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COVID-19 Infection Triggering Rhino-Orbital Mucormycosis –A Review of 2 Cases

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Abstract **Case Report**

The corona virus disease has spread rapidly on a global scale. Superinfections and coinfection in covid-19 pneumonia are still under exploration. Amongst secondary infection, fungal infections are ten times more common. We present two cases of rhino-orbital mucormycosis after covid-19 infection.

Keywords: Mucormycosis, rhino-orbital, post COVID-19 infection.

INTRODUCTION

The corona virus disease has spread rapidly on a global scale [1, 2]. Superinfections and coinfection in covid-19 pneumonia are still under exploration [3]. Amongst secondary infection; fungal infections are ten times more common [3]. As the nature of the disease is not completely understood, it is not clear whether this is a complication of the disease or its management. Mucormycosis is an aggressive fungal infection and increasing trend is observed during COVID-19 pandemic. We present two cases of COVID-19 infection triggering rhino-orbital mucormycosis to highlight the aggressive clinical course and morbidity of this infection.

CASE REPORT

Case-1

52 year old male patient presented with fever, headache and swelling of right eye since 10 days. There was complete loss vision of right eye. On examination there was ptosis of right eye with proptosis and opthalomoplegia (Fig -1). The patient gave a history of COVID-19 infection 15 days back and was newly diagnosed case of diabetes mellitus type-2. Investigations done are shown in box-1.Biopsy from infected site revealed mucormycosis. The patient was treated with inj liposomal amphotericin and inj H. Actrapid and supplementation with zinc, oral calcium and multivitamins**.** Exentration of right eye and Functional Endoscopic Sinus Surgery with debridement was done. Histopathological examination of samplings from eyeball, periorbital soft tissue and soft tissue from paranasal sinuses revealed fungal hyphae of mucormycosis which were confirmed with PAS and GMS stain (Fig-6,7). Postoperative amphotericin was continued for 8 days and patient was discharged after repeat MRI.

Case-2

58 year old male complained of nasal stuffiness, facial pain and swelling of right eye which was progressive in nature since 10 days. There was complete loss of vision with redness and swelling of right eye (Fig- 2). The patient gave a history of COVID 19 infection 15 days back and was a known case of diabetes mellitus type-2 and on medications since 16 years. The patient was treated with inj liposomal amphotericin and inj H. Actrapid and supplementation with zinc, oral calcium and multivitamins**.** Exentration of right eye and Functional Endoscopic Sinus Surgery with debridement were done. Investigations done are shown in Fig-3 and Box-2. HPE revealed mucormycosis with mixed inflammation and giant cell reaction, areas of hemorrhage and necrosis (Fig-4, 5). Postoperative amphotericin was continued for 10 days and patient was discharged after repeat MRI report.

DISCUSSION

Mucormycosis is one of the most fulminant forms of zygomycosis which is caused by Mucorales species of the phylum Zygomcota [4]. It is a lethal infection seen in immunocompromised hosts most commonly candidates with diabetes mellitus, leukemia, iatrogenic immunosuppressive and acquired immunodeficiency syndrome. Paltauf in 1885 initially described this infection[5].Though the incidence rate is low varying from 0.005 to 1.7 per million people, there

is significant increase in the wake of ongoing COVID-19 pandemic [6]. COVID-19 patients have started developing this fulminant infection during middle and later stages of the disease [7]. Both of our patients developed this infection in late stage of COVID-19 disease. Disease can manifest as one of the different clinical forms such as rhino-orbital, pulmonary, cutaneous, gastrointestinal, central nervous system and miscellaneous [8, 9]. Rhinoorbital presentation is the most common presentation as seen in our cases.

General characteristics

Mucormycosis are saprophytic fungi present in dust decaying material, hospital ward rooms and air conditioners. They grow fast and show irregularly shaped large non septate hyphae with wide angle.

