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Case Report

Post Covid-19 Cerebellar Mucormycosis Without Apparent Rhino-Orbital or Ear Involvement – A Case Report

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Abstract

Fungal infection of the central nervous system, especially intracranial mucormycosis are very rare. It is not an independent disease, but a secondary opportunistic infectious disease. There is an increase in the incidence of mucormycosis in post Covid-19 infection patients. It can be attributed to impairment of barrier defense, dysfunction of phagocytes and lymphocytes and the use of immunosuppressive medications such as steroids and toclizumab. There is usually some evidence of rhino-orbital or ear involvement in the cases in intracranial mucormycosis. We present a rare case of a 48 year old male patient with a history of Covid-19 infection who presented with apparent isolated cerebellar mucormycosis.

Keywords: *Covid-19, Mucormycosis, Intracranial Mucormycosis*

Key Message: *Cases of invasive mucormycosis have increased in this Covid era. Patients with Covid-19 infection are susceptible to mucormycosis because of impairment of barrier defense, dysfunction of phagocytes and lymphocytes and the use of immunosuppressive medications such as steroids and toclizumab. Treating clinicians need to be aware of the possibility of mucormycosis, in such patients particularly in those with underlying comorbidities. Early diagnosis and treatment of secondary fungal infections can substantially reduce morbidity and mortality.*

Introduction

Fungal infections of the central nervous system, especially cerebral mucormycosis are very rare. With the advent of the Covid-19 pandemic, the incidence of this disease has exhibited an increasing trend. A hallmark of mucormycosis infection is the presence of extensive angioinvasion with resultant vessel thrombosis and tissue necrosis. [1] In later stages of Covid-19 infection, epithelial-endothelial barrier integrity is compromised which predisposes the patient to invasive mucormycosis.[2] Additionally, corticosteroid treatment affects the ability of macrophages to prevent the germination of the spores of these fungi.[3] It can spread to the intracranial compartment either through local

invasion by nasal and orbital mucormycosis or through the blood circulation.[4] The former route is the most common and is responsible for the majority of the cases of intracranial mucormycosis. We report a rare case of a 48 year old male patient with a history of Covid-19 infection and corticosteroid treatment who presented with cerebellar mucormycosis without apparent nasal or orbital involvement.

Case Report

A 48 year old male patient presented to our OPD with complaints of headache, dizziness and imbalance while walking since last seven days. On neurological examination the patient was conscious and oriented to time place and person with no limb or facial weakness. His ENT examination was unremarkable. His cerebellar signs were positive on right side. He had no medical history of hypertension or diabetes mellitus. He had ha history of mild Covid-19 infection two months ago for which he was hospitalized for five days and was treated with antivirals and dexamethasone.

His MRI Brain with Contrast revealed a 21x26x23 mm ill defined T1W hypointense [Fig. 1] and T2W hyperintense [Fig. 2] lesion involving then right side inferior medial cerebellar hemisphere reaching towards right side vermis region with perilesional edema. The lesion showed diffusion restriction on DWI images and a peripheral ring like contrast enhancement [Fig. 3]. The overall picture was suggestive of an abscess formation.

The patient underwent full workup to detect the source of the abscess. His Chest X-ray, USG abdomen and MRI PNS and Orbit with Contrast revealed no abnormalities. Considering his history of Covid-19 infection, a nasal swab for KOH testing was also sent which also turned out normal.

The patient was posted for surgery and neuronavigation guided excision of the cerebellar abscess was performed. The lesion was grayish-white in color and also contained minimal amount of pus. The excised lesion was sent for histopathological examination.

Histopathology report revealed cerebellar tissue showing areas of necrosis, collection of inflammatory cells comprising of histiocytes, lymphoplasmacytic cells & neutrophils and broad, aseptate fungal hyphae [Fig. 4] which were positive on Grocott methenamine silver stain [Fig. 5]. The overall picture was diagnostic of mucormycosis.

The patient was then started on injection Amphotericin-B at the dose of 5mg/kg/day for 14 days and then was shifted to oral Posaconazole maintenance therapy at 300mg/day.

