Cerebral Mucormycosis in Context with COVID-19 Infection

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Sir,

Rhino-orbital-cerebral mucormycosis (ROCM) is an uncommon infection caused by the angiotropic fungus belonging to the order Mucorales, which almost always occurs in immunocompromised hosts (uncontrolled diabetes mellitus, hematologic cancers, and solid organ or hematopoietic stem cell transplants). The suspicion or diagnosis of ROCM triggers a medical as well as surgical emergency, as delay in treatment increases morbidity and mortality.1 In India, after the second peak of COVID-19 infection, there was a surge in cases of mucormycosis implicating complex interplay of various factors such as an ideal environment of low oxygen, high glucose, acidic medium, high iron levels, and decreased phagocytic activity of white blood cells due to immunosuppression coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators.2 Here we present a clinical profile and outcome of ROCM at our institute.

After getting permission from the IEC-IRB-PG research, an observational prospective study of 14 patients was carried out at a single-center tertiary care hospital over a period of 3 months.

The significant findings of our study are:

- During the time of admission, 12 patients (85.71%) had SpO2 ≥90 and only two
patients had SpO₂ < 90. The patients with high oxygen requirements had died (4–28.57%); whereas out of eight patients on room air, seven were discharged and only one died (p-value = 0.008). This finding suggests that patients with high oxygen requirements have higher mortality (Table 1).

- On radiological evaluation, computed tomography of the paranasal sinus (PNS) and magnetic resonance imaging of brain + orbit + PNS of six expired patients showed involvement of ≥3 sinuses (n = 5), cavernous sinus (n = 4) with proptosis (n = 2), and infraorbital extension. Whereas involvement of ≥3 sinuses (n = 5), frontal lobe (n = 5), optic nerve with infraorbital extention and other central nervous system (n = 8) without cavernous sinus involvement were seen in eight discharged patients. This suggests that patients in whom infection has extended to cavernous sinus had higher mortality.

- Six (75%) out of eight discharged patients had undergone sinuscopy and debridement, whereas three (50%) out of six expired patients had surgical intervention mentioned above. This result suggests that early surgical intervention could reduce mortality in ROCM however larger studies are required to throw further light.

Other data collected during the study suggest that all 14 patients were diabetic (seven known cases and seven freshly diagnosed), with higher mortality among uncontrolled diabetics. Six patients received steroids (high dose methylprednisolone and low dose dexamethasone) as a part of COVID-19 treatment but no significant effect on mortality. The main presenting complaints were local symptoms such as orbital swelling, orbital pain, headache, and facial pain. Thirteen patients (92.86%) were COVID positive (recent and past) with 100% mortality in those having recent COVID infection, and only one patient had no past history of COVID (discharged). All 14 patients were not vaccinated for COVID-19 infection. Case fatality was 42.86% (six patients) and 57.14% (eight patients) were discharged.

On laboratory evaluation, almost all the patients had raised inflammatory markers (neutrophil-lymphocyte ratio, C-reactive protein, ferritin, and lactate dehydrogenase) with low serum albumin. All the patients had received lyophilized amphotericin-B maximum for up to 28 days. The patients who developed nephrotoxicity and had estimated glomerular filtration rate < 10 were given liposomal amphotericin-B. The major side effects on receiving amphotericin-B were hypokalemia (n = 13), nephrotoxicity (n = 9), hypocalcemia, and hypomagnesemia in decreasing order.

To conclude, in our study, we have observed that there was no significant difference in mortality among age group, gender, or severity of COVID-19 infection. Major presenting complaints were local symptoms involving orbit. Thirteen patients had history of COVID infection (recent and past). However, all the patients with recent COVID infection died (Table 1). Patients with higher oxygen requirements had higher mortality compared to those who were on room air. Cavernous sinus involvement in ROCM patients could be considered as a poor prognostic marker as observed in our study. However, this part of study should be explored further. We also observed that early surgical intervention and antifungal treatment are beneficial for patients in form of less morbidity and mortality among them. Major side effects of amphotericin-B were nephrotoxicity (64.29%) and dyselectrolytemia (50%).

### Table 1: Association of COVID-19 infection with outcome in patients with ROCM

<table>
<thead>
<tr>
<th>History of COVID-19 infection</th>
<th>Discharged</th>
<th>Death</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Past COVID-19</td>
<td>7 (53.85%)</td>
<td>2 (15.39%)</td>
<td>9 (69.23%)</td>
</tr>
<tr>
<td>Recent COVID-19</td>
<td>–</td>
<td>4 (30.77%)</td>
<td>4 (30.77%)</td>
</tr>
<tr>
<td>Total</td>
<td>7 (53.85%)</td>
<td>6 (46.15%)</td>
<td>13</td>
</tr>
</tbody>
</table>

Past COVID-19—those patients who were COVID positive within past 6 months but not at the time of admission; Recent COVID-19—those patients who are COVID positive at the time of admission

###References
