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Research Article

Neurological Manifestations of Mucormycosis in Covid-19

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Abstract

Background: Mucormycosis has emerged as an opportunistic infection during COVID-19 pandemic. It mostly affects the paranasal sinus, orbits, skin, gastrointestinal tract and brain. Intracranial spread has a poor prognosis and high fatality. It has been termed as "Rhino-orbital-cerebral mucormycosis".

Objective: To study about the incidence of neurological features of mucormycosis in COVID-19 patients in tertiary care hospital.

Materials and Methods: This is an observational study done in a tertiary care hospital. COVID-19 infection was detected with reverse transcriptase - polymerase chain reaction (RT-PCR). The diagnosis of mucormycosis was confirmed with computed tomography (CT) paranasal sinus, nasal washings and nasal cavity tissue biopsy. CT and magnetic resonance imaging of brain was done.

Results: 30 patients presented with fever, headache, visual loss, decreased sensation over the face, hemiparesis, seizures. The neurological deficits observed were visual loss (n = 12), multiple cranial nerve palsy (n = 20), stroke (arterial = 15, venous = 8), infective encephalopathy (n = 10). The cranial nerves affected were oculomotor, trochlear, abducens (n = 20) followed by optic (n = 12), trigeminal (n = 9) and facial nerve (n = 5). Diabetes mellitus and COVID-19 were the associated risk factors.

Conclusion: There is increasing incidence of neurological complications in mucormycosis during COVID-19 pandemic. Judicious use of corticosteroids, strict hyperglycemic control can help us in reducing the no. of mucormycosis cases and its neurological complications.

Keywords: COVID-19; Rhino-Orbital-Cerebral Mucormycosis; Neurological Manifestations; Amphotericin; Stroke; Orbital Apex

Background

The mortality rate has increased during this second wave of COVID-19 pandemic, which is attributed to not only to COVID 19, but also to another disease namely Mucormycosis. Mucormycosis is commonly called "black fungus". It can occur as a concomitant infection or within 10 days of COVID-19 infection. Mucormycosis is a rapidly progressive fatal disease that affects nasal sinus, lungs, skin, orbits, gastrointestinal tract and brain.

The angioinvasive nature of the fungi causes rapid dissemination to distant sites of the body followed by sepsis and death. Rhino-orbital- cerebral mucormycosis is one of the manifestations of mucormycosis which is fatal. When the neurological manifestations of mucormycosis is evident, it becomes far more difficult to cure it. Patients have presented with neurological features when there is infective stroke, internal carotid artery occlusion, cavernous sinus thrombosis and intracranial extension to orbital apex.

Aim

To study the neurological features seen in mucormycosis in COVID-19 patients in tertiary care hospital.

Materials and Methods

This is an observational study done in from xxxxxxxxxx hospital May-December 2021. The patients of age 18 to 70 years admitted in mucormycosis ward with concomitant COVID -19 or within 10 days of COVID-19 infection were included in this study.

COVID -19 infection was diagnosed with reverse transcriptase – polymerase chain reaction (RT-PCR). The diagnosis of mucormycosis was confirmed with computed tomography paranasal sinus, nasal washings and biopsy of the tissue taken from affected nasal cavity. Computed tomography (CT), magnetic resonance imaging (MRI) of brain magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) was done to find cause of the neurological deficit.

Informed consent was taken from each patient considered in this study. Patients who were drowsy, written informed consent was obtained from families of the patient before enrolling into the study.

Observations

120 cases of mucormycosis have been in Tertiary Care Hospital in Southern India since May 2021. The patients commonly presented with fever, unilateral eye swelling (proptosis), facial pain, rhinitis. The incidence of neurological complications in mucormycosis was 16.6%.

30 patients presented with neurological features of fever, headache, visual loss, decreased sensation over the face, weakness of one half of the body, seizures. The neurological deficits observed were visual loss (n = 12), multiple cranial nerve palsy (n = 20), stroke (n = 20), altered sensorium (n = 10). The cranial nerves mostly commonly affected are oculomotor, trochlear, abducens (n = 20) followed by optic(n = 12), trigeminal (n = 9) and facial nerve (n = 5).

