Chronic Invasive Aspergillosis with Fulminant Mucormycosis Sparing Palate in a Post-COVID-19 Patient - A Case Report

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Abstract

Rationale: COVID-19 patients, especially immunocompromised or severely ill, have a higher probability of suffering from invasive fungal infections. Patient Concerns: A 41-years-old male reported with pain and heaviness in the face for the past 20 days. Patient had tested COVID-19 positive 20 days back and was recently diagnosed with diabetes mellitus. On histopathological examination numerous hyphae resembling *mucor* and asper fungi were evident. Diagnosis: Chronic invasive aspergillosis with fulminant mucormycosis sparing palate. Treatment: Since the lesion was spreading very rapidly the patient was referred to an isolation facility for further management. Outcomes: We have postulated few hypothesis for the coinfection of aspergillosis and mucormycosis in our patient. Take-away Lessons: It is important for the clinicians to systematically screen post COVID-19 patients for fungal infections, especially in immunocompromised and severely ill patients.

Keywords: Aspergillosis, coinfection, COVID-19, mucormycosis, mycoses

Introduction

The pandemic COVID-19 continues to be a significant problem worldwide.[1] COVID-19 patients, especially immunocompromised or severely ill, have a higher probability of suffering from invasive fungal infections.[2,3] Recently, a more dangerous and potentially deadly infection, invasive fungal sinusitis, resulting from mucormycosis in post-COVID-19 patients has been observed.[4] The most common causes attributed to the rise of mucormycosis in COVID-19 patients are the excessive use of corticosteroids, uncontrolled diabetes, and long-term stays in the ICU.[5] We hereby report a case of chronic invasive aspergillosis with fulminant mucormycosis sparing palate in a post-COVID-19 patient. To the best of our knowledge, no case reports with invasive aspergillosis with fulminant mucormycosis in post-COVID patients have been reported in the literature.

Case Report

A 41-year-old male reported pain and heaviness in the face for the past 20 days. He also complained of multiple swellings with pus discharge from the upper jaw and mobility of the upper teeth for the past 10 days. The patient had tested COVID-19 positive 20 days back and was hospitalised for the same for seven days. He noted facial swelling and blackish green nasal discharge within few days of being hospitalised. The patient was recently diagnosed with Type II diabetes mellitus (capillary blood glucose (CBG) – 317 mg/dl) and also gives a history of steroid administration for eight days during hospitalisation for COVID-19. On examination, swelling was present in relation to the left maxillary sinus [Figure 1a]. Multiple sinus openings were evident in relation to the attached gingiva of 13–23 region. The palatal mucosa appeared normal [Figure 1b]. No ulceration or pus discharge

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was evident on the palatal mucosa. Cone-beam computed
tomography revealed osteolytic changes involving bilateral
maxillary sinus with thinning of palate and haziness in the
right and left maxillary sinus [Figure 1c]. Based on the patient
history and clinical examination, a provisional diagnosis of
mucormycosis was given. On histopathological examination,
numerous tightly packed thin septate hyphae branching at
acute angle along with many fruiting bodies (conidial heads)
were evident [Figure 2a and b]. Several areas of broad aseptate
hyphae branching at 90° and aseptate broad hyphae branching
at obtuse angle were also present [Figure 2c and d]. There was
also evidence of extensive areas of tissue necrosis and necrotic
bone. Based upon the above histopathological findings, the
diagnosis of chronic invasive aspergillosis with fulminant
mucormycosis in a post-COVID-19 patient was reported. Since
the lesion was spreading very rapidly, the patient was referred
to an isolation facility for further management.

**Discussion**

Diabetes mellitus, immunosuppressive therapy, and systemic
immune alterations of COVID-19 infection may lead to
secondary infections.[6] Patients with COVID-19 show
increased expression of inflammatory cytokines, and
impaired cell-mediated immunity with decreased CD4- and
CD8-positive T-helper cell counts, indicating susceptibility to
fungal coinfections.[2] In the early stages, the infected tissue
may appear normal, thereafter progressing to erythema and
subsequent development of black, necrotic eschars.[7] Over
the past few months, our institute has seen a sudden rise in cases
of invasive fungal infections, specifically mucormycosis in
post-COVID-19 patients. A black necrotic intranasal or palatal
eschar is highly suggestive of mucormycosis.[7] Majority of
the cases of mucormycosis which are reported in the literature
present with a palatal ulcer. Interestingly, our patient showed
nasal discharge with swelling near the sinus region sparing the
palate. Due to the COVID-19 infection, the clinical symptoms
of mucormycosis seem to be varying. Aspergillosis usually
affects the sinus mucosa with destruction of the nasal cavity,
and adjacent structures such as orbit and brain.[8] Palatal
mucosa is less commonly affected in aspergillosis when
compared to mucormycosis. Aspergillosis could have been
the first organism to cause disease in our patient, followed
by mucormycosis. *Mucor* fungi could have followed the path
of aspergillosis and hence sparing the palate. The presence
of palatal ulcer should not be considered as the only clinical
manifestation of mucormycosis and hence is important for
the clinicians and pathologists to increase awareness of these
varying degrees of clinical.

