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Imaging of COVID-19 Patients to assess predisposing factors causing mucormycosis

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***Abstract*---**Introduction: With the second wave of Covid 19, the incidence of mucormycosis has seen an upsurge in patients recovered from Covid 19 infection. Aims & Objectives: The present study aims to describe the various symptoms reported by the patients and to describe the various CT findings in the patients suffering from Mucormycosis. Materials and methods: This prospective study was done on 21 post Covid cases from May 2021 to July 2021 at Department of Radiology, VMKV Medical College & Hospitals. Patients who have presented with chest complaints and symptoms of sinusitis such as facial pain, headache, nasalblock, orbital swelling and pain were subjected to CT-Chest, CT-PNS. Imaging findings were correlated with clinical history and findings. Results: Radiological findings showed involvement of ethmoid 19/21(90.78 %) maxillary 17/21 (80.95 %) sinus, followed by sphenoid13/21 (61.90%) and frontal 6/21(28.57 %).Out of 2 patients studied, 15 patients (71.43%) had type 2 diabetes mellitus, 5(23.81%) patients had chronic renal failure, 5(23.81%) patients developed acute renal failure and 2(9.52%) patients received immunosuppressive therapy due to myelodysplastic syndrome. Conclusion: Early diagnosis, control of predisposing factors prompt initiation of antifungal therapy and radical debridement of involved sinuses are very essential for improving outcomes.

***Keywords*---**COVID-19, paranasal sinuses, ROM (Rhino orbital mucormycosis).

Introduction

Covid 19 is associated with significant increase in secondary fungal infection due to immune system dysfunction. Covid 19 patients on prolonged hospitalization, admitted in ICU or on ventilator are more likely to present with fungal co infection.[1] The widespread use of corticosteroids for Covid 19 treatment may further allows opportunistic fungal infections.[2] Mucormycosis is a potentially fatal fungal infection affecting predominantly immunosuppressed patients. Patients with uncontrolled diabetes, hematological carcinomas or recipients 'of organ transplantation are more vulnerable to Mucormycosis [3,4] In susceptible patients, mucormycosis is characterized by direct invasion with marked tissue necrosis of adjacent structures followed by angioinvasion from the nasal and sinus mucosa into the orbit and brain.[5]

SARS COV 2 infection impairs the function of pancreatic beta cells, thereby resulting in ketoacidosis. Patients with ketoacidosis are at increased risk of developing rhinocerebral Mucormycosis.Mucorales depends on the host iron for their metabolic requirements. Hence the acidic pH of diabetic ketoacidosis and high free iron may predispose to rhino cerebral Mucormycosis. Impaired phagocytic action, increased interleukins (IL-1 and IL-6) along with tumor necrosis factor-alfaand persistent lymphopenia may also contribute to increased susceptibility to Mucormycosis among Covid 19 patients. [3,5]

In case of delayed diagnosis, the prognosis of Mucormycosis is relatively poor in immunocompromised patients. Without early identification and treatment, Mucormycosis can lead to intra orbital and cerebral complication. Imaging modalities can help clinicians in proper diagnosis, monitor the disease status and to predict the prognosis of affected patients.[6].

Though Mucormycosis was know for a longer period of time, the present pandemic of COVID infection waves had led to a parallel increase in Mucormycosis cases. The challenging factors were their atypical presentations. The present study aims to shed some light to the different types of presentation that Mucormycosis get presented among the COVID 19 patients. The objective of present study was to describe the various symptoms reported by the patients and to describe the various CT findings in the patients suffering from Mucormycosis.

Materials and Methods

Study design: retrospective hospital based descriptive study.
Study period: 2 months
Study population: Patients admitted to the hospital and diagnosed with Mucormycosis.

Inclusion criteria

- Patients who had been diagnosed to have Mucormycosis.
- Patients who are willing for CT-PNS screening.

Exclusion criteria

- Patients who are not willing for study.
- Patients who are claustrophobic.

Study tool: A semi structured pretested interview schedule.

- CT was done using 16 SLICE MULTIDETECTOR CT (GE Revolution ACTs).
- MRI was done using SIEMENS 1.5 TESLA Scanner.

All the patients who had fulfilled the inclusion criteria had been included into the study and subjected to an interview initially. During which the data on sociodemographic characteristics and more detailed history on symptoms were collected. The collected data were entered into the interview schedule. Following the interview to all the participants, CT – Chest and CT – PNS were taken. The findings of whish were also entered into the interview schedule. The completed interview schedule thus obtained for each patient were recorded and numbered individually for future reference. Further evaluation was done with the help of MRI if needed.

Statistical analysis

All the data thus collected were entered into Microsoft excel 2019 spread sheet and the master chart was made. The master chart was then imported into SPSS (Statistical software for social sciences) software 19 version for statistical analysis. Both quantitative and qualitative data were present in the variables collected. The quantitative variables were expressed using mean and standard deviation, while the qualitative variables were expressed using percentages and proportions.

