

Selection of study participants
Selection process: All patients referred to the Department of Radio diagnosis with clinical diagnosis of Rhino-orbito-cerebral Mucormycosis in severe covid19

Inclusion Criteria
Patient presenting with symptoms of sinusitis, facial pain or swelling, proptosis, or decreased vision,radiological evidence of bone destruction and orbit/brain infiltration and tissue biopsy with pathological evidence of tissue invasion, vessel occlusion, and non-pigmented non-/pauci-septate hyphae with variable width or the same typical fungal appearance in microbiological culture

Exclusion criteria
Patients in whom CT and MRI contraindicated.

Measurements and data collection
Procedure for measurements including process for standardization: Semi-structured questionnaire to collect data on socio demographic variables
Details of data to be collected: CT and MRI findings of ROCM

Statistical details
(data management, data analysis plan and major statistical results).
Data were entered in MS EXCEL worksheets
Analysis done using appropriate software
Qualitative variables will be expressed as percentages and proportions and studied by using Chi-square test.
Quantitative variables will be expressed in mean, standard deviation and confidence intervel and studied by using students t test.

Observation and Results
25 cases with ROCM were identified over 8 months from May 2020 to December 2020. 17 of which were male. The demographic and clinical data of the cases are detailed inTable1. The mean (SD) age of the cases was 57.4 years. 18 of the 25 cases (72%) had a positive SARS-CoV-2 RT-PCR test result at the time of diagnosis with ROCM. 4 cases (16%) tested negative for COVID-19 at the time of diagnosis but had a prior positive test record and had

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been admitted for treatment, with symptoms of ROCM appearing 2 days following discharge. The remaining 3 cases (12%) had negative SARS-CoV-2 RT-PCR results on diagnosis of ROCM and no prior record of positive COVID-19 testing. All patients concurrently positive for SARS-CoV-2 had moderate to severe disease and were treated for COVID-19 in accordance with the national guidelines for COVID-19.

No.	Age	Sex	Comorbidities	Diabetic control	Covid testing	Sinonasal involvement	Orbital involvement	Cerebral invasion	Debride-ment	Outcome
1	43	F	DM	Poor	Positive	+	+	+	+	Death
2	37	M	ALL	NA	Positive	+	+	+	+	Recovery
3	69	M	DM	Poor	Prior	+	+	+	_	Death
4	70	M	DM,CKD	Poor	Positive	+	+	+	+	Death
5	63	F	DM, IHD	Poor	Prior	+	+	+	+	Death
6	56	F	DM	NA	Prior	+	+	-	+	Recovery
7	51	M	DM	Poor	Negative	+	+	+	_	Death
8	61	M	DM	Poor	Negative	+	+	-	+	Recovery
9	47	F	ALL	Poor	Prior	+	+	+	+	Recovery
10	69	M	DM,HTN	Poor	Positive	+	+	+	+	Recovery
11	72	M	DM,CKD	Poor	Positive	+	+	-	-	Death
12	55	F	DM	Poor	Positive	+	+	-	+	Recovery
13	48	M	DM	Poor	Positive	+	+	+	+	Recovery
14	49	F	DM	Poor	Negative	+	+	-	+	Recovery
15	52	M	DM	Poor	Positive	+	+	+	+	Recovery
16	56	M	DM	Poor	Positive	+	+	-	+	Recovery
17	48	M	DM	Poor	Positive	+	+	-	-	Recovery
18	55	M	DM	Poor	Positive	+	+	+	+	Recovery
19	68	M	DM	Poor	Positive	+	+	+	+	Death
20	57	M	DM	Poor	Positive	+	+	+	-	Recovery
21	55	F	DM	Poor	Positive	+	+	+	+	Recovery
22	59	M	DM	NA	Positive	+	+	+	+	Recovery
23	63	F	DM	Poor	Positive	+	+	-	+	Recovery
24	68	M	DM	Poor	Positive	+	+	-	+	Recovery
25	65	M	DM	NA	Positive	+	+	-	+	Recovery

Table 1. Demographic and clinical data of the 25 cases presenting with rhino- orbito- cerebral mucormycosis (ROCM)

DM-Diabetes mellitus, CKD- Chronic kidney disease, ALL- Acute lymphoblastic leukemia, HTN-Hypertension, NA- Not applicable,M- Male, F- Female

18 of the 25 cases(72%) had poorly controlled diabetes mellitus, 2 cases(8%) had a hematological malignancy, 2 cases (8%) had chronic kidney disease and 1 case(4%) had ischemic heart disease. The number of cases identified during the interval is much higher than the numbers presenting in the prior 2 years during equivalent intervals than those reported in the literature in different settings in the pre-pandemic era.

The initial presenting signs of the cases were lid edema, conjunctival chemosis , diminution of vision, proptosis, facial edema, nasal crusts and total ophthalmoplegia. MRI is a valuable modality that can be used to diagnose mucormycosis infections involving sino-nasal region, orbits, and possible intracranial extension. The multiplanar capabilities of MRI with its superior soft tissue depiction are helpful in delineating the anatomical extent of disease as well as its complications.

