



## CASE SERIES: A SPECTRUM OF FUNGAL INFECTIONS IN COVID-19

## General Medicine

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## ABSTRACT

Corona virus Disease 2019 (COVID-19) pandemic is causing a major health crisis across the globe. With the increasing number of fungal infections associated with COVID-19 being reported, it is imperative to understand the spectrum of such infections. Most documented cases have been reported in patients with diabetes mellitus or treatment with immunomodulators. The most common causative agents are Aspergillus, Candida or Mucorales. This series aims to portray the spectrum of fungal infections associated with COVID-19.

## KEYWORDS

COVID-19, opportunistic fungal infections, Aspergillosis, Mucor mycosis, Candidiasis

## INTRODUCTION

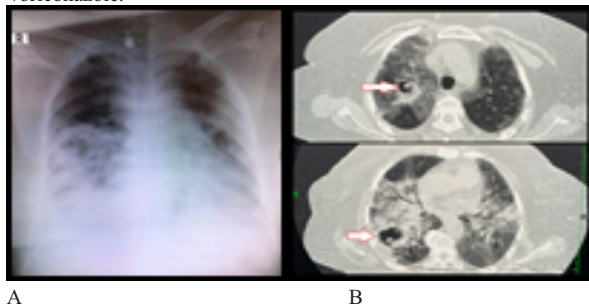
Approximately 5% of patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) experience severe lung damage due to viral replication, the ensuing cytokine storm and complex inflammatory processes(1). This can lead to secondary infections early after the disease onset (2). While super-infections have been rarely reported in the beginning of the current COVID pandemic, they are now on the rise, particularly reports about secondary fungal disease. While the pathogenesis is incompletely understood, there are several immunological mechanisms that may contribute to the development of fungal diseases (3). COVID-19 associated pulmonary aspergillosis (CAPA), Candida and Mucormycosis have been reported more frequently than others.

## CASE 1

A 59 year old female, a known case of type-2 diabetes since 6 year presented with complaints of cough with fever since 5 days. Upon admission, SpO<sub>2</sub> - 80% on room air. RT-PCR for COVID-19 was positive. The patient was started on supplemental oxygen and treatment for COVID-19.

In spite of all measures, patients condition steadily deteriorated. HRCT-thorax revealed thick walled cavitary lesions in the right upper and lower lobes (Fig 1). Sputum for fungal stain showed septate hyphae with narrow angle branching and culture grew Aspergillus fumigatus.

This was a case of CAPA. The patient was treated with intravenous Voriconazole.



**Fig 1.** A. Chest X-ray showing bilateral lower lobe inhomogenous opacities with a cavity in the right lower zone. B. Concurrent HRCT-thorax showing consolidation (air bronchogram) and multiple thick walled cavities (arrows) with dependent content in upper and lower lobes of right lung.

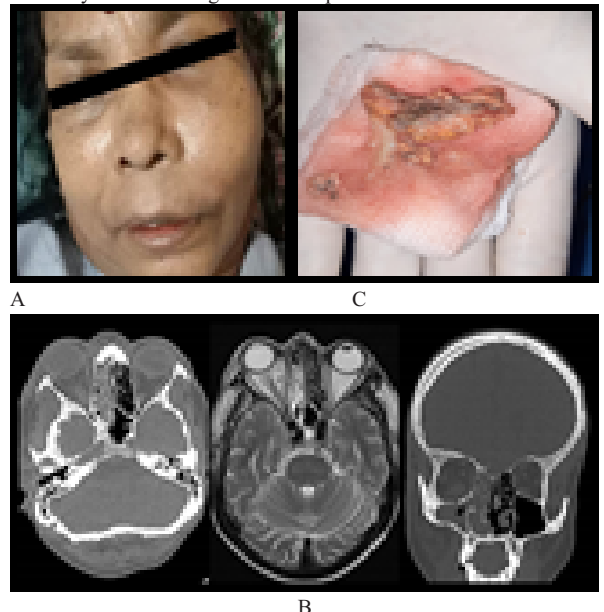
## CASE 2

A 58 year old female who was a known case of type-2 diabetes since 8 years was admitted with complaints of shortness of breath and fever

since 3 days. RT-PCR for COVID-19 was positive. On day 8 of admission, she complained for facial swelling (Fig 2.).

Plain and contrast MRI of paranasal sinuses was suggestive of mucormycosis of bilateral ethmoid and maxillary sinuses with spread to left premaxillary soft tissue plane. The patient underwent FESS and debridement. Tissue samples (Fig 2.) were sent for microbiological and histological examinations (HPE). HPE showed several, broad, twisting, ribbon-like non-septate fungal structures morphologically consistent with mucormycosis both within the necrotic and viable tissue. Vascular invasion by fungal structures, associated with thrombosis.

This was a case of COVID-19 pneumonia with rhino-sinusal mucormycosis occurring in a diabetic patient.



**Fig 2.** A. Left sided facial swelling. B. MRI-PNS showing bilateral ethmoid and maxillary sinuses with spread to left premaxillary soft tissue plane. C. Necrotic debrided sample.