Results

This study included 15(71.43%) men and 6(28.57%) women, with mean age of 73.1±7.7 years (range: 61-88 years). 15 patients (71.43%) had type 2 diabetes mellitus, 5(23.81%) patients had chronic renal failure, 5(23.81%) patients developed acute renal failure and 2(9.52%) patients received immunosuppressive therapy due to myelodysplastic syndrome. All these patients had severe COVID 19 associated ARDS and were on treatment with steroids. Elevated D-dimer value was observed for all patients. All patients received heparin therapy. All 21 patients were diagnosed with mucormycosis during COVID 19 treatment and time interval between COVID 19 diagnosis and mucormycosis diagnosis was 10 to 25 days.All these patients were treated in ICU due to ARDS caused by Covid 19 and all tested RTPCR positive.Left eye was involved in 12 patients (57.14%) and right eye was involved in 10 (47.62%) patients (Table1). The common presenting symptoms were proptosis 21/21(100%), conjunctival hyperemia 18/21(85.71%), decreased vision 6/21(28.57%), orbital pain 18/21(85.71%), ptosis 14/21 (66.67%), endophthalmitis 12/21 (57.14%) (Fig:1)

Table 1: Demographic and clinical characteristics of Covid 19 patients with rhinocerebral mucormycosis

Age (years) Gender/eye involved	Systemic diseases	Predisposing medications	CT Chest (severity score)	Involved PNS	Outcome
73/F/Right	HTN/DM	IV.Dexa (5 days) Tocilizumab (5 days)	CORADS 6 SS: 5/25	Maxillary, ethmoid, frontal	Success
80/M/Left	ARF/DM	IV.Dexa (7 days)	CORADS 6 SS: 11/25	Ethmoid, sphenoid	Success
60/M/Right	HTN/DM/CRF	IV.Dexa (6 days) Tocilizumab (5 days)	CORADS 6 SS:18/25	Maxillary, ethmoid, sphenoid, frontal	Failure
72/M/Left	HTN/COPD	IV.Dexa (9 days)	CORADS 6 SS: 7/25	maxillary	Success
63/M/Left	MDS	IV.Dexa (6 days) Tocilizumab (5days)	CORADS 6 SS: 5/25	Maxillary, ethmoid, sphenoid, frontal	Success
60/M/Left	ARF/CAD/HTN	IV.Dexa (9 days)	CORADS 6 SS: 20/25	ethmoid, sphenoid, frontal	Failure
74/F/Right	DM/HT/AF	IV.Dexa(9 days)	CORADS 6 SS: 15/25	Maxillary, ethmoid, sphenoid	Success
74/M/Left	HTN/DM/CRF	IV.Dexa (6 days) Tocilizumab (5days)	CORADS 6 SS: 3/25	Maxillary, ethmoid.	Failure
84/M/Left	DM	IV.Dexa (10days)	CORADS 6 SS: 12/25	Maxillary, ethmoid	Success
70/M/Right	HTN/DM	IV.Dexa (6 days) Tocilizumab (5days)	CORADS 6 SS: 13/25	Maxillary, ethmoid, sphenoid	Success
78/M/Right	HTN/DM/ARF	IV.Dexa (7days) Tocilizumab (5days)	CORADS 6 SS: 7/25	Maxillary, ethmoid, frontal	Success
61/M/Right	DM/CRF	IV.Dexa (8days)	CORADS 6 SS: 12/25	Maxillary, ethmoid, sphenoid, frontal	Failure
59/F/Left	DM	IV.Dexa (9 days)	CORADS 6 SS: 5/25	Maxillary,	Success
62/M/Right	MDS	IV.Dexa (6 days) Tocilizumab (5days)	CORADS 6 SS: 9/25	Maxillary, ethmoid, sphenoid, frontal	Success
66/F/Right	DM	IV.Dexa (9 days)	CORADS 6 SS: 10/25	Ethmoid, sphenoid, frontal	Success
60/M/Left	CRF	IV.Dexa (9 days)	CORADS 6 SS: 2/25	Maxillary, ethmoid,	Success
80/F/Right	DM	IV.Dexa (10days)	CORADS 6 SS: 12/25	Maxillary, ethmoid, sphenoid	Success
59/M/Left	HTN/ARF	IV.Dexa (6days) Tocilizumab (5days)	CORADS 6 SS: 7/25	Maxillary, ethmoid,	Success
63/M/Right	DM/CRF	IV.Dexa (9days)	CORADS 6 SS: 10/25	Maxillary, ethmoid, sphenoid,	Success
65/F/Left	DM/ARF	IV.Dexa (8days)	CORADS 6	Maxillary,	Failure

