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Original Research Paper

Radiodiagnosis

ROLE OF COMPUTED TOMOGRAPHY SCAN IN POST-COVID SINO-NASAL MUCORMYCOSIS WITH CLINICO-EPIDEMIOLOGICAL CORELATION

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ABSTRACT

- **OBJECTIVE:**
- To evaluate the spectrum of radiological findings in post-COVID sinonasal mucormycosis cases
- To evaluate the demography, comorbidities and treatment modalities used in these patients which may be attributable to development of sinonasal mucormycosis after recovery from COVID-19 disease.
- **MATERIALS AND METHODS:** In this retrospective study, 80 out of 793 patients who came for follow-up after recovering from COVID pneumonia, had symptoms related to paranasal sinus and orbit. CECT PNS and orbit was performed in them and 69 patients had positive CT findings. Clinico-epidemiological data was recorded. The correlation between CT findings and clinical history was performed by Chi2 test. P value <0.05 was considered as statistically significant.
- **RESULTS:** Majority - 48 (69.5%) belonged to age group between 40-60 years. Diabetes mellitus was the most common comorbid condition seen in 58 (84%) patients. The treatment history during COVID-19 disease revealed administration of intravenous or oral steroids in 54 (78.2%) patients, Injection Remdesivir in 48 (69.5%), broad-spectrum antibiotics in 36 (52.2%). 15 (21.7%) were given non-invasive ventilation and 7 (10.1%) needed invasive ventilation.

Ethmoidal sinus- 68 cases (98.5%) and maxillary sinus- 65 cases (94.2%) were most frequently affected sinus. Intraorbital extension of the soft tissue was seen in 37 (53.6%) and intracranial extension was seen in 11 (15.9%) cases. On follow-up, fungal hyphae were detected in 39 (56.5%) cases via KOH mount or biopsy.

- **CONCLUSION:** The widespread use of steroids/monoclonal antibodies/broad-spectrum antibiotics/oxygen therapy for treating COVID-19 may lead to the development/exacerbation of pre-existing fungal diseases. Health care professionals should act promptly when there is a suspicion of mucormycosis.

KEYWORDS : COVID-19, mucormycosis, invasive fungal sinusitis, CECT PNS

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infection caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[1] Since the detection of first case in December 2019 at Wuhan, China, there has been various twist and turn regarding pathophysiology, symptoms, treatment, and complications of COVID-19 disease. To add to this misery, there has been an advent of a more dangerous and potentially deadly complication: that of invasive fungal sinusitis resulting from mucormycosis. [2]

Mucormycosis is a fungal disease caused by Rhizopus, mucor and absidia. Because of the low virulence potential, it may be present in the nasal mucosa of healthy people as a commensal.[3] If the patient becomes immunosuppressed, this fungus may germinate within the paranasal sinuses, and spread intracranially or to other nearby structures such as the orbit. COVID-19 disease is a immunocompromised state, and with addition of comorbidities like diabetes mellitus, HIV positive status, malignancies; the scenario worsens.[4]

Over the past few months, our tertiary teaching hospital has witnessed a massive rise in post-COVIDinvasive fungal sinusitis cases with quite a significant number of cases requiring life-saving operative procedures. In this article we have studied various imaging findings of post COVID invasive fungal sinusitis and correlated demography, comorbidities and treatment modalities used in these patients which may be attributable for this fatal disease.

MATERIALS AND METHODS

1. ETHICS

The study was discussed with the ethical committee of out institution and as it is a retrospective observational study, the ethical approval was waived off.

2. SELECTION AND DESCRIPTION OF PARTICIPANTS

Our retrospective study deals with 793 patients who came for follow-up 10-14 days after turning RTPCR negative in COVID follow-up clinic. All the patients were once RTPCR positive and underwent treatment. They were evaluated and 80 (10.1%) patients were found with symptoms related to paranasal sinuses and orbit. These patients were referred to the Radiology department for CT scan of PNS and orbit. 69 (8.7%) patients had some imaging findings in CT scan.

We also collected epidemiological data from these 69 patients and retrospectively evaluated the usage of drugs like Remdesivir, methylprednisolone, oral steroids, and zinc. We also evaluated the potential risk factors of the patients like diabetes mellitus, hypertension, immunocompromised state, or any known malignancies.

3. TECHNICAL INFORMATION:

CT plain study of PNS and orbit was done using Philips 256 slice Spiral CT machine. Contrast scans were performed using Inj. Iohexol 350mgI/ml when required to look for intracranial and intraorbital extension.