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On radiological assessment (Figures 2,3,4,5), the imaging findings were sinonasal and orbital infiltration (including 'guitar pic' sign, cavernous sinus infiltration, internal carotid artery infiltration, and cerebral abscess. COVID-19 coinfection was neither associated with specific presenting signs of ROCM nor did it affect our management course. All cases received medical treatment for ROCM including measures to control the general condition, underlying risk factors, and complications, together with systemic antifungals and antibiotics to prevent secondary bacterial infection. 15 cases (60%) were fit to undergo surgical debridement, five of which (20%) had a non-salvageable eye globe on the affected side that was sacrificed during surgery. The final outcome was recovery and discharge in 18 patients (72%) and death due to complication in 7 patients (28%), three of which had COVID-19 and two had received systemic steroids.

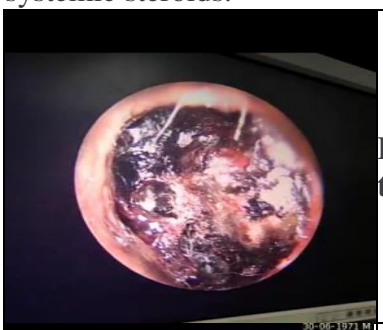

Figure 1: Endoscopic view demonstrating black necrotic tissue filling the right nasal cavity.

Figure 2: Axial non contrast CT reveals destructive sinonasal soft tissue mass

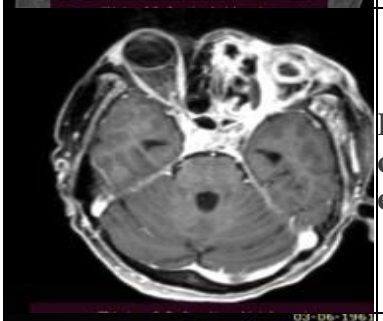

Figure 3: Contrast enhanced MRI showing orbital and cavernous sinus infiltration with lack of expected enhancement in left cavernous sinus.

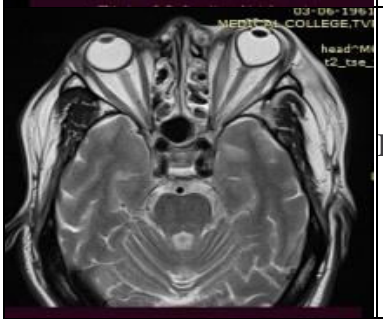

Figure 4: Axial T2WI showing 'Guitar pic sign' in left orbit

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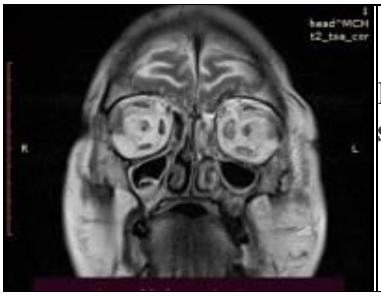

Figure 5: Coronal T2WI showing black turbinate signon left side

Discussion

We report the various imaging findings of ROCM in patients with covid 19 infection which were higher than those cases without covid 19 infection. Multiple case reports and series described ROCM—or invasive maxillofacial fungal infection-in SARS-CoV-2-positive patients but with no evidence of an actual spike in case numbers.

Possible implication of COVID-19 in the development of ROCM may include impaired host defenses against the fungus by viral-induced lymphopenia or the therapeutic use of corticosteroids and/or hydroxychloroquine, both likely to impair phagocytic immune-cell response, which is the major defense mechanism against mucormycosis.[2] It is worth noting that hydrocortisone was given for severe cases. Other implicated factors for COVID-19 in ROCM development may include aggravated disruption of blood sugar control and general debilitation in diabetic patients and/or late seeking of medical care during lockdown resulting in more DKA events.

There further remains the remote possibility that our reported spike is an incidental one, partly attributable to increased referral of complicated cases to our more-equipped center, However, 15 ROCM cases presenting over the period of6 months to a single center is still a high rate when viewed in the context of literature reports.

Imaging findings of mucormycosis include mucosal thickening and/or opacification of the involved paranasal sinuses. Majority of the lesions appear hypointense on T1-weighted images and variable to hyperintense on T2-weighted images. Low signal intensity of fungal elements on T2-weighted images along with restricted diffusion on DWI may be seen. Hypertrophy of nasal turbinates with nasal secretions is seen with nasal involvement. Post-contrast enhancement can be seen in the thickened mucosa and involved tissues. However, areas of non-enhancing soft tissue may be seen within the affected turbinates and/or paranasal sinuses, known as the “black turbinate sign”. This sign may help in the early detection of nasal mucormycosis.[10]

Extrasinus extension into orbital compartment, face is commonly encountered and may further extend into the infratemporal fossa, cavernous sinus, skull base, and intracranial compartment. Post-treatment follow-up MRI may be needed in some cases.

Conclusions

Rhino-orbital mucormycosis can have aggressive necrosis of the involved paranasal sinuses and orbits with or without cerebral extension. Hence, the correct diagnosis is imperative as prompt antifungal drugs and surgical debridement can significantly reduce mortality and morbidity. There is an increased rate of ROCM cases presenting to our center during COVID-19 pandemic.

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