			SS: 8/25	ethmoid,	
70/M/Left	DM	IV.Dexa (10days)	CORADS 6 SS: 5/25	Ethmoid, sphenoid	Success

Time interval between onset of symptoms and diagnosis of rhino orbital mucormycosis was 1 week. Fungal culture yield growth in all patient samples and KOH mount showed presence of fungal elements.CT chest was obtained to assess the percentage of involvement of lung in covid 19 patients. All patients showed multifocal, bilateral and peripheral ground glass opacities with posterior segment predominance and few patients had traction bronchiectasis and dilatation of vessels at the area of ground glass opacities. Severity on CT was estimated by percentage of involvement of each lobe.CT scan and/ or MRI demonstrated paranasal sinusitis, and most commonly involved were ethmoid 19/21(90.78%) maxillary 17/21 (80.95%) sinus, followed by sphenoid 13/21 (61.90%) and frontal 6/21(28.57 percent) (Table :1).Visual acuity improved in 4 patients.

Figure 1: Presenting symptoms of Covid 19 patients with rhinocerebralmucormycosis

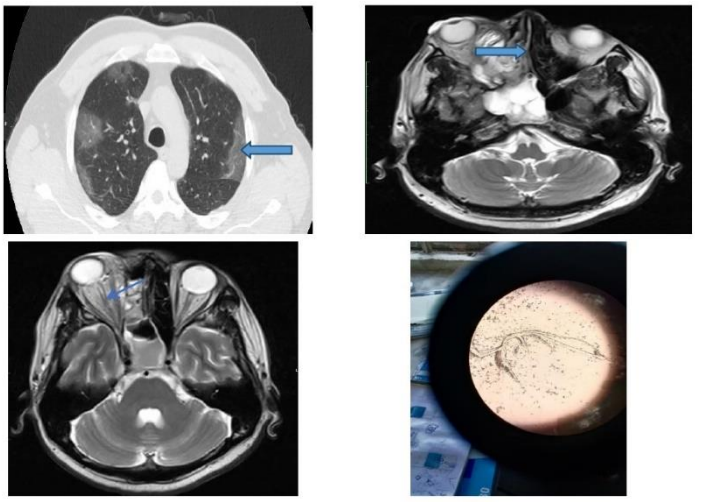

Figure 2: A 50 Years male patient CT Chest shows bilateral diffuse GGO, MRI: mucosal thickening with T2 hypointensity noted within the right maxillary sinus, ethmoidal sinus, nasal cavity and bilateral sphenoid sinuses. Minimal mucosal thickening noted in the right frontal sinus.Right orbit: intra and extraconal fat stranding noted. Medial rectus, inferior rectus and superior oblique muscles appears bulky. Minimal collection noted along the medial wall of right orbit. Proposes of the right eyeball with pre-septal edema. KOH Mount: Shows fungal elements.

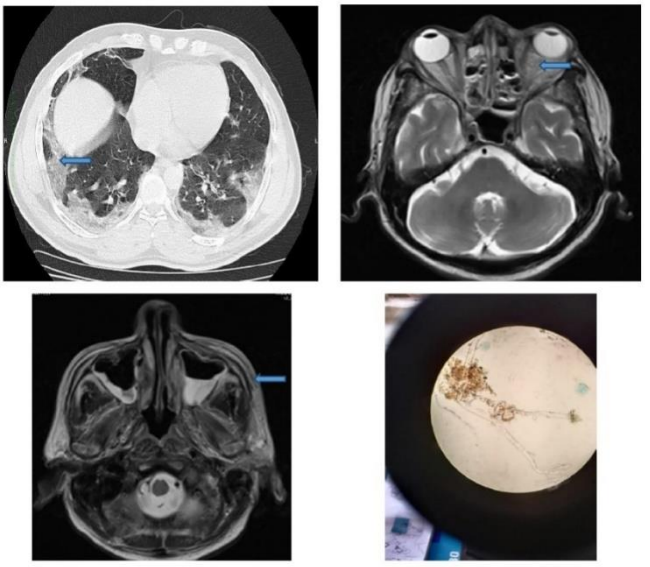

Figure 3: A 60 years old male, CT chest: diffuse bilateral ggo (subpleural), MRI: Mucosal thickening with T2 low signal areas noted in right superior turbinate of nasal cavity and moderate mucosal thickening with T2 low signal areas noted in B/L ethmoid, maxillary, and left frontal sinuses. Ill defined enhancing soft tissue with ebema noted in inferomedial extraconal space of B/L orbit, more in left orbit with thickening of bilateral medial and inferior recti. KOH mount: Fungal elements are seen clearly.