Pathogenesis

The route of transmission for organism is air borne through asexual spores and invasion occurs in paranasal sinuses and respiratory tract. The fungus being extremely angioinvasive results in thromboembolism and subsequent infarction [10]. In diabetic patients raised levels of serum free iron favours growth of this organism. In patients with diabetic ketoacidosis, increased levels of serum free iron occurs due to acidemia which causes release of iron form binding protein such as transferrin [11]. Neutropenia and raised serum iron are risk factors for the infection. Our cases showed increased serum ferritin and neutrophilia.

CLINICAL FEATURES

Rhino-orbital mucormycosis affects paranasal sinuses after inspiration of spores and spreads to eye and brain. Symptoms include sinus pain, fever, headache, congestion and soft tissue swelling. Symptoms generally appear 2-3 weeks after recovery of COVID 19 infection. Our patients presented 2 weeks after recovery from COVID -19 infections. Progression of disease occurs rapidly extending to neighbouring tissue causing thrombosis and necrosis with painful brown blood eschar on the maxilla. Extension to the eye may cause blurred vision or complete blindness. Disease can spread to central nervous system from eyes causing altered sensorium, cranial neuropathies or cerebral abscess [12]. Our cases presented with facial pain, orbital cellulitis with phlegmon and opthalmoplegia of eye with complete loss of vision.

DIAGNOSIS

Early diagnosis of mucormycosis is critical so that treatment can be started at early as possible. Clinical features and radiological investigations are not sufficient for diagnosis. Definitive diagnosis is essential which requires a direct identification of fungal hyphae in histopathology slides or fungal culture obtained from the site of infection. Initiation of treatment should not be delayed waiting for cultures. Positive report on smear or histopathology should be sufficient for initiating treatment. Polymerase chain reaction enables rapid diagnosis. Imaging modalities are useful in defining extent of disease and to detect cavernous sinus thrombosis.

TREATMENT

Immunosuppressive medications particularly steroids should be stopped immediately. In diabetic ketoacidosis, aggressive management to rapidly restore blood sugar level and acid base balance is essential. Iron administration should be avoided as it aggravates the disease. For complete eradication of mycosis debridement is needed. If not done, tissue necrosis and vessel thrombosis may result in more damage [13]. Amphotericin deoxycholate is primary therapeutic antifungal agent. Non-conventional agents include antidiabetic, iron chelating agents, statins, granulocyte transfusion, cytokines and hyperbaric oxygen which increase survival rate [14].

CONCLUSION

Mucormycosis is an aggressive fungal infection and spike in cases have been observed during COVID pandemic era. Impaired cellular and humoral responses in COVID- 19 disease triggers this fungal infection. Treatment with anti-inflammatory and immunosuppressive drugs further raise the risk of mucormycosis. Histopathological study offers a definitive diagnosis and plays an important role in initiation of treatment. Clear understanding of the pathogenesis of the disease is needed to offer new strategies for prevention and treatment of mucormycosis.

Fig-1: Right eye. Orbital cellulitis (Case-1)

Fig-2: Redness and swelling of eye (Case-2)

Fig-3: MRI-Maxillary sinusitis (fungal) with invasion into right orbit (Case-2)

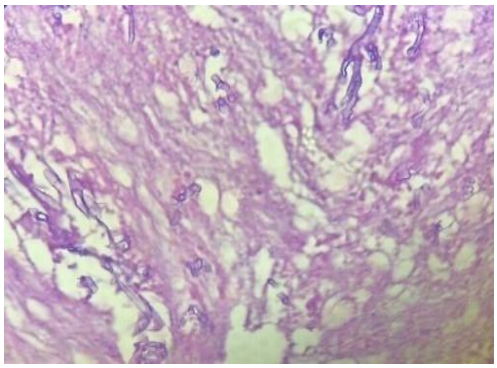

Fig-4: Broad aseptate fungal hyphae stained with H &E (400X)

