Covering Letter

To,

The Editor

Sub: Submission of Manuscript for Publication

Dear Sir,

We intend to publish an article entitled **"The Aftermath of COVID-19 Pandemic- Rhino-Orbital Mucor-mycosis"** in your esteemed journal as a Letter to the Editor.

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Support:-nill

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Thanking you,

Yours' Sincerely,

Signature

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Type of Article: Case Report

Title of the Article: **"The Aftermath of COVID-19 Pandemic- Rhino-Orbital Mucor-mycosis"**

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The Aftermath of COVID-19 Pandemic- Rhino-Orbital Mucormycosis. A Case Report

Abstract:

Infections of paranasal sinuses are very commonly encountered in general population. They are known to flare up more in the immunocompromised conditions. Orbital involvement occurs in cases of neglected chronic infections. SARS-CoV-2 or COVID-19 has adversely hit the world causing a heavy death toll, now pandemic seems to trail off very slowly; but permanent serious central and visual disabilities will persist.

We have noticed a steep rise in cases of rhino-orbital mucormycosis in last few months. We present here the cases in which convalescent COVID-19 patients presented with acute onset symptoms that had progressed very fast leading to visual loss and intra-cranial extension of the fungus.

Key-words: Rhino-orbital mucormycosis, COVID-19 aftermath, Infection control, Sinusitis

Key Messages:

COVID-19 infection is a multi-system disorder; it produces long-lasting effects on immunity, heart and respiratory system and permanently damages vision by entering the orbit due to ascending fungal infection via para-nasal sinuses. Not only does the infection produces the impact, but the drug treatment employed also seems to play a role in the damage.

Introduction:

The outbreak of Severe Acute Respiratory Syndrome (SARS) was reported in 2002-3. Later the H1N1 and SARS in 2009-10 enabled WHO to define surveillance on respiratory infectious diseases. [1]

The pathogen was novel RNA β- coronavirus and the disease was named as SARS-CoV-2 or COVID-19 with reported case fatality rate of 6% to 0.25%. [2, 3 and 4]

This global epidemiological crisis of COVID-19 put severe burden on responsiveness to infection control. It is proven that COVID-19 causes over-activation of innate immune response leading to multi-organ damage. In addition to affecting the major systems like respiratory, cardiovascular and GIT, SARS-CoV-2 targets retinal vessels also causing pyo-granulomatous uveitis, choroiditis and macular micro-vascular impairment. [5] It also remains dormant in paranasal sinuses for months after acute phase infection is cured and precipitates Rhino-orbital Mucor-mycosis.

Fungal rhino-sinusitis is an ascending infection with serious life and vision threatening consequences. We are reporting 10 such cases that were operated for Functional Endoscopic Sinus Surgery (FESS) within a period of less than 3months after COVID-19 infection.

Case History:

The patients we have reported are either known or newly diagnosed diabetics; they had history of hypertension and IHD and were under treatment in COVID-19 wing of our institution. They were subjected to anesthesia as an emergency procedure for vision and life-saving purpose. Majority were under the care of physicians and few were in immediate post-operative period after some emergency surgery. The presenting complaints for ENT consultation were headache, fever, swelling and pain in either eye and pain over face on the same side. They were receiving intravenous medications for the underlying medical and/or surgical conditions in the form of oral hypoglycaemic, or insulin, anti-hypertensives, statins, antibiotics and intravenous antifungals. Anti-inflammatory agents and corticosteroids were also given for symptomatic relief.

Pre-anesthetic evaluation was done after taking due precautions for COVID-19 and mostly patients were found to be cases for anticipated difficult intubation due to compromised oral and dental hygiene, fungal discoloration and occasional bleeding on touch of throat and palate. Mask holding was also difficult due to pain and proptosis. Positioning for airway ease was restricted due to stiffness. Pre-operative preparation included pre and intra-operative optimal blood sugar control, control of hydration status due to post- COVID-19 poor general condition and inability to drink and swallow freely due to painful and /or obstructing fungal lesions and anticipated hypotension due to ongoing anti-fungal therapy.