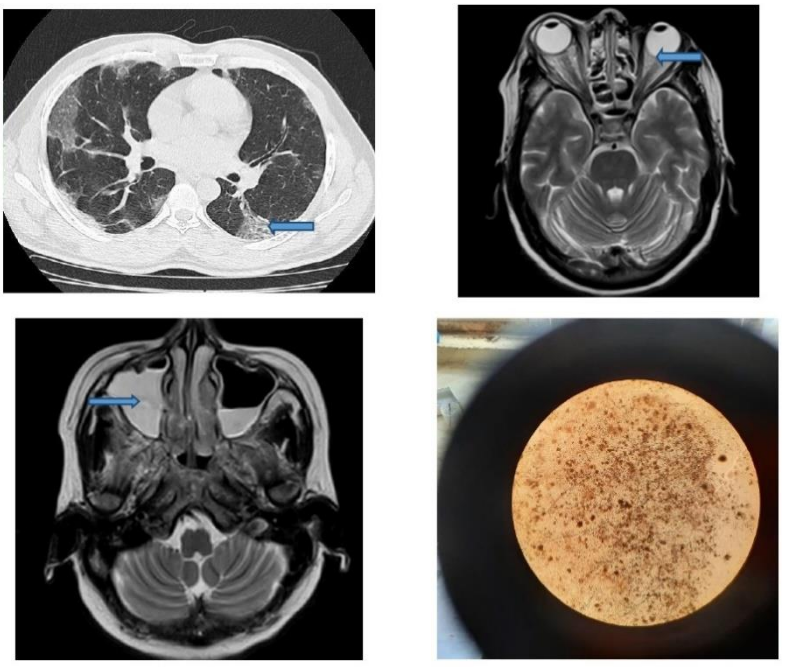

Figure 4: 65 years male CT chest: diffuse bilateral GGO (periphery), MRI: Mild right orbital proptosis. Moderate edema in intra and extraconal space of the right orbit with associated thickening of right extraocular muscles. Subtle edema in extraconal space of left orbit around the left inferior rectus muscle.Above findings are in favour of sino nasal fungal infection with bilateral orbital cellulitis R > l. Koh mount: Fungal elements are seen clearly.

Discussion

With the advent of second wave, rhino orbital mucormycosis in Covid patients has increased widely. Mostof the people affected by severe COVID-19 have other predisposing conditions such as type 2 diabetes mellitus, hypertension etc.Critically ill COVID-19 patients are candidates for very high-risk rhino orbital mucormycosis[5]. The present study was hospital based descriptive study carried out with the objective of describing the symptoms most commonly occurred among those suffered from mucormycosis infections and the pattern radiological findings in them.

In the present study,15 patients (71.43%) had type 2 diabetes mellitus. Similar study reports from Indian have showed 61.4% Covid 19 patients with diabetes as comorbidity. Patients with uncontrolled diabetes are more prone to opportunistic infection[8,9]. Singh AK et al also reported that the presence of diabetes as a comorbid condition among those suffered from COVID had a positive association with the development of Mucormycosis[10]. The above association could be due to the fact that the diabetics can become immunocompromised over a period of time.

In our study the common presenting symptoms were proptosis 21/21(100%), conjunctival hyperemia 18/21(85.71%),decreased vision 6/21(28.57%), orbital pain 18/21(85.71%), ptosis 14/21 (66.67%), endophthalmitis 12/21 (57.14%). A

similar study by Nurettin Bayram et al have reported rhinocerebralmucormycosis with presenting symptoms and signs asproptosis (100%), ophthalmoplegia (63.6%), orbital pain (81.8%), conjunctival hyperemia or chemosis (81.8%), ptosis (63.6%), fixed and dilated pupil (63.6%), vision loss (63.6%), endophthalmitis (54.5%) and decreased vision (27.3%). frequency of endophthalmitis. Increased frequency of endophthalmitis was reported in non COVID-19 studies. (11,12). Another study by Al-Tawfiq JA et al in the year 2021 reported that rhinocerebral and rhinoorbital mucormycosis were reported in higher frequency among the cases admitted[13].

The most commonly involved sinuses were ethmoid 19/21(90.78%), maxillary 17/21 (80.95%) sinus, followed by sphenoid 13/21 (61.90%) and frontal 6/21(28.57%). A study conducted by Gupta et al have reported the involvement of ethmoid sinus (90.9%), followed by maxillary sinuses (81.8%). The coexistence of ROM and severe COVID-19 infection is associated with higher mortality rate[14-16]. Antifungal treatment along with radical debridement of infected and necrotic tissue with drainage of infected paranasal sinuses should be performed to minimize the fungal load in the tissue.

Conclusion

This study showed diabetes as predominant predisposing factor associated with mucormycosis in Covid of patients. The frequency of ethmoid sinus involvement was observed in our study. Proptosis was the common presenting symptom of rhinocerebral mucormycosis

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