Among the 30 patients, 19 were male patients and 11 were female patients. The intracranial involvement was evidenced by intracranial extension to basifrontal leptomeninges (n = 5), extension to cavernous sinus (n = 6), to orbital apex (n = 7), internal carotid artery occlusion (n = 6). The visual loss is due to orbital apex syndrome and optic neuritis which was confirmed by magnetic resonance of brain.

21 patients were having mucormycosis with concomitant COVID-19 and 9 patients developed within 10 days of COVID-19 infection. 18 mucormycosis patients had type 2 diabetes mellitus and COVID-19; 12 patients had only COVID-19 as risk factor.

Patients have been given corticosteroid therapy as a treatment for COVID-19 and were given injectional liposomal amphotericin B, Posaconazole and surgical debridement for mucormycosis. In 4 patients orbital exenteration was also done.

Out of 30 patients, 11 patients had died. (Case fatality rate - 37%).

CT scan brain, MRI brain, MRA, MRV of cerebral vessels and CT paranasal sinus was done. It showed infarction in frontal lobe (n = 10), parietal lobe (n = 8), temporal and occipital lobe(n = 6), extension to cavernous sinus and cavernous sinus thrombosis (n = 8), internal carotid artery occlusion(n = 6) and leptomeningeal enhancement (n = 5) with features of fungal sinusitis in maxillary ± frontal sinus with erosion of roof frontal sinus.

The biopsy taken from the tissue or crust in the nasal cavity showed necrotic areas admixed with mixed inflammatory cell infiltrates with hyphal forms of mucormycosis.

Discussion

Mucormycosis is caused by fungi which belong to family *Mucoraceae,* Mucorales order of Zygomycetes class. Arnold Paultauf was the first to describe about mucormycosis. The fungi in this family are Mucor, Rhizopus, Rhizomucor and Absidia [1].

It affects people with immunocompromised state i.e., diabetic ketoacidosis, uncontrolled diabetes mellitus, organ transplant patient on immunosuppressive therapy, corticosteroid therapy, malignancies (lymphoma and leukemia), and AIDS (acquired immune deficiency syndrome) [2,3].

They are found in soil and decaying products. Mode of infection is via inhalation of fungal sporangiophores or direct inoculation of fungi through lacerated skin or disrupted mucosa [4,5].

The fungus lodges in the paranasal sinus and spreads to orbits, brain, meninges through invasion of blood vessels by hyphae causing infarction and tissue necrosis giving the appearance of black discoloration to nasal palate and secretions [4,5]. The necrosed tissue acts as a nidus for fungal growth [6-8].

In immunocompetent persons, the spores and hyphae are destroyed by phagocytosis by mononuclear and polymorphonuclear cells. Patients with neutropenia, impaired phagocyte function, uncontrolled diabetes mellitus become susceptible to mucormycosis. High glucose levels favour the growth of the fungi [13,14].

Intracranial involvement occurs via by way of the superior orbital fissure, ophthalmic vessels, and cribriform plate, through the carotid artery, or possibly via a perineural route [1-5,7].

The angioinvasive nature and ability for bone destruction are responsible for rapid dissemination from nasal cavity to orbits and intracranial extension in rhino-orbito-cerebral mucormycosis.[4] The mucormycosis from ethmoid sinus spread through the lamina papyracea into the orbit, extraocular muscles, and optic nerve [5,11,12]. Vascular invasion causes thrombosis of cavernous sinus and infarction in brain parenchyma.