After ensuring adequate PPE, use of N95, face shields and availability of aerosol control measures, appropriate risk consent was checked and intravenous line was accessed. Electrocardiography (ECG), pulse oximetry, non-invasive BP (NIBP) monitors were connected. A difficult intubation cart was kept ready. Patients were pre-medicated with injection glycopyrrolate 4µg/kg, injection fentanyl 2µg/kg, intravenously. After pre-oxygenation with 100% oxygen, patient was induced with injection propofol 1% -100 mg in titrated dose. The palatal perforation if present was covered with gauze and intubated with proper size cuffed reinforced endotracheal tube after relaxation with injection succinylcholine 2 mg/kg body weight. The injection xylocard 1.5 mg/ kg was used to attenuate laryngoscopy response.

Intra-operative blood sugar monitoring was also done. The patients were maintained with oxygen, nitrous and isoflurane 1% or sevoflurane with controlled ventilation. Muscle relaxation was maintained with injection atracurium 0.5mg/kg. On completion of surgery, reversal was given and after ascertaining adequate muscle power and patients were extubated and shifted to recovery with 100% oxygen with 2 L/min. The rest of the post-operative period was monitored either in ward or in ICU depending upon the clinical condition. Annexure 1 shows the detailed description of the cases. Fig. 1 shows the intra-operative endoscopy view of the fungal infection.

Discussion

Occurrence of Sinusitis, either allergic, non-allergic or infective, has been commonly reported to be existing in general population. Up to 90% cases are of fungal etiology. [6] In our institution the number of surgeries done in ENT Theater over last three years is shown in figure 2. In the year 2021 we noticed a steep rise (almost four times) in number of FESS cases for removal of mucormycosis, when compared with the last two years.

Chakraborty et al [7]have reported that the rational approach towards prognosis and treatment of fungal sinusitis is less understood which explains the high incidence.

Fungal rhinosinusitis is often an ascending infection affecting the orbit via vascular invasion of fungal hyphae of mucorales. It is an opportunistic infection often found in immunocompromised patients. [8]

Our reported cases were post- COVID-19 patients who received aggressive immunosuppressive treatment along with central venous catheterization during their hospital/ICU stay for COVID-19 treatment.

Patients with invasive fungal infections have Cryptococci or pneumocystis infections. The use of antifungal agents changes the epidemiology of Candida albicans to non-albican candida strains as reported by David Enoch et al. [9] The explanation for high mortality rates of such patients as reported by David Enoch et al are due to resistance to antifungal agents, underlying serious medical diseases, seropositive status and inability to achieve early source control.

P. Castelnuova et al [10] have studied fungal sinusitis cases (1050 patients) over a period of three years. They observed Aspergillus fumigatus (76.9% cases) as the most often occurring myecetes and have reported patients presenting with facial algia, followed by nasal obstruction with C.T. features showing focal areas of non-homogeneous intensity, metal like endo-sinus calcifications in 84.4%.

In our cases, common C.T. features were invasive fungal sinusitis with bony erosion with intra orbital and intra cranial extension. Soft tissue thickening was seen in maxillary, sphenoid, ethmoidal sinuses due to fungus. MRI showed features of sinusitis with bone destruction intracranial and intra orbital extension with optic neuritis and temporal lobe abscess was also present in some. CT Thorax showed Ground Glass Opacities, crazy paving appearance, sub-pleural fibrotic bands with interstitial thickening in peri-broncho-vascular and peripheral sub-pleural regions confirming the classical covid picture.

