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Clinical Profile of Rhino-Orbital-Cerebral Mucormycosis in Post-Covid Patients

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Abstract

Background: During the Covid-19 pandemic, several complications were being reported in patients who have recovered post-covid. One such lethal complication being reported in patients who had underwent treatment for Covid 19 infection in India in recent times, is a fungal disease called Mucormycosis or the black fungus. The aim of this retrospective observational study is to find out the clinical presentation, diagnostic nasal endoscopy findings and involvement on MRI scanning in the patients of post covid mucormycosis at CPR hospital Kolhapur from July 2021 to October 2021. **Objective** To study different clinical features of Post covid rhino-orbital-cerebral mucormycosis. To study diagnostic findings of Post covid rhino-orbital-cerebral mucormycosis patients and to study involvement on MRI in patients with Post covid rhino-orbital-cerebral mucormycosis**. Materials and methods** This is retrospective observational study and will be carried out in tertiary care center in Western Maharashtra from 1 July 2021 to 31 October 2021. Study population includes post-covid patients presenting with symptoms of rhino orbital-cerebral mucormycosis**. Results** A total of 229 patients of post covid 19 mucormycosis patients were included in the study. Out of 229 patients , ptosis was seen in 77 patients (32.77%), periorbital swelling in 73 patients (31.06%), ophthalmoplegia in 43 patients (18.30%), proptosis in 45 patients (19.15%), decreased vision in 56 patients (23.83%), palatal ulcer in 46 patients (19.57%), loosening of maxillary teeth in 25 patients (10.64%), toothache in 21 patients (8.94%), orbital pain in 38 patients (16.17%), headache in 51 patients (21.70), facial numbness in 14 patients (5.96%), facial pain with swelling in 40 patients (17.02), discoloured nasal discharge in 48 patients (20.43%) and nasal obstruction in 16 patient (6.81%). On diagnostic nasal endoscopy (DNE) out of 229 patients 151 patients (64.26%) had blackish crusting and 50 patients (21.28%) had mucopurulent discharge. On MRI involvement, out of 229 patients 229 patienst (100%) had sinus involvement, 122 patients (53.27%) had eye involvement, 9 patients (0.04%) had brain involvement, 13 patients (0.056%) had oral cavity involvement **Conclusion** Patients should be made aware of strict glycemic control and limited use of corticosteroids. Patients should seek immediate medical attention if develops headache, pain, facial swelling, diminution of vision so that timely medical action may be taken for ensuring survival. Surgical debridement of necrotic tissue is cornerstone of

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treatment which also provides sample for immediate fungal microscopy by KOH wet mount and Giemsa stain to provide quick possible diagnosis for timely management of the patients.
Level of Evidence Level 2. Retrospective observational study
Keywords Mucormycosis, Post Covid, Rhinoorbito-cerebral

Introduction:
Rhino-orbito-cerebral mucormycosis (ROCM) is a fulminant fungal infection associated with high morbidity and mortality rates [1–3]. Diabetes is the most common predisposing factor for ROCM [4, 5]. Other predisposing factors include malignant hematological disorders, metabolic acidosis, deferoxamine and glucocorticoid therapy, and chronic renal failure [6, 7]. Opportunistic fungi, belonging to the order Mucorales, are responsible for this rapidly progressing fatal infection [8–11]. Among the several Mucorales genera, species from the genus Rhizopus are the most common causes of ROCM and are detected in the majority of cases, followed by Lichtheimia, Mucor, Rhizomucor, Saksenaea, Apophysomyces, and Cunninghamella [12, 13]. Following the inhalation of fungal spores that are present in the environment [14], the fungi colonize the nasal/sinus mucosa and cause infection in neighboring areas including the orbit, cavernous sinus, and brain [15].
The Mucoralean fungi have angio-invasive ability and cause thrombosis of blood vessel leading to tissue necrosis [16]. It is believed that acidosis facilitates the invasion of blood vessel walls by these fungi because these fungi have keto-reductase system, which activate in acidic pH caused by uncontrolled diabetes [17].
This is a retrospective observational study done at CPR hospital Kolhapur to find out various clinical features on presentation in Post-Covid Rhino-Orbito-Cerebral mucormycosis

Materials And Methods
After the second wave of Covid 19, there was a rapid increase in the number of Covid associated mucormycosis cases in the city during April 2021. Due to multi system involvement patients were managed combinedly by various departments including ENT, ophthalmology, Medicine, neurosurgery. The ENT wards were converted into a Mucor ward. Patients with active covid 19 infection were isolated from the covid 19 recovered patients. The present study is retrospective observational study conducted at CPR hospital Kolhapur. A total of 229 cases of post covid mucormycosis confirmed by microbiological/histopathological evaluation were included in study in the study period from to
Data was collected from history, clinical symptoms and signs, diagnostic nasal endoscopy findings and imaging reports and outcomes were tabulated and analysed.