Patients with ischemic stroke presented as aphasia, hemiparesis and monoparesis. Patients had restricted extraocular movements and hypothesia of forehead and cheeks due to involvement of oculomotor, trochlear, abducens, ophthalmic and maxillary division of trigeminal nerve due to extension to cavernous sinus and thrombosis of cavernous sinus. Patients had presented with features of orbital apex syndrome with complete ophthalmoplegia, visual loss and hypoesthesia of forehead (involving the optic, oculomotor, trochlear, abducens nerves). In 3 cases leptomeningeal spread was detected in MRI brain. 3 patients had internal carotid artery occlusion.

Orbital apex syndrome is common presentation of mucormycosis [8-10].

The patients were treated with liposomal amphotericin B, and surgical debridement of necrosed tissue was done [15-17]. Patients were given antiplatelets (Aspirin /clopidogrel), Statins (ischemic stroke), inj. Heparin, antiedema measures (inj. Mannitol) and inj. Phenytoin and lorazepam for seizures.

Treatment with corticosteroids with huge numbers of diabetic patients as well as COVID-19 infection has increased the risks of

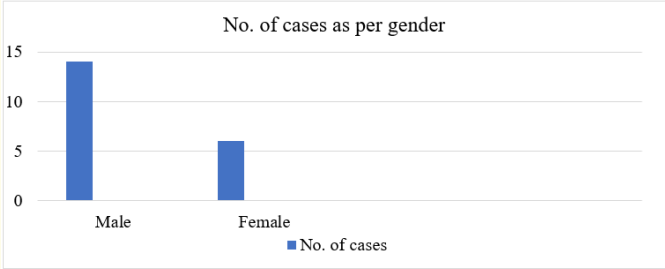

Chart 1: Males are prone to be affected than females.

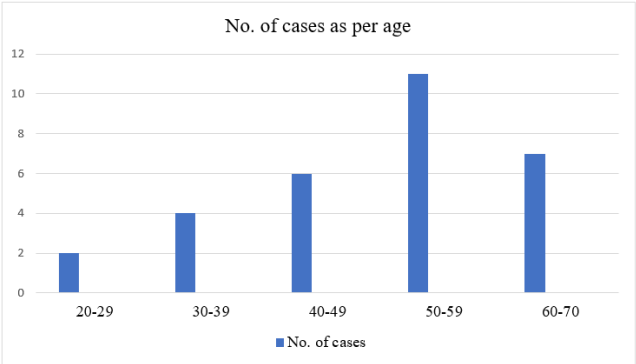

Chart 2: Patients with age more than 50 year of age are more predisposed to rhino-orbito-cerebral mucormycosis.

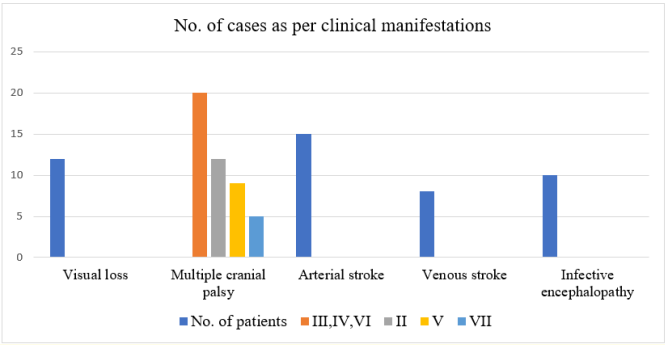

Chart 3: The most common neurological symptoms are headache, visual loss, complete ophthalmoplegia, unilateral facial sensory loss, facial palsy, seizure, weakness of upper and lower limb in one half of body.

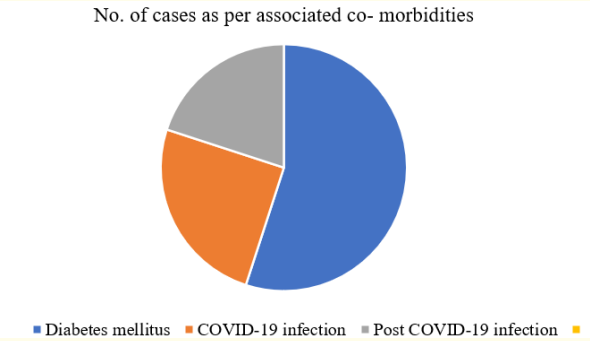

Chart 4: Patients with diabetes mellitus with COVID-19 infection have increased risk of acquiring mucormycosis.