The acute pulmonary injury in SARS-CoV-2 is due to release of pro-inflammatory cytokines like IL-1, 2, and 6 and TNF-alfa. National Health Commission of China has included Tocilizumab a novel monoclonal antibody that competitively inhibits binding of IL-6 to its receptor, in COVID -19 treatment. It binds soluble as well as bound IL-6 receptors and hinders pro-inflammatory effects of the virus. [11]

Surgery of sinuses (FESS) has been reported to be curative for fungal ball without further pharmacologic treatment. In cases of fulminant invasive mycoses surgery prevented endo-cranial complications. High doses of systemic Amphotericin B, control of underlying disease; it is given in 2-6 h infusions to reduce the severity and frequency of side effects of rapid administration. Amphotericin B is primary antifungal therapy for patients with opportunistic fungal infections although antifungals have poor penetration ability at the site of infection. [12]

Our patients received it in dose of 1 mg/kg body weight titrated over 3 days. Hypokalaemia, hypomagnesemia, fever, chills, dyspnoea, and hypotension are common side effects of Amphotericin B. Allergic reactions, seizures, anaemia, and thrombocytopenia are less likely to occur but are well-documented. Renal function is also impaired, and a permanent decrease in the glomerular filtration rate is likely.

Our patients commonly had hypotension intraoperatively with occasional arrhythmias that responded to treatment with lidocaine. We were careful about renal, electrolyte, coagulopathy, hemodynamic, and respiratory aberrancies during anaesthesia for these patients with due risk for all major systemic functions.

Conclusion

The true burden of the pandemic was because of rapidly spreading acute respiratory infection and fast mutating trends of the virus. With the advent of latest technologies, the understanding of clinical course was possible. Due to effective treatment modalities death toll appears to be under control. However the serious post- COVID-19 consequences are gradually being observed.

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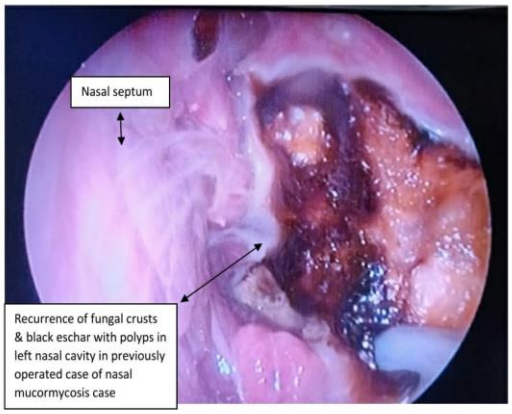
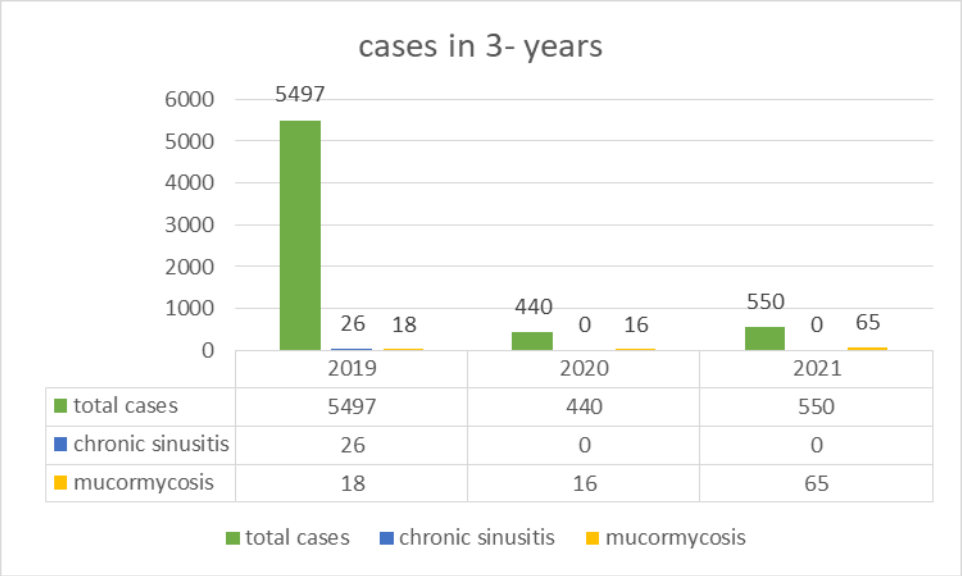
Fig.1 Fungal Black Eschar and Polyps



POST COVID FUNGAL BLACK ESCHAR AND POLYPS IN AN OPERATED CASE OF NASAL MUCORMYCOSIS

Fig.2 Number of cases in ENT Theater in last three years.



