



# COVID-19 and fungal infection: An opportune time

Ivan A. Jones\*, G. Dominic Rodriguez

Department of General Medicine, Kauvery Hospital, Trichy, Tamilnadu, India

\*Correspondence: [keitch.jones@gmail.com](mailto:keitch.jones@gmail.com)

**Abstract:** The COVID-19 pandemic which originated in Wuhan, China in late 2019 and paralyzed the world in 2020 posed unique problems to certain high-risk groups, especially the elderly and the diabetics. The increased incidence of fungal infections that were noted in COVID-19 patients deserve close attention and have to be managed expeditiously. Four patients recovered and one patient succumbed to infection and thrombotic complication. Meticulous glycemic monitoring, insulin therapy, minimizing antibiotic use and very safe handling of intravenous lines should be practiced to prevent these serious infections.

**Keywords:** COVID-19; hyperglycemia; steroids; fungal infections, mucormycosis; *Candida* sp.

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## 1. Introduction

Diabetics were among the high-risk group prone for developing severe COVID pneumonia [1–4]. Apart from viral disease, life threatening fungal infections also occurred either as co-infections or as a complication post treatment.

From our COVID care centre, we have compiled the data of five patients in whom we encountered fungal infections and its management.

Several causes for increased fungal infections in diabetic patients are postulated.

- (1). Chronic hyperglycemia predisposes to rhinocerebral mucormycosis and patients could present with the same as co-infection, along with COVID-19 pneumonia [1].
- (2). COVID-19 infection itself has been noted to cause hyperglycemia through several mechanisms [5].
- (3). Medications used for treatment of COVID-19 such as steroids, tocilizumab (IL-6 receptor antibody) and antibiotics can lead to fungal superinfection.
- (4). Prolonged hospital stays, indwelling urinary catheters and central venous catheters coupled with antibiotic use, leads to increased chance of fungal infection.

These infections manifest as Urinary Tract Infections (UTI), Blood Stream Infections (BSI), fungal pneumonia or fungal rhino-orbital-cerebral infection.

Prompt diagnosis, involvement of surgical and medical teams and appropriate antifungal therapy are crucial in determining patient recovery [4].

## 2. Case Presentation

### 2.1. Case 1

A 54-year-old male who was a diabetic, hypertensive and hypothyroid presented with history of fever and cough for 10 days, dyspnea for four days, black discharge from left nostril for two days, along with swelling of left eye. On examination, he had eschar and ulceration in left middle meatus, decreased infra-orbital sensations, ptosis and complete ophthalmoplegia in left eye. Pupils were sluggishly reacting on left side and finger counting was impaired. Nasal swab examination revealed aseptate broad based branching fungal hyphae with right angled branching suggestive of zygomycetes species.

CT thorax revealed features of COVID-19 pneumonia. Blood investigations revealed diabetic ketoacidosis and severe renal failure. A provisional diagnosis of rhino-orbital mucormycosis was made. Endoscopic debridement of sinuses, left maxillectomy and left orbital exenteration was done. He was treated with amphotericin B, antibiotics, insulin and hemodialysis. Post operatively patient developed seizures, aspiration and gastrointestinal bleeding requiring intubation and mechanical ventilation.

CT-brain revealed bifrontal infarcts with hemorrhagic transformation – likely due to cerebral venous thrombosis. Systemic anticoagulation could not be done due to active gastrointestinal bleeding. Subsequently patient developed features of DIC and succumbed to his illness in spite of treatment measures.

This was a case of COVID-19 pneumonia and rhino-orbital mucormycosis occurring as co-infection due to poor glycaemic control in a diabetic patient and it was associated with diabetic ketoacidosis and renal failure.

#### 2.2. Case: 2

A 67-years-old male was admitted with complaints of right sided chest pain of 10 days duration. He was a diabetic/hypertensive who was recently treated for COVID-19 pneumonia with steroids. CT thorax with contrast revealed thick-walled cavity in right upper and lower lobe. Cardiac assessment revealed CAD–LAD territory with moderate LV dysfunction. Bronchoscopy was done, aseptate fungal hyphae was identified in smear. TB-PCR was negative. Patient was diagnosed to have fungal pneumonia and was started on IV amphotericin B and then switched to oral posaconazole. He was also treated with insulin for glycaemic control and cardiac medications were given. He was discharged on oral antifungal and complete resolution occurred after prolonged oral anti-fungal therapy.

This was a case of post COVID–fungal pneumonia occurring in a diabetic patient who received steroids for COVID-19 pneumonia.

#### 2.3. Case: 3

A 74-years-old male who was diabetic and treated for severe COVID-19 pneumonia and had been discharged two weeks earlier without any oxygen requirement presented with symptoms of cough with expectoration, fever of 1-week duration. His current medications included oral steroids methylