To Determine The Role Of Imaging Findings On Computed Tomography (CT) And Magnetic Resonance Imaging (MRI) Predictive Of Acute Invasive Rhino-Orbito-Cerebral Mucormycosis (ROCM) In COVID 19 Patients

Dr. Tapan P. Solanki*, Dr. Avni M .Patel, Dr. Sahil N. Shah**, Dr. Vikas Kagathara*, Dr. Ujas Dhakan*****

*3Rd Year Resident, **Assistant Professor, ***1St Year Resident, Department Of Radio-Diagnosis; SVP Hospital; Smt. NHL Municipal Medical College; Ahmedabad

Abstract: Background: There is a sudden rise of fungal infection with coronavirus disease. This is attributed to the immunomodulation by the disease and the drugs used, diabetes mellitus, steroid use, oxygen inhalation using dirty water, use of zinc and iron supplements, etc. Early diagnosis and prompt medical and surgical intervention is the mainstay of treatment. This can greatly reduce the high morbidity and mortality associated with this disease. The objective of the retrospective study is to describe the imaging findings of acute invasive rhino-orbito-cerebral mucormycosis (ROCM) in 58 patients with severe acute respiratory syndrome coronavirus 2, from SVP hospital with proven mucormycosis. Special emphasis is placed on the signal patterns of sinonasal mucosa, the earliest and most common findings. Material And Methods: We report the sinonasal, orbital and neuroimaging findings in patients of suspected acute invasive ROCM. A total of 58 patient's scans were analyzed. The study comprises cases performed at two different imaging modalities and a tertiary care hospital from March 23, 2021 to September 1, 2021. All the patients had positive reverse transcriptase polymerase chain reaction test for severe acute respiratory syndrome coronavirus 2 and were hospitalized with clinically severe disease as per the guidelines laid down during the second wave in India. They were on intravenous steroids and oxygen. Thirty patients (52%) had diabetes mellitus. All of them presented with headache, facial and/or orbital pain, periorbital puffiness with decreased vision, during the course of treatment. CT or MRI examination of the paranasal sinuses, orbits and brain was done, with intravenous contrast wherever possible. The presence of mucormycosis was confirmed by histological diagnosis in all of them following clinico-radiological diagnosis of acute invasive ROCM. Result: Computed tomography (CT) and magnetic resonance imaging (MRI) of 58 patients showed most commonly involved sinuses as maxillary and ethmoid sinuses together. Sino-nasal mucosal thickening was the most common finding. Periantral infiltration preceded orbital, cerebral complications, with grossly intact bones. Sinus wall erosions were seen in only patients and maxillary alveolar arch erosion were frequent findings. CT showed hypodense soft tissue thickening or fat stranding as the predominant finding in involved areas, while MRI showed T2 iso- to hyperintense mucosal thickening with T2 hypointense component as the main finding. Conclusion: MRI is better at demonstrating early mucosal abnormalities, turbinate necrosis, devitalized tissues, orbital apex involvement and intra-cerebral extension. Imaging findings of inflammatory tissue infiltration adjacent to the paranasal sinuses in premaxillary, retroantral fat, facial muscles, pterygopalatine fossa, temporal, infratemporal fossa and extraconal orbital- fat along with typical patterns of sinonasal mucosal thickening should raise the suspicion of acute invasive fungal etiology given the short duration of history and immunocompromised status. High incidence of periantral and orbital extension of the disease is suggestive of acute invasive form of fungal infection. Also the rapidly progressive inflammatory changes without much bone involvement should suggest the suspicion of ROCM. Bony, cerebral and vascular involvements are relatively late complications. [Solanki T Natl J Integr Res Med, 2022; 13(4): 01-06, Published on Dated:10/07/2022]

Key Words: Rhino-Orbito-Cerebral Mucormycosis (ROCM), COVID-19 Infection, Periantral Extension, Sinonasal Imaging

Author for correspondence: Dr. Sahil N. Shah, Assistant Professor, Department Of Radio-Diagnosis; SVP Hospital; Smt.NHL Municipal Medical College; Ahmedabad. E-Mail: tapansolanki77@gmail.com Mobile: 7990982658

Introduction: Coronavirus disease 2019 (COVID-19), attributed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a global pandemic by the World Health Organization (WHO) in March 2020[1]. A myriad of potential complications from COVID-19 are being increasingly appreciated, including the heightened vulnerability to secondary bacterial and fungal infections. The immune dysregulation associated with COVID-19 is further aggravated

by concomitant medical conditions such as diabetes mellitus, and the widespread use of immunosuppressive agents and broad-spectrum antibiotics[2]. In addition, COVID-19 patients are more susceptible to develop secondary infections if they have decompensate pulmonary functions or require invasive mechanical ventilation. The rate of in-hospital secondary bacterial and fungal infection has been reported to be approximately 8%.Previous reports observed that fungal infections were more likely to develop during the more advanced stages of COVID-19 infection with substantially higher mortality among patients with a fungal co-infection[3].

Mucormycosis is known to affect immunocompromised patients. It is an opportunistic infection leading to invasion of blood vessels by fungal hyphae, causing infarction and necrosis of a variety of end-organ host tissues[4]. Rhino-orbital infection with the mucorales species of fungus portends a poor prognosis with a mortality rate reaching 50%, even with appropriate treatment. Since the start of COVID-19 pandemic, there has been a renewed interest about secondary fungal infections. The Indian subcontinent has witnessed a sudden and alarming surge in the number of mucormycosis cases in patients of COVID-19.

There needs to be a heightened awareness about mucormycosis among patients with COVID-19, since both conditions in combination may lead to significant morbidity and mortality. However, there has been a tremendous increase in the 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. Ours is a descriptive observational study.

Aims And Objectives: To determine the role of imaging findings on computed tomography(CT) and magnetic resonance imaging (MRI) predictive of acute invasive rhino-orbito-cerebral mucormycosis (ROCM) in COVID 19 patients.

Material & Methods: This is a descriptive observational study. We report the sinonasal, orbital and neuro imaging findings in patients of suspected acute invasive ROCM. A total of 58 patient's scans were analyzed. The study comprises cases performed at two different imaging modalities and a tertiary care hospital from March 23, 2021 to September 1, 2021. All the patients had positive reverse transcriptase polymerase chain reaction test for severe acute respiratory syndrome coronavirus 2 and were hospitalized with clinically severe disease as per the guidelines laid down during the second wave in India. They were on intravenous steroids and oxygen. Thirty patients (52%) had diabetes mellitus. All of them presented with headache, facial and/or orbital pain, periorbital puffiness with decreased vision, during the course of treatment. CT or MRI examination of the paranasal sinuses, orbits and brain was done, with intravenous contrast wherever possible. The presence of mucormycosis was confirmed by histological diagnosis in all of them following clinico-radiological diagnosis of acute invasive ROCM.

Inclusion Criteria: All patients with COVID-19 infection proved positive by RT-PCR who underwent CT PNS and MRI PNS with brain and histopathological proven invasive mucormycosis. No age or sex predilection.

Exclusion Criteria: We excluded patients with unavailable RT-PCR results and negative biopsy reports for mucormycosis.

Imaging: CT scans were performed on multislice Philips machines using a routine paranasal sinuses protocol with 120 kV and 200 mA tube current. Multiplanar MR imaging was performed on 3.0 T Siemens MRI machines for brain, orbit and paranasal sinuses. T1 weighted, T2 weighted, fluid attenuated inversion recovery (FLAIR). Diffusion weighted images were also obtained. All the cases were assessed for involvement of the paranasal sinuses, nasal cavities, orbits and brain.

On CT, partial/ complete sinus inflammatory changes and bony erosions were evaluated. On MRI, signal alterations in the mucosa were evaluated. Involvement of the periantral soft tissues, orbits, brain parenchyma and adjacent bones was also assessed. The imaging findings were broadly categorized into groups based on the extent of regional involvement, namely sino-nasal, periantral, orbital, bony and intracranial and vascular involvement. Descriptive statistical methods were used for analysis.

Figure 1: Periantral Fat Stranding With Hypodense Mucosal Thickening With Hyperdense Component In Right Maxillary Sinus (Red Arrow Suggests Periantral Fat Stranding Or Involvement) , (Yellow Arrow Indicates Normal Normal Periantral Fat On Left Side) (On Axial Image Of CT PNS).

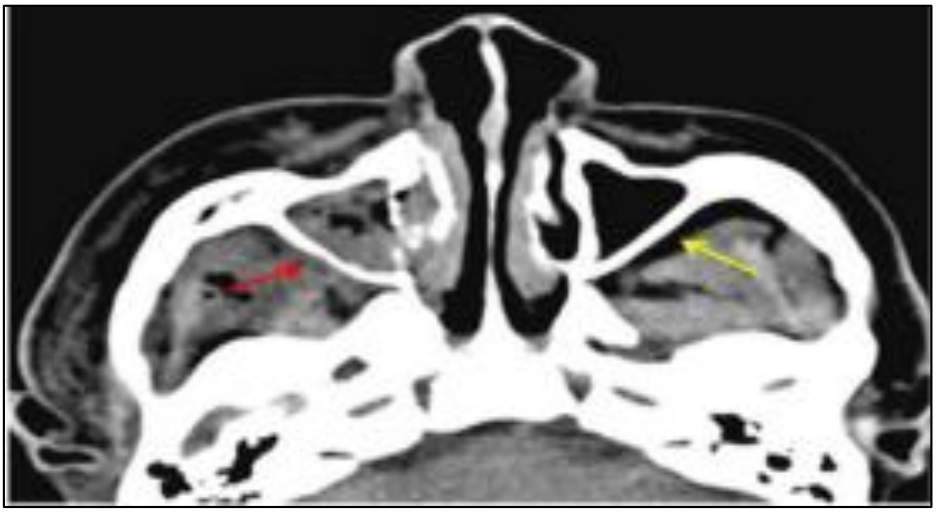


Figure 2: Hypodense Mucosal Thickening In Left Maxillary Sinus With Erosion Of Floor Of Left Orbit (Red Arrow) (On Coronal Images Of CT PNS).

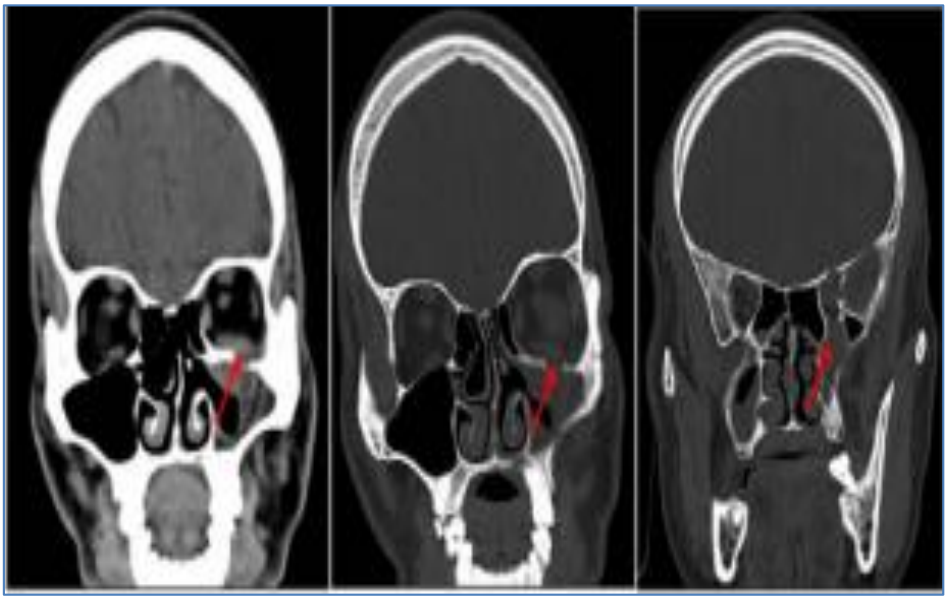


Figure 3: Hyperintense Mucosal Thickening (Red Arrow) With Hypointense Contents (Devitalised Tissue) (Green Arrow) In Right Sphenoid Sinus (On Axial T2WI).

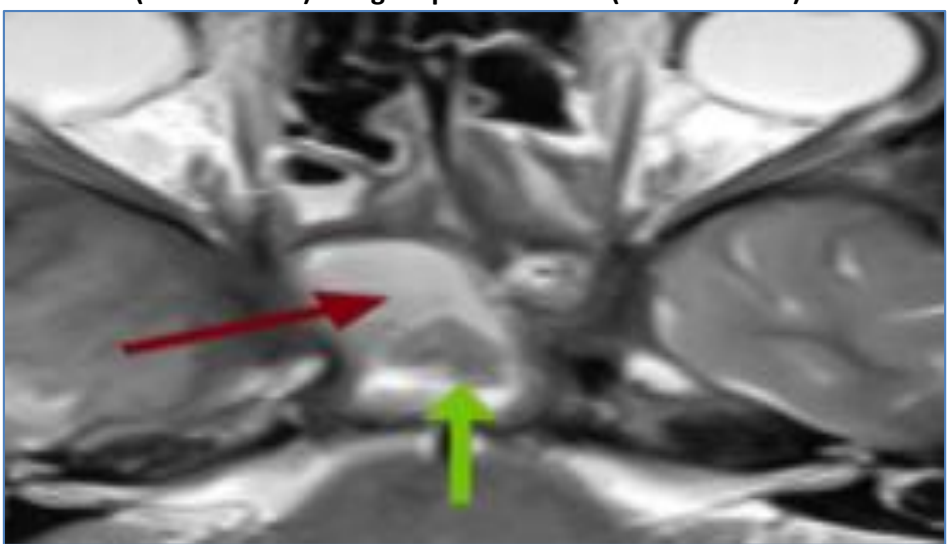
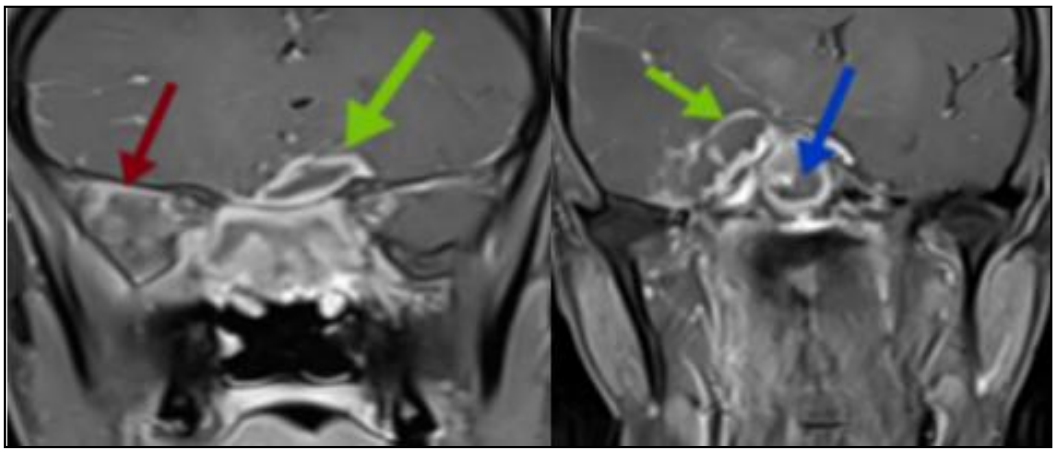
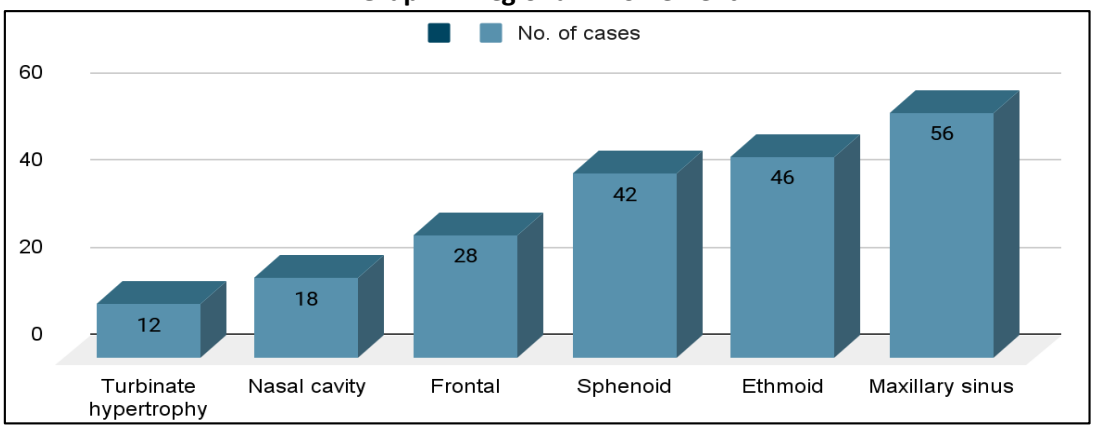


Figure 4: Intracranial Extension In Form Of Pachymeningeal Enhancement In Right Frontal Region And Peripherally Enhancing Abscess In Midline (Green Arrow) And Non-Enhancing Hypointense Component (Blue Arrow) In Right Sphenoid Sinus. (On Coronal Post Contrast T1FS Images).