	2019	2020	2021
total cases	5497	440	550
chronic sinusitis	26	0	0
mucormycosis	18	16	65

Table -1 Case details

SN	PRESENTATION	PASTHISTORY- Diabetes (DM) Hypertension (HT) Ischemic Heart Disease (IHD)	AIRWAY EXAMINATION Mallampatti grade (MPC) Nasal Endoscopy (NE)	INVESTIGATIONS Computed Tomography (CT) Magnetic Resonance Imaging (MRI)
1	Blurring of vision, watering right eye	IHD- 10 years, DM- 1 month	NE- full of crust, right middle turbinate not identified	MRI- Sinusits with bone destruction intracranial and intra orbital with optic neuritis with Rt temporal lobe abscess CT Thorax Bilateral pleural effusion with atelectasis of underlying lungs with areas of ground glass opacities. Perihilar vessel engorgement with peri bronchovascular thickening
2	Right orbital swelling, headache	DM- since 5 years CABG- 3 years back HT- since3 years	MPC- grade III	CT Thorax- Patchy areas of Ground Glass Opacties, crazy paving appearance, subpleural fibrotic bands
3	Left Eye- loss of vision Diplopia	DM- since 3 months	MPC- grade III NE- full of black crusts	MRI- Sinusits with bone destruction intracranial and intra orbital with optic neuritis
4	Left eye swelling	DM- since 8 years HT- since 7 years	MPC – grade III	CT Thorax- Multiple patchy confluent Ground Glass Opacities with interstitial thickening in peribronchovascular and peripheral subpleural regions of both lungs CT brain- Hyperdense foci in both side maxillary, ethmoidal, sphenoidal sinuses with bony erosion.
5	Headache, decrease in left vision, difficulty opening mouth	DM- since 1year	MPC- grade III	CT Thorax- Multiple Ground Glass Opacities with thin fibrolinear fibrotic changes in both lungs CT brain & paranasal sinuses- Polypoidal mucosal thickening of sphenoidal, ethmoidal and maxillary sinuses & both osteomeatal complexes widened.
6	Decreased left eye vision, left eye	DM- since 2years	Tracheostomy in situ	MRI brain-

	swelling			Pan sinusitis, left orbital cellulitis with left optic nerve extension CT neck, thorax- Signs of aspiration pneumonitis with mucormycosis with right emphysema.
7	Right periorbital pain with headache	DM – since 5 years	MPC- grade III	CT brain- Non enhancing soft tissue thickening in maxillary, sphenoid, ethmoidal sinuses suggesting fungal sinusitis
8	Loss of vision in left eye, peri orbital pain and headache, shortness of breath	Asthma- since 3 years Tuberculosis3 years back DM since 1 month	MPC- grade III	CT brain- Invasive fungal sinusitis with bony erosion with intra orbital and intra cranial extension
9	Swelling of left eye lid, decreased left eye vision	DM since 20 years, IHD since 2years Percutaneous Transluminal Coronary Angioplasty done twice in last 3 years	MPC grade IV	CT brain & paranasal sinuses- Soft tissue density in pansinuses with left orbital cellulitis. CT Thorax- Multiple patchy areas of resolving Ground Glass Opacities with fibrotic change in lung fields with multiple subpleural bands.
10	Presented and operated acute pancreatitis 3months back. Black colouration & palatal perforation since 2 months	DM-since 9 months, Jaundice since 3months. HT- recent	MPC-grade III Poor dentition, missing teeth.	CT paranasal sinuses- Right Maxillary sinusitis, bony erosion, intracranial extension, intra-orbital extension. MRI brain- Mucosal thickening in right .maxillary, ethmoidal sinus. Extension in pterygopalatine fossa and orbit.