LETTER TO THE EDITOR

Cerebral Aspergillosis Complicating COVID Recovery

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Dear Editor,

Sir, as we see the coronavirus disease-2019 (COVID-19) wave sweeping through the whole world, it has also set as a new host for secondary bacterial and fungal infections. In light of the recent studies revealing the high incidence of COVID-19-associated pulmonary aspergillosis—CAPA, we would like to highlight a rare complication of the same with its systemic spread involving the brain parenchyma.[1–4] We report a case of cerebral aspergillosis in a patient with SARS COVID pneumonia, who had secondary pulmonary fungal cavitary lesion followed by cerebral invasion, which eventually turned out to be fatal.

Our patient was a 38-year-old immunocompetent man, who had presented to our emergency from a local hospital, with history of breathing difficulty, fever, and cough for 10 days. He had tested positive for COVID-19 and had worsening hypoxemia, requiring oxygen supplementation. His initial CT chest scan showed bilateral ground-glass opacities with CT severity index (CTSI) ~ 6/25, which had progressed to ~22/25, by the time he reached to us (Fig. 1). In ICU, the patient was received in ICU with low oxygen level, SpO_2 ~ 85% on oxygen support with fraction of inspired oxygen (FiO_2) ~ 0.6 on Venturi mask. Management was started on lines of severe COVID pneumonia with methylprednisolone in dose of 5 mg/kg in two divided doses for 3 days, antiviral and broad-spectrum antibiotics, and placed on high-flow nasal cannula support @ 0.8 FiO_2. In view of evident cytokine storm, he was administered bevacizumab. Tocilizumab was not given due to the past history of old treated pulmonary Koch's.

In view of worsening respiratory failure, he was placed on mechanical ventilation at FiO_2 ~ 1.0. The patient showed an improvement on steroids and bevacizumab. He was extubated after 4 days of ventilation and placed back on high flow nasal cannula (HFNC) support with FiO_2 ~ 0.5. During his further course of illness, he had secondary infection evident by persistent leukocytosis and sputum yielding *Klebsiella pneumoniae* (carbapenem-resistant bug). Antibiotics were upgraded accordingly, and posaconazole was added empirically, considering the use of steroids and immunomodulators. He continued to be on HFNC support with FiO_2 ~ 0.5, and steroids were tapered in a protocolized manner.

We did a follow-up third CT chest at 30 days of illness, which showed a new finding of air-filled cavitary lesion in the left lower lobe along with mild pneumomediastinum (Fig. 2). A high suspicion

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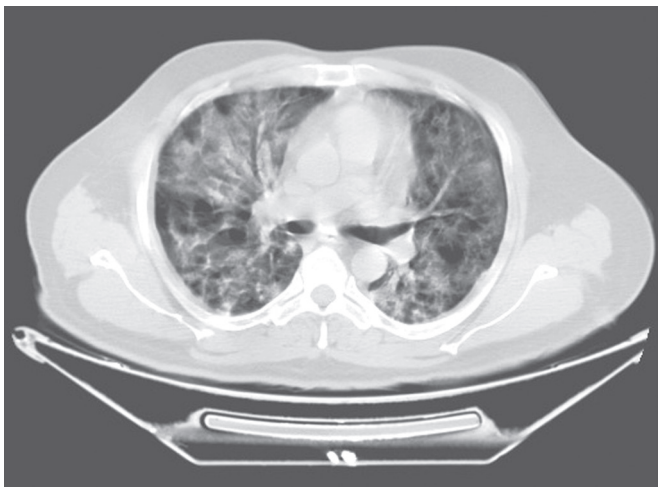

Fig. 1: HRCT chest showing diffuse ground-glass opacifications in bilateral lungs with CTSS 22/25

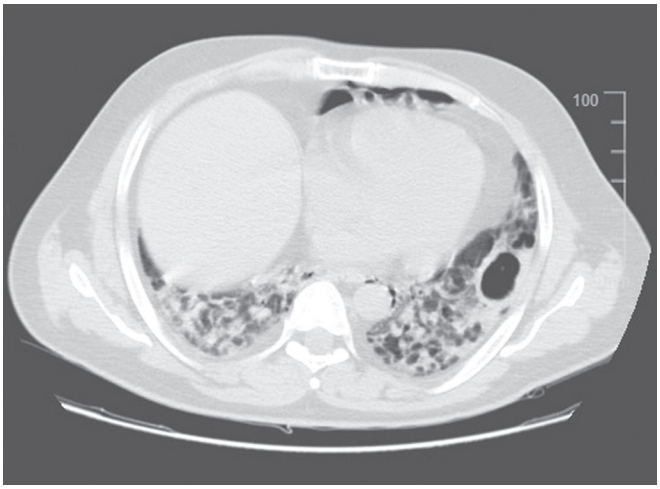

Fig. 2: HRCT chest showing GGOs with reticulations scattered in all lobes of both lungs along with air-filled cavitary lesion in lateral basal segment of the left lower lobe

of fungal pneumonia was kept, and micafungin was added to posaconazole. We saw a good clinical response, and his FiO_2 came down to 0.3.