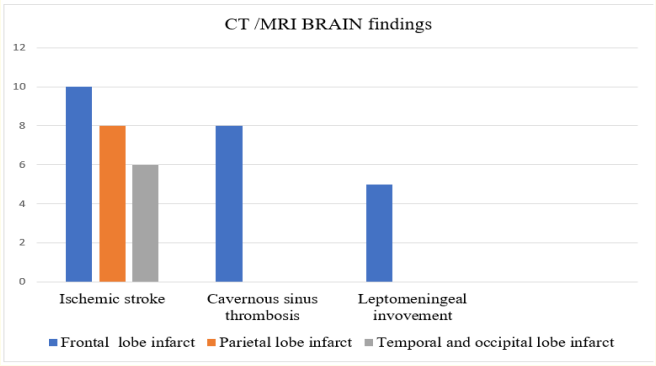

Chart 5: In ischemic stroke, the anterior circulation is more prone for infarction than posterior circulation. In venous circulation, cavernous sinus is more affected.

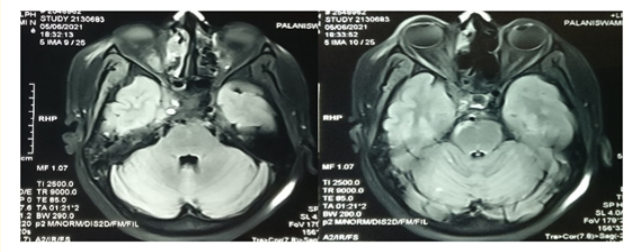

Figure 1: Ischemic stroke – CT Brain showing acute infarct in left frontal lobe, parietal lobe and occipital lobe.

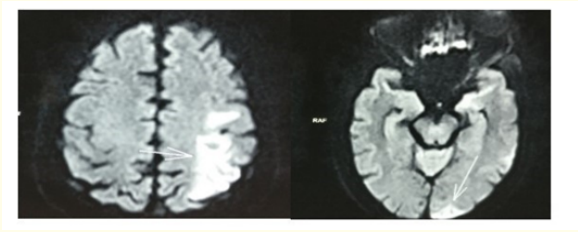

Figure 2: Diffusion weighted imaging of brain showing diffusion restriction in the left frontoparietal and occipital lobe suggestive of acute infarction.

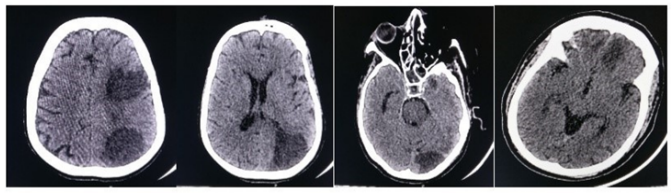

Figure 3: Cavernous sinus invasion- Magnetic resonance imaging of brain T2 FLAIR- Skull base extension with right cavernous involvement.

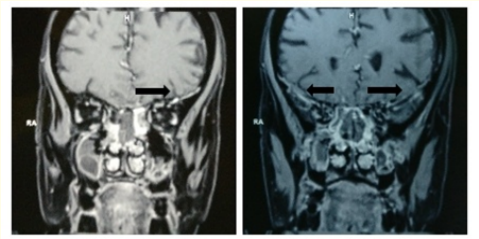

Figure 4: Meningeal invasion- Basifrontal leptomeningeal enhancement.

acquiring mucormycosis (Chart 1-5 and Figure 1-4).

Conclusion

There is increasing incidence of neurological complications in mucormycosis during COVID-19 pandemic. Judicious use of corticosteroids and strict hyperglycemic control can help us in reducing the no. of mucormycosis cases and its neurological complications.

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