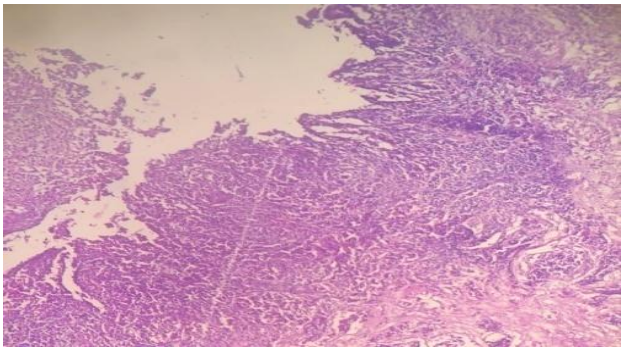

Fig-5: Inflammatory reaction to fungal hyphae (400X H&E)

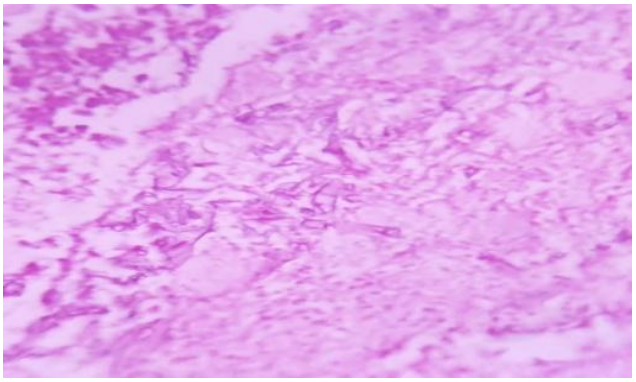

Fig-6: Fungal Hyphae confirmed with PAS stain (400X)

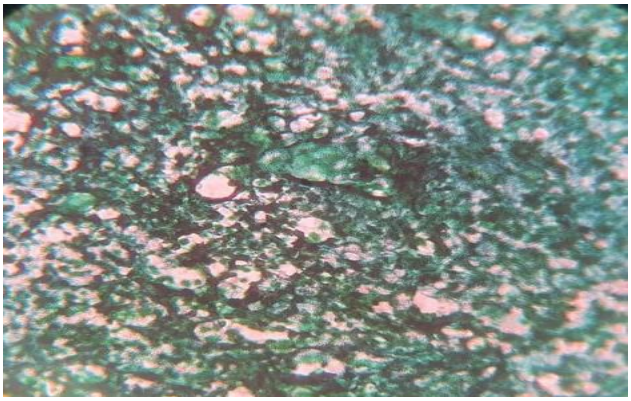

Fig-7: Fungal hyphae stained with GMS (400X)

Table-1: Investigations - Case-1

Hb	11.1gm/dl (13.0-17.0 gm/dl)
TLC	5300/cumm with Neutrophilia-86% (4000-11000/mm^3) (>75%)
ESR	70 mm/ 1 hour (Male 0-15mm/1 hour)
BSL(F)	304mg/dl (70-110mg/dl)
HBA1C	6.6% (4-6%)
URINE EXAMINATION	Urine sugar +++ (absent), Proteins & Ketones absent (absent)
SERUM FERRITIN	1514 ng/ml) (Male-21.8-276 ng/ml)
D-DIMER	1mg/L (0-0.5 mg/L)

Table-2: Investigations - Case-2.

Hb	11.3gm/dl (13.0-17.0 gm/dl)
TLC	9300/cumm with Neutrophilia-85% (4000-11000/mm^3) (>75%)
ESR	75mm/1 hour (Male 0-15mm/1 hour)
BSL(F)	225mg/dl (70-110mg/dl)
HBA1C	6.8%
URINE EXAMINATION	Urine sugar + (absent), Proteins + & Ketones –Negative (absent)
SERUM FERRITIN	1120ng/ml (Male-21.8-276 ng/ml)
D-DIMER	1.5 mg/L (0-0.5 mg/L)

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