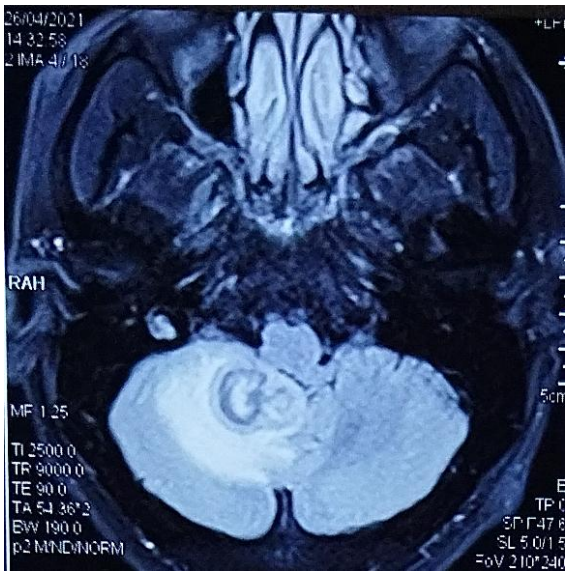

Fig 1: MRI brain showing T1 hypointense cerebellar lesion.

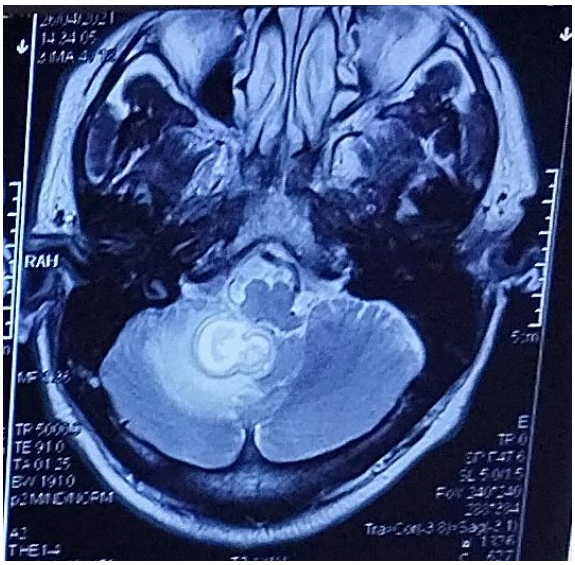

Fig 2: MRI brain showing T2 hyperintense cerebellar lesion.

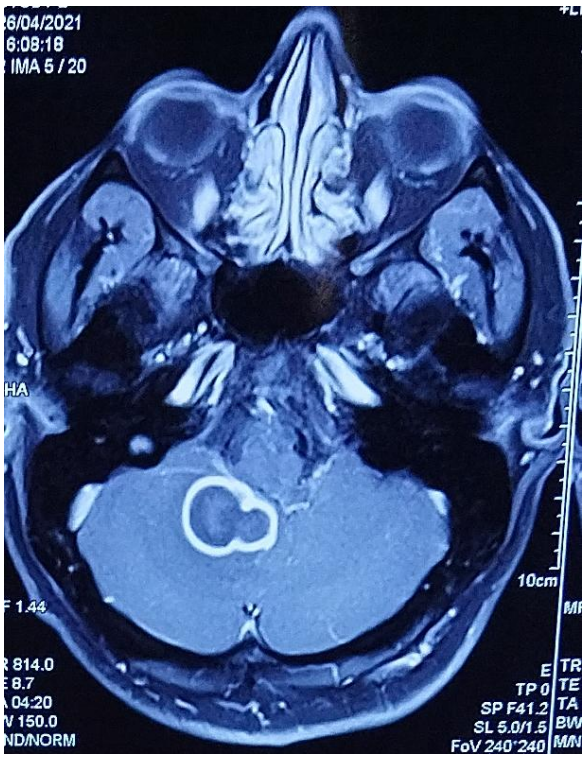

Fig 3: MRI brain showing lesion with post contrast ring like enhancement.