4. CT FEATURES

We evaluated the patients radiologically in detailed manner with respect to sinus and bony involvement, intraorbital extension, extraocular muscle involvement, optic nerve involvement, orbital cellulitis and abscess, intracranial extension.

5. STATISTICS

Collected data was entered into Microsoft Excel software and coded. Charts and tables were prepared using Microsoft word and excel software. Descriptive data was presented in frequency and percentage. The correlation between CT

findings and clinical history was performed by Chi2 test. P value <0.05 was considered as statistically significant and statistical software STATA version 14.2 was used for data analysis.

RESULTS

1. DEMOGRAPHIC AND CLINICAL DATA OF ENTIRE COHORT

48 (69.5%) out of 69 patients were male. Majority - 48 (69.5%) belonged to age group between 40-60 years. Diabetes mellitus was the most common comorbid condition seen in 58 (84%) patients.**[TABLE 1]** Most frequent complain of patient was orbital and nasal swelling in 40 (58%) cases.**[TABLE 2]**65 (94%) of them underwent institutional treatment. The treatment history during COVID-19 disease revealed administration of intravenous or oral steroids in 54 (78.2%) patients, Injection Remdesivir in 48 (69.5%), broad-spectrum antibiotics in 36 (52.2%), Tocilizumab in 8 (11.6%) patients**[FIG1]**. 34 (49.3%) patients needed supportive oxygen therapy with or without bag & mask. 15 (21.7%) were given non-invasive ventilation and 7 (10.1%) needed invasive ventilation. 13 (18.8%) patients did not need oxygen therapy at all.

2. RADIOLOGICAL FINDINGS

Most frequent sinuses to be involved were ethmoidal sinus- 68 cases (98.5%) and maxillary sinus- 65 cases (94.2%).Poorly enhancing soft tissue with hyperdense component **[FIGURE 2A]** within and associated rarefaction & bony erosion of the walls of sinuses and turbinates were frequently seen. Intraorbital extensionof the soft tissue was seen in 37 (53.6%)**[FIGURE 3,4]** and intracranial extension was seen in 11 (15.9%) cases. **[FIGURE 5,6]** Cavernous sinus was involved in 3 (4.3%) patients, with 1 (1.4%) showing frank thrombosis **[FIGURE 7]**. Palatal perforation was seen in 8 (11.6%)**[FIGURE 2B]** and sinus wall perforation was seen in 10 (14.5%) cases.

3. FOLLOW-UP: 15 (21.7%) patients underwent Functional Endoscopic Sinus Surgery (FESS). Fungal hyphae were detected in 39 (56.5%) cases via KOH mount or biopsy.

DISCUSSION:

Mucormycosis is a fungal disease caused by Rhizopus, mucor and absidia. These fungi are present in the environment surrounding us. Because of the low virulence potential, it may be present in the nasal mucosa of healthy people as a commensal. (3)

If the patient becomes immunosuppressed, this fungus may germinate within the paranasal sinuses, and spread intracranially or to other nearby structures such as the orbit. [5]We knew from before that diabetic and immunocompromised states are predisposing factors for mucormycosis.

COVID-19 is a virus which makes the patient immun ocompromised by affecting multiple systems in the body with decrease in CD4+ T and CD8+ T cells. Moreover COVID-19 patients who are diabetic, HIV positive and have cancer previously are immunocompromised from before. [6]

During the SARS-CoV infection spread in 2003, fungal infection was found in 14.8–27 per cent, and it led to25–73.7 per cent in all causes of death.[7-9] SARS-CoV and SARS-CoV-2 share similar prevalence rates and biological and clinical characteristics as they belong to the same species. [10]

Previously, few such incidental case reports have been published, but a firm association between COVID-19 and increased fungal infections can now be clearly seen. Mehta and Pandey reported a single case of a 60-year-old male with rhino-orbital mucormycosis associated with COVID-19 in September 2020. [11]

White et al. studied 135 adults with COVID-19 infectionand reported an incidence of 26.7 per cent for invasive fungal infections. [12]

In this study, we have come across various presentations of the invasive fungal sinusitis ranging from pansinusitis, to intraorbital & intracranial extension, cavernous sinus thrombosis, palatal perforation, etc. The exact role of a radiologist is to delineate the anatomy and variants of paranasal sinuses, the extensions of the disease and complications if any. This will help the treating surgeon to take an operative decision and reduce the risk of surgical complications. [13-16]