Clinical presentation
From history, the clinical presentation each patients were noted. It includes ptosis (picture 1), periorbital swelling (picture 2), ophthalmoplegia, proptosis, decreased vision, palatal ulcers, loosening of maxillary teeth, toothache, orbital pain, headache, facial numbness, facial pain with swelling, discoloured nasal discharge, nasal obstruction.

Diagnostic nasal endoscopy (DNE)
DNE was performed in each and every patient of post covid mucormycosis and findings were noted. Most common were blackish crust (picture 3) and mucopurulent nasal discharge (picture 4). This documented DNE findings were used for this study.

MRI SCAN

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Each patient of post covid mucormycosis in this study underwent MRI imaging to find out the extent of disease and look for involvement of sinuses, orbit, oral cavity and brain and the findings were tabulated and analysed.
These patients underwent medical and surgical management according to the need of disease process. Medical management included injection Amphotericin B and Posaconazole. And surgical management included Functional Endoscopic Sinus Surgery (FESS), total and partial maxillectomy, endoscopic orbital clearance and open exenteration.

Picture 1

Picture 2

Picture 3

Picture 4

Results
A total of 229 patients of post covid 19 mucormycosis patients were included in the study. Mean age of patients in study was 51.13 ± 12.9145. Out of 229 patients,161 were males and 68 were females. All patients included in study were confirmed RT PCR positive Covid 19 cases who developed mucormycosis.
The most common comorbidity associated with Invasive fungal sinusitis was Diabetes Mellitus followed by Hypertension. Different clinical presentation of post covid mucormycosis patients were studied.
Out of 229 patients , ptosis was seen in 77 patients (32.77%), periorbital swelling in 73 patients (31.06%), ophthalmoplegia in 43 patients (18.30%), proptosis in 45 patients (19.15%), decreased vision in 56 patients (23.83%), palatal ulcer in 46 patients (19.57%), loosening of maxillary teeth in 25 patients (10.64%), toothache in 21 patients (8.94%), orbital pain in 38 patients (16.17%), headache in 51 patients (21.70), facial numbness in 14 patients (5.96%), facial pain with swelling in 40 patients (17.02), discoloured nasal discharge in 48 patients (20.43%) and nasal obstruction in 16 patient (6.81%). (Figure 1)
On diagnostic nasal endoscopy (DNE) out of 229 patients 151 patients (64.26%) had blackish crusting and 50 patients (21.28%) had mucopurulent discharge. (Figure 2)
On MRI involvement, out of 229 patients 229 patienst (100%) had sinus involvement, 122 patients (53.27%) had eye involvement, 9 patients (0.04%) had brain involvement, 13 patients (0.056%) had oral cavity involvement (Figure 3). Out of 229 patients 98 patients (42.8%) had only sinuses involvement, 109 patients (47.5%) had both sinus and eye involvement, 6 patients (0.026%) had sinus and oral cavity involvement, 3 patients (0.013%) had sinus and brain involvement, 7 patients (0.030%) had sinus, oral cavity & eye involvement, 6 patients (0.026%) had sinus, eye & brain involvement.

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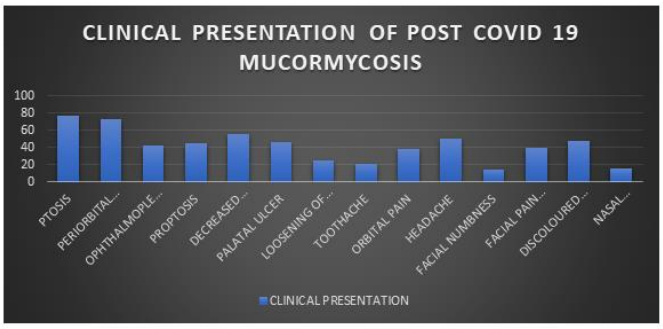