As our patient was recovering, he had insidious onset of weakness in the left lower limb progressing to the whole left side of the body over 24 hours. He had been conscious, oriented, but had a power of around 2/5 in lower limbs. Nerve conduction studies (NCS) was suggestive of polyneuropathy. Suspecting Guillain-Barre syndrome (GBS) for asymmetrical presentation, cerebrospinal fluid (CSF) was done, which showed exudative picture with total leucocyte count (TLC) ~ 275, N 92, and negative cultures. MRI brain revealed multiple peripheral enhancing lesions showing diffusion restriction with T1 central hyperintensity with T2 hypointensity and blooming on multiecho gradient recalled echo (GRE) images in bilateral cerebral hemispheres, left cerebellar hemispheres, and pons with mild perilesional edema, which are suggestive of infective eitiology: fungal (Figs 3 and 4). Considering the new lesions be of

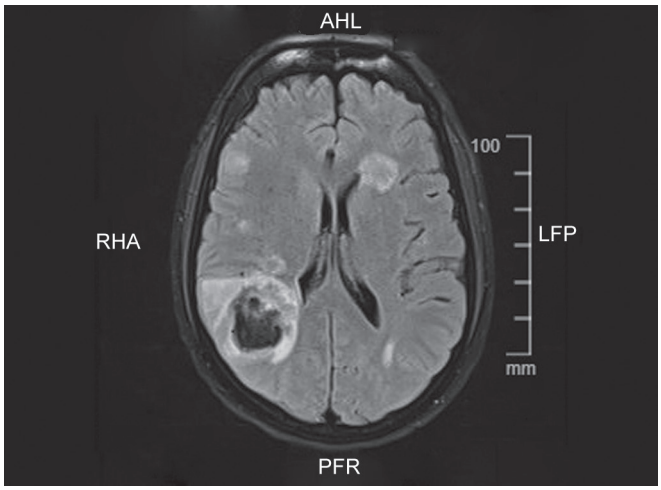

Fig. 3: MRI T2WI showing hemorrhagic lesion in right parieto-occipital lesion with other hyperintense lesions close to the left frontal horn

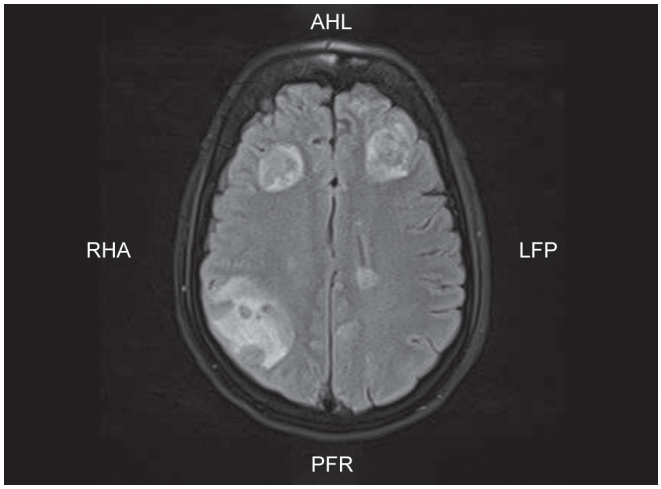

Fig. 4: MRI flair image showing multiple hyperintense lesions in bilateral frontoparietal area

fungal origin, we shifted him onto liposomal amphotericin for better central nervous system (CNS) penetration and other antifungals were taken off. But he had a rapid neurological deterioration as he became drowsy and had seizures. He had to be re-intubated and mannitol, and antiepileptics and dexamethasone were started. Neurosurgery opinion was sought, and he was taken up for right parieto-occipital decompressive craniotomy with cavity excision after formal family consent.

Post-decompression, he didn't improve and had Glasgow Coma Scale (GCS) E1 Vt M1,with severe brainstem dysfunction, and on postoperative day 4, unfortunately he died. Histopathologic report of brain tissue revealed hyaline septate fungal hyphae with acute angle branching suggestive of aspergillus.

So, with this case, the authors would like to highlight the rapid invasion of the fungal infection despite treating with antifungals in a timely manner. We had seen cerebral involvement, with mucor but with aspergillosis, it had been a rare presentation. Its incidence in immunocompetent patient is very rare, and in ongoing COVID pandemic, till date, there is only one reported case of fatal disseminated aspergillosis in immunocompetent patient with COVID-19 due to *Aspergillus ochraceus* by Hakamifard et al.[5]

We wish to emphasize on the early need of identification of invasive fungal infection in COVID patients who are receiving steroids and immunomodulators. This case adds on to data reflecting high mortality due to the rapid fungal invasiveness. The need of hour is to evaluate the incidence and the dynamics of invasive fungal infection in the course of COVID-19 and formalize preventive strategies and environmental measures and management algorithms to decrease morbidity and mortality.

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