There are mainly three phases of COVID-19 infection. The viral replication, the cytokine storm phase, and the recovery phase. During the second wave of COVID, we have seen that the cytokine storm phase of the patients was prolonged and severe. [17-18]

Hence, we as doctors had to give methylprednisolone via intravenous route for a prolonged period in high dosages. In addition to it, people in home isolation used to take oral steroids for longer duration as it was part of COVID treatment protocol for home isolation patients.Steroids are type of drugs that make the patients more immunocompromised. Hence it makes the patient more susceptible to mucormycosis. [19]Zinc was prescribed from first wave of COVID-19 as an agent to boost immunity. But there is a catch to it. It has been seen that zinc acts a facilitator for fungal survival and metabolism. Moreover, zinc chelators have been seen to act similarly as amphotericin B as an anti-fungal agent. [20]

TABLES

TABLE 1: Co-morbidities of the patients

Associated Co-morbidities	No. of cases (%)
Hypertension	18 (26.1%)
Diabetes	58 (84%)
Hemoglobinopathy	6 (8.7%)
HIV	4 (5.8%)
Coronary artery disease	10 (14.5%)
Malignancy	5 (7.2%)

TABLE 2: Clinical features of the patients

CLINICAL FEATURES	NO. OF CASES (%)
Nasal swelling	40 (58%)
Cheek swelling	35 (50.7%)
Haemoptysis	13 (18.8%)
Eschar formation	14 (20%)
Cough & Cold	20 (29%)
Fever	26 (37.6%)
Altered Sensorium	5 (7.5%)
Tooth ache	20 (29%)
Blurring of vision	24 (34.8%)
Jaw swelling	25 (36.2%)

FIGURES

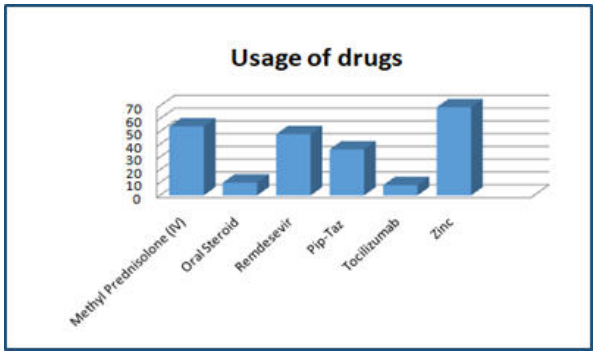

FIGURE 1: Bar diagram showing usage of various drugs in the patients during COVID-19 disease.

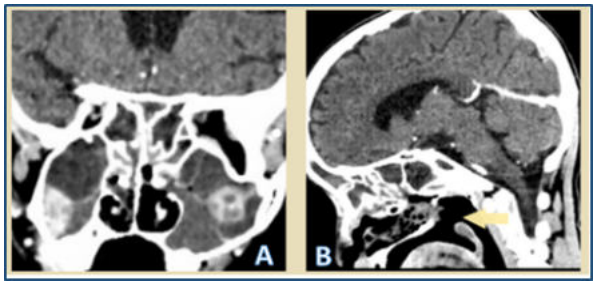

FIGURE 2:CECT PNS study **A.** Expansile soft tissue density seen in bilateral maxillary sinus with hyperdense component within, likely fungal etiology. **B.** Sagittal view of same patient showing a defect in the soft palate suggestive of **palatal perforation.**

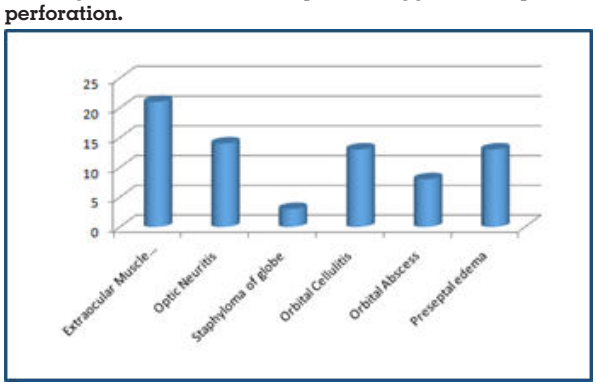

FIGURE 3: Bar diagram showing different intraorbital complications.

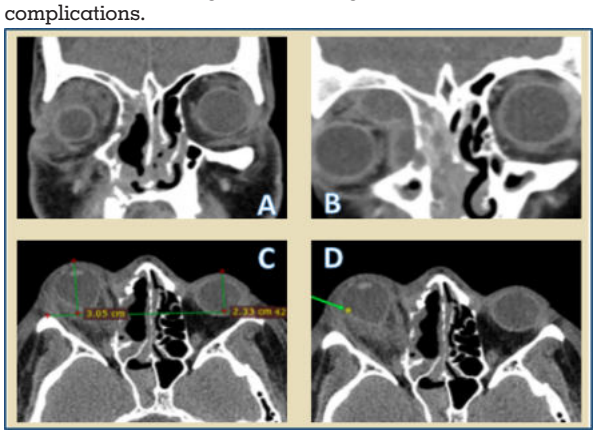

FIGURE 4: CECT PNS study **A.**There is intra and extraconal fat stranding in right orbit; extraocular muscles appear bulky and heterogeneous. **B.** There is relatively well defined peripherally enhancing intraorbital extraconal loculated collection involving superior and medial compartment of right orbit s/o **intraorbital abscess formation.C.** There is resultant **proptosis** of right eye. **D.** Focal deformity involving posterior aspect of right eye globe suggestive of **staphyloma**.

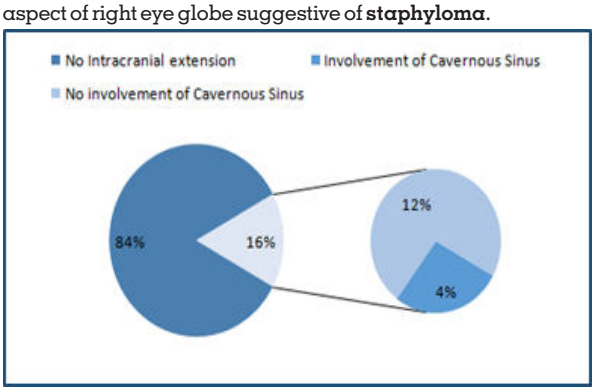

FIGURE 5: Pie-chart showing intracranial extension in 16% cases and involvement of cavernous sinus in 4% cases.

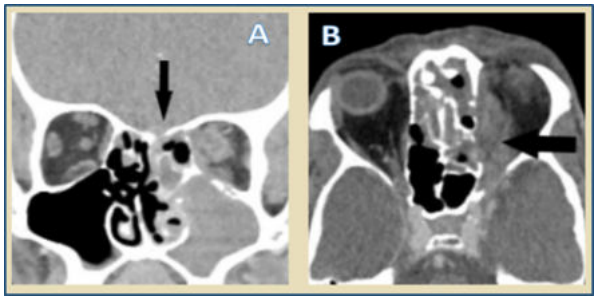

FIGURE 6:CECT PNS study**A.** There is erosion of cribriform plate with **minimal intracranial extension** of the soft tissue. Olfactory fossa appears effaced. The left optic nerve appears bulky with enhancement s/o **optic neuritis.B.** There is erosion of left lamina papyracea with intraorbital extension of soft tissue. It is extending posteriorly through the orbital apex and **reaching upto cavernous sinus** in left without any obvious thrombosis.

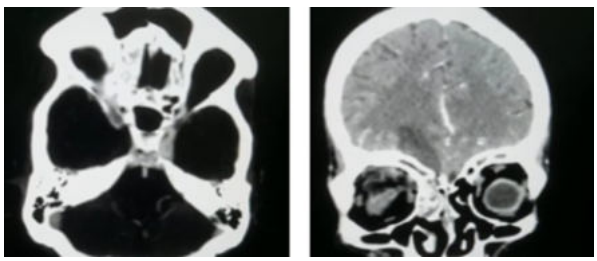

FIGURE 7: CECT PNS study reveals thrombosis of right cavernous sinus and cavernous segment of right ICA. There is associated erosion of cribriform plate with intracranial extension seen in form of hypo density in right basifrontal lobe.

CONCLUSION:

Rapid disease progression and angioinvasive character of mucormycosis is responsible for its severity. The widespread use of steroids/monoclonal antibodies/broad-spectrum antibiotics/oxygen therapy for treating COVID-19 or any underlying comorbidities may lead to the development/ exacerbation of pre-existing fungal diseases. Healthcare professionals should act promptly when there is suspicion of mucormycosis. A multidisciplinary approach should include the prompt diagnosis and treatment with antifungals, surgery, plus the reversal of the underlying condition.

ABBREVIATIONS: SARS-CoV-2- Severe Acute Respiratory Syndrome Coronavirus-2, COVID-19- Coronavirus Disease-19, CECT- Contrast Enhanced Computed Tomography, PNS-Paranasal Sinus, RTPCR- Reverse Transcriptase Polymerase Chain Reaction

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