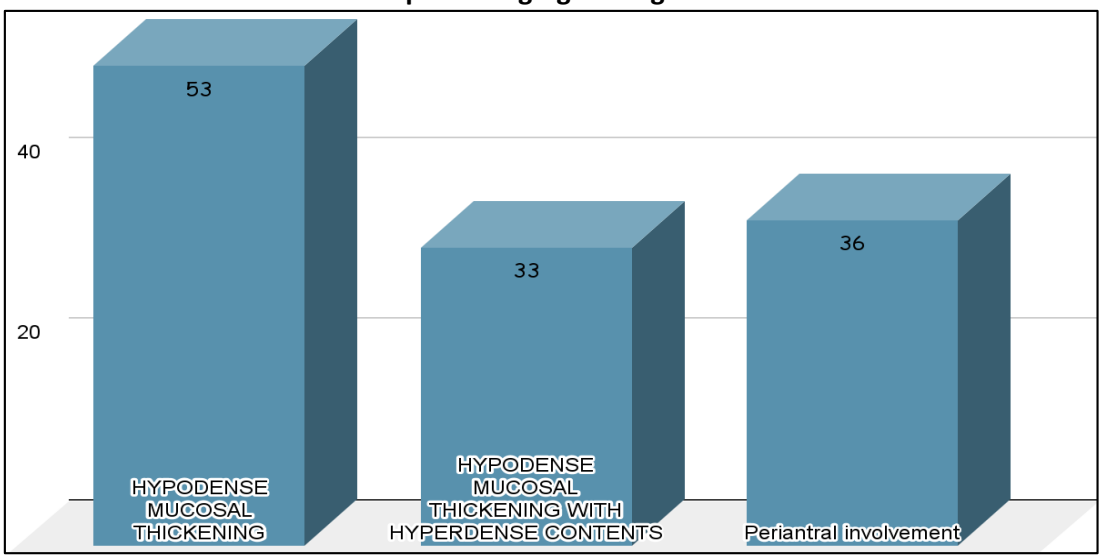


Results: Computed tomography (CT) and magnetic resonance imaging (MRI) of 58 patients showed most commonly involved sinuses as maxillary and ethmoid sinuses together. Sino-nasal mucosal thickening was the most common finding. Periantral infiltration preceded orbital, cerebral complications, with grossly intact bones. Sinus wall erosions were seen in only patients and maxillary alveolar arch erosion were frequent findings. CT showed hypodense soft tissue thickening or fat stranding as the predominant finding in involved areas, while MRI showed T2 iso- to hyperintense mucosal thickening with T2 hypointense component as the main finding[5].