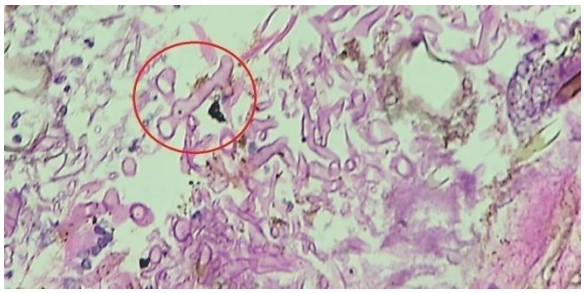

Fig 4: HE stain showing broad aseptate fungal hyphae.

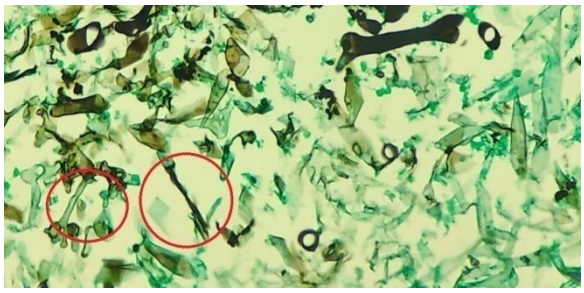

Fig 5: Grocott methenamine silver stain showing broad aseptate fungal hyphae.

Discussion

Invasive mucormycosis is not an independent disease, but a secondary opportunistic infectious disease. Mononuclear and polymorphonuclear phagocytes of normal hosts kill mucorales by generation of oxidative metabolites and defensins; hence neutropenic patients and those with dysfunctional phagocytes are susceptible to develop invasive mucormycosis.[3] In Covid-19 there is lymphopenia and in advanced infections viral replication accentuates the inflammatory response.[2] This leads to an imbalance between neutrophil and lymphocyte action making the patient more susceptible to systemic fungal infections. Administration of steroids results in neutrophilic leukocytosis and the impaired ability of leukocytes to migrate to the site of inflammation. Prolonged use of glucocorticoids is known to increase the risk of the patient to many opportunistic infections. [5] Recent published evidence says that Covid-19 is a pro-coagulable state and there is increased incidence of thrombotic events. [2] This pro-coagulable state provides a perfect ground for the angioinvasion of mucor due to vessel thrombosis and leading to disseminated infections.

Mucor could invade the intracranium through many routes. [4] It can colonize the nasal mucosa and cause mucosal degeneration & necrosis expanding to paranasal sinuses and then by eroding their wall spread intracranially. It can also invade the orbit directly from the nasal cavity and paranasal sinuses and then spread intracranially by entering the orbital vessels or the optic canal. These two routes are the most common and account for approximately 75% of cases of intracranial mucormycosis. Rarely can they also spread in the cranium through the blood circulation. In our case there was no apparent orbital or nasal-paranasal involvement, suggesting that it may have spread through the hematogenous route from a distant focus.

Once spread intracranially, mucor forms an abscess in the brain parenchyma which present with signs and symptoms as any other space occupying lesions like headache, mental status changes, focal neurological deficits and seizures. [6] MRI brain shows a T1 hypointense and T2

hyperintense lesion with surrounding edema showing a ring like enhancement on contrast administration just like any other brain abscess.[7] CT and MRI of the nasal and orbital tissues are necessary to look for the primary causative lesions. Definitive diagnosis requires histopathological examination of the specimen to look for aseptate fungal hyphae and can be confirmed using Periodic Acid Schiff stain and Grocott methenamine silver stain. [8] Treatment consists of immediate craniotomy and excision of the abscess. The patient may also require extensive surgery to remove the primary nasal or orbital lesions. [9] Once mucormycosis has been confirmed the patient has to be started on injectable Amphotericin-B and then can be shifted to maintenance oral Posaconazole therapy. Glycemic control is also an integral part of the treatment of mucormycosis. [10]

Conclusions

Patients with Covid-19 infection are susceptible to mucormycosis because of impairment of barrier defense, dysfunction of phagocytes and lymphocytes and the use of immunosuppressive medications such as steroids and toclizumab. Although most of the cases of intracranial mucormycosis have evidence of nasal or orbital involvement, some patients may present with isolated intracranial involvement. Treating clinicians need to be aware of the possibility of mucormycosis, in such patients particularly in those with underlying comorbidities. Early diagnosis and treatment of secondary fungal infections can substantially reduce morbidity and mortality.

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