The finding of hyphal forms of *Aspergillus* is not very common
in biopsies; detection of fruiting bodies of *Aspergillus* in
histopathological section is a rare finding. The hyphal forms
of *Aspergillus* can be confused with the hyphal forms of
other fungi, but when fruiting bodies are present, diagnosis
is possible at the histopathology level itself.[9] Fruiting bodies
(conidia) of aspergilli develop from mycelia in areas of high
oxygen tension or severe infections.[9] Our case showed chronic
invasive aspergillosis along with mucormycosis. There are two
possibilities for this occurrence, we could not ascertain whether
aspergillosis was followed by mucormycosis and henceforth

![Figure 1: Photomicrograph showing (a) Multiple sinus openings in relation
to attached gingiva of 13-23 region (black arrow) (b) Nasal discharge with
apparently normal palatal mucosa (white arrow) (c) CBCT with osteolytic
changes involving bilateral maxillary sinus with thinning of palate. CBCT:
Cone-beam computed tomography](image1)

![Figure 2: Photomicrograph showing (a) Aspergillus fruiting bodies
dissipating spores, (b) Fruiting bodies (black arrow) with Mucor hyphae
(yellow arrow), (c) Numerous broad aseptate hyphae, (d) Narrow
septate hyphae (black arrow), broad aseptate hyphae (green arrow),
broad tortuous Mucor hyphae (yellow hyphae), and hyphae showing
branching (dark blue arrow)](image2)
becoming a fulminant disease, or there was coexistence of these two infections together post-COVID. We have postulated few hypotheses for the coinfection of aspergillosis and mucormycosis in this case [Figure 3]:

1. Radiograph of this patient showed bilateral haziness suggestive of sinusitis? This leads to poorly drained sinus and blocked ostium. At this stage, patient would have inhaled asper followed by mucor spores leading to its coinfection

2. Noninvasive aspergillosis such as aspergilloma could have led to invasive aspergillosis due to COVID infection and steroid therapy. During the course of steroid therapy, the patient could have encountered Mucor spores probably from the hospital (iatrogenic), which could be the reason for coinfection of mucormycosis and aspergillosis

3. COVID-19, diabetes mellitus, and steroid therapy can lead to immune dysregulation, which could have led to invasive aspergillosis and tissue necrosis. At this stage, Mucor spores would have entered the sinus, as the ability of Mucor spores to cause infection depends upon mucosal barrier, environmental factors, and virulence of organism, and as the tissue of the nasal or sinus mucosa was already destroyed by the aspergillosis infection, there would have been an easy entry of these fungi, leading to a coinfection of aspergillosis and mucormycosis

4. COVID-19 along with diabetes mellitus and corticosteroid therapy lead to a combined infection of chronic invasive aspergillosis and mucormycosis due to immune dysregulation.

While invasive aspergillosis and mucormycosis infections are often grouped together under the umbrella of invasive fungal sinusitis, studies have found very different clinical outcomes and treatment strategies between these two infections.

Figure 3: Hypothesis for the coinfection of aspergillosis and mucormycosis
Trief et al. reported that the treatment of mucormycosis and aspergillosis differs, amphotericin B is the preferred antifungal for mucormycosis, and when a diagnosis of invasive *Aspergillus* is made, amphotericin B is switched to voriconazole as this agent was demonstrated to be superior.[10] It is important to note that voriconazole does not have reliable activity against mucormycosis.[7] We recommend clinicians to systematically screen post-COVID-19 patients for fungal infections, especially in immunocompromised and severely ill patients.

**Conclusion**

Post-COVID-19 patients should receive fungal pathogen surveillance, including periodic cytology and culture to identify these fungal infections at the earliest and prevent subsequent comorbidity. Effort must be made to obtain accurate diagnosis including a tissue biopsy if required to confirm the diagnosis. Possibility of a concurrent infection with other fungal infections should also be kept in mind.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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