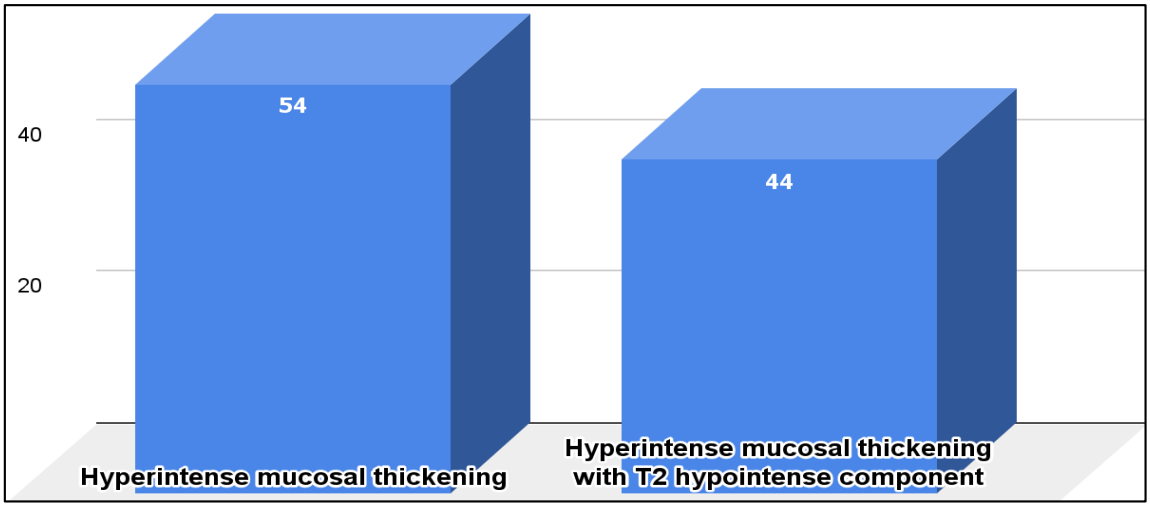
Graph 1: Regional Involvement



Graph 2: Imaging Findings of CT



Graph 3: Imaging Findings of MRI (No. Of Cases)



Discussion: our study, the majority of the patients (60%) were between 35 –60 years of age. Acute invasive ROCM can progress in a few hours to days with orbital and CNS involvements, it can be as high as 50–80%. In a setting of COVID-19, 24 % mortality. In our study, the patients with intracranial involvement or extensive orbital involvement or bilateral sino-nasal extension. The low mortality in our series may be the result of early detection of the disease due to high index of suspicion or already hospitalized status of the patients. Imaging helps in early diagnosis, assessing the extent of involvement and diagnosing complications.

This can help in guiding debridement and further medical and surgical planning. Here, the differential diagnosis which could be considered includes bacterial infection/cellulitis, inflammatory pseudotumor, paranasal sinus tumor, Grave's disease, carotico-cavernous fistula and cavernous sinus thrombosis. However, in bacterial etiology, blindness is a much later finding and early visual loss would favor the diagnosis of ROCM. Also the rapidly progressive inflammatory changes without much bone involvement should suggest the suspicion of ROCM[6]. The final diagnosis, however, rests on histopathology.

There is overexpression of inflammatory cytokines, impairment of cell-mediated immune response and decreased CD4+T and CD8+T cell counts in most of the COVID-19 patients, indicating their susceptibility to fungal co-infection. Studies also show that SARSCoV and SARS-CoV-2 belong to the same species and have similar biological and clinical characteristics and prevalence. Based on the studies on SARS in 2003, it was found that the incidence of fungal infection in SARS patients was 14.8–27% . Also, fungal infection was accounted for as the main cause of death in SARS patients, ranging up to 25–73.7% of death. This makes it all the more important for early identification of concomitant fungal infections in patients suffering from COVID-19. There were few limitations in our study. Firstly, we had a limited number of patients. Secondly, contrast enhanced MRI could not be performed in all the cases.

Limitations: Our study has few limitations; first, a retrospective study was done in one center and larger multicentric studies are needed to further understand the nature of this novel complex illness. We did not include patients who are operated for sinus surgery.

Conclusion: Early diagnosis and prompt medical and surgical intervention is the mainstay of treatment. Early clinical signs are often underappreciated, but prompt imaging may help in timely diagnosis. CT and MRI are the imaging tools that can assess the complete extent of disease.

MRI is better at demonstrating the extra-sinus, orbital, intracranial and vascular complications. Periantral infiltration and extraconal orbital extension even without bony erosion is a significant observation in acute invasive form.

Awareness and careful attention should be given to the subtle but often present radiological features of sinonasal mucosal thickening. MRI is better at demonstrating early mucosal abnormalities, turbinate necrosis, devitalized tissues, orbital apex involvement and intra-

cerebral extension. Imaging findings of inflammatory tissue infiltration adjacent to the paranasal sinuses in premaxillary, retroantral fat, facial muscles, pterygopalatine fossa, temporal, infratemporal fossa and extraconal orbital- fat along with typical patterns of sinonasal mucosal thickening should raise the suspicion of acute invasive fungal etiology given the short duration of history and immunocompromised status. High incidence of periantral and orbital extension of the disease is suggestive of acute invasive form of fungal infection[7,8].

Also the rapidly progressive inflammatory changes without much bone involvement should suggest the suspicion of ROCM. Bony, cerebral and vascular involvements are relatively late complications.

Abbreviations: ROCM: Rhino-orbito-cerebral mucormycosis; COVID-19: Coronavirus disease-19; RT-PCR: Reverse transcriptase polymerase chain reaction; SARS-CoV2: Severe acute respiratory syndrome corona virus 2; CT: Computed tomography; MRI: Magnetic resonance imaging.

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