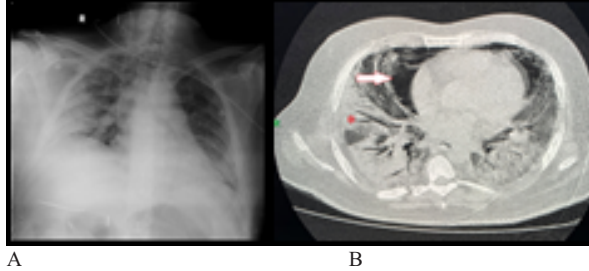
## CASE 3

A 38 year old male with no known co-morbidities presented with severe breathlessness since a week and was admitted to the ICU. He was diagnosed with COVID-19 ( RT-PCR positive). The patient was started on NIV and treatment for severe COVID pneumonia. Despite the efforts, patients condition worsened and was put on mechanical

ventilation.

HRCT-Thorax revealed CT severity of 23/25 with secretions in the tracheo-bronchial tree and pneumomediastinum (Fig 6). ET secretions for fungal stain showed budding yeast cells with pseudo-hyphae and culture grew *Candida kefyr*. However, the patient succumbed to his illness, despite the treatment measures with broad spectrum antifungals.

This was a case of COVID-19 pneumonia with pulmonary candidiasis co-infection.

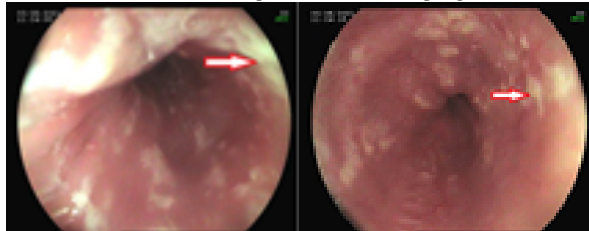


**Fig 3.** A. Chest X-ray suggestive of bilateral inhomogenous opacities. B. Concurrent HRCT-Thorax showing consolidation (\*air bronchogram), GGO's and pneumomediastinum (arrow).

#### CASE 4

A 61 year old female, diabetic since 3 years treated for COVID-19 15 days back, presented with epigastric pain, loss of appetite, difficulty in swallowing, generalised weakness, dry cough for which upper GI endoscopy was performed which revealed multiple thick adherent whitish plaques throughout the entire length of the esophagus suggestive of oesophageal candidiasis. The patient was treated with Flucanazole 150 mg BD for 15 days.

This was a case of COVID-19 pneumonia with esophageal candidiasis.



**Fig 4.** Endoscopic image showing multiple thick adherent whitish plaques (arrows) throughout the entire length of the esophagus.

#### DISCUSSION

Several causes have been postulated for increased fungal infections in COVID-19 patients such as co-morbidities, drugs, oxygen and even COVID-19 itself.

1. Chronic hyperglycemia, which is an immuno-suppressive condition predisposes to fungal infections.
2. COVID-19 infection itself has been noted to cause hyperglycemia through several mechanisms (4).
3. Medications used for treatment of COVID-19 such as immuno-modulators (steroids, tocilizumab, baricitinib) and antibiotics can lead to fungal superinfection.
4. Prolonged hospital stays, indwelling urinary catheters, central venous catheters, nasogastric tubes and invasive mechanical ventilation lead to increased chance of fungal infection.
5. A sustained and substantial reduction of the peripheral lymphocyte counts, mainly CD4 T and CD8 T cells, has been observed in COVID-19 patients (5).
6. Other factors like use of industrial grade oxygen, poor patient hygiene, lot of observational studies and a lack of RCT's creating confusion among doctors and increased patient to health care provider ratio are contributing factors for the increase in opportunistic fungal infections in COVID-19.

#### CONCLUSION

A high degree of suspicion is necessary to diagnose fungal infections in COVID-19. Once diagnosed, should be treated with an aggressive approach and a multidisciplinary team comprising of pulmonologists, physicians, infectious disease specialists, critical-care team, ENT

surgeons, ophthalmologists, oro-maxillary-facial surgeons, plastic surgeons and neuro-surgeons for the best possible outcome. However, the treatment is expensive, for longer durations and with unfavorable outcomes.

#### Patients Consent

The authors certify that they have obtained all appropriate patient consent forms. 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.

#### REFERENCES

1. Mehta, P., McAuley, D. F., Brown, M., Sanchez, E., Tattersall, R. S., & Manson, J. J. (2020). COVID-19: consider cytokine storm syndromes and immunosuppression. *The Lancet*, *395*(10229), 1033-1034.
2. Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., ... & Cao, B. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*, *395*(10229), 1054-1062.
3. Hoenigl, M. (2020). Invasive Fungal Disease complicating COVID-19: When it rains it pours. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America*.
4. Wu, L., Girgis, C. M., & Cheung, N. W. (2020). COVID-19 and diabetes: Insulin requirements parallel illness severity in critically unwell patients. *Clinical Endocrinology*, *93*(4), 390-393.
5. Li, H., Liu, L., Zhang, D., Xu, J., Dai, H., Tang, N., ... & Cao, B. (2020). SARS-CoV-2 and viral sepsis: observations and hypotheses. *The Lancet*, *395*(10235), 1517-1520.