Figure 1

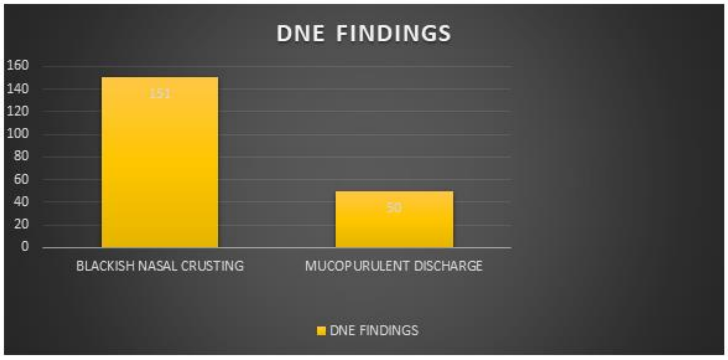

Figure 2

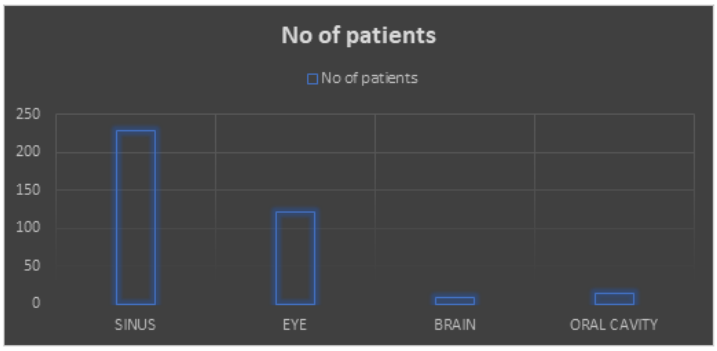

Figure 3

Discussion

Coronavirus disease is caused by SARS-CoV2 virus which has infected millions of people globally so far. COVID-19 infection has hit India badly during the second wave. The most common symptoms of covid-19 remain fever, dry cough and fatigue. People above 60 years of age, with cardiac and pulmonary problems, obese, diabetic are at higher risk of becoming critically ill. People who have had COVID-19 infection whether hospitalized or not continue to experience fatigue, respiratory and neurological symptoms for some time. The COVID- 19 infection dysregulates CD4 + and CD8 + cells disturbing the innate immunity which increases the chances of secondary fungal and bacterial infections. COVID-19 patients have more pro-inflammatory (IL-1, IL-2, IL-6, tumor necrosis factor- alpha) cytokine levels and less CD4 interferon-gamma expression which increases the risk of invasive fungal infection in them. Mucormycosis and aspergillosis are important opportunistic systemic mycoses. Their spores are inhaled in immunocompromised states which germinate in nasal cavity, paranasal sinuses, lung orbit and brain which may lead to death.

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Hyperglycemia in diabetic patients disrupts immune response and affects cellular immunity, causes defective phagocytosis, suppresses cytokine production and results in failure to attack microbes causing invasion by secondary fungal infections. COVID-19 infection virus (SARS-Cov 2) itself causes hyperglycemia as the virus damages the pancreatic islets due to cytokine storm. So, the blood glucose levels increases significantly in already diabetic patients when infected with COVID-19.

The second wave of COVID-19 infection caused extensive use of corticostroids as a part of COVID-19 management either as hospital care or at home under online supervision. Glucocorticosteroids have anti-inflammatory and immunosuppressive effects. Steroids antagonizes IL-1, IL-6, TNF and microbicidal activities of activated macrophages.

Some studies have shown that prolonged use of corticosteroids to control cytokine storm contributed to more susceptibility to fungal infection due to their immunosuppressive behaviour. Steroids also affects glycemic status causing hyperglycemia. According to WHO, if COVID patient is initiated on steroids, blood glucose monitoring should be done as before breakfast, lunch and dinner and after dinner also.

The Indian Council of Medical Research, in May 2021, came up with guidelines for the screening, diagnosis, and management of mucormycosis in the time of Covid 19. The chief warning signals to suspect mucormycosis in Covid 19 patients, people with diabetes, and immunosuppressed individuals enlisted include sinusitis, nasal congestion, blackish or bloody nasal discharge, local pain on the cheekbone, unilateral facial pain, numbness or swelling, blackish discoloration over nasal bridge/palate, toothache, teeth loosening, jaw involvement, blurred or double vision with pain, fever, skin lesion, thrombosis and necrosis (eschar), chest pain, pleural effusion, hemoptysis and worsening of respiratory symptoms (ICMR, 2021).

In this study, the most common clinical presentation was found out to be ptosis followed by periorbital swelling and most common DNE finding was blackish crusting in nasal cavity. Frank symptoms like palatal discoloration/ulceration, palatal perforation, diplopia, proptosis, ophthalmoplegia and ptosis are clear indications for starting antifungal therapy without histopathological report.

DNE followed by nasal swabs for KOH mount was done for every patient. There are many cases where KOH microscopy could not detect the fungus but histopathology could demonstrate the presence of fungal elements. This is mainly due to inadequate fungal hyphae, trapped fungal hyphae in mucosa preventing it to come in contact with stains, inter observer variability and improper sampling technique.

Conclusion

Primary aim of this study was to report the characteristics of Post COVID- 19 patients who presented with rhino-orbital-cerebral mucormycosis. Patients should be made aware of strict glycemic control and limited use of corticosteroids. Patients should seek immediate medical attention if develops headache, pain, facial swelling, diminution of vision so that timely medical action may be taken for ensuring survival. Surgical debridement of necrotic tissue is cornerstone of treatment which also provides sample for immediate fungal microscopy by KOH wet mount and Giemsa stain to provide quick possible diagnosis for timely management of the patients.

Vigilance among the clinicians and spreading awareness in the public health care system remains crucial in successfully managing Mucormycosis and subsequent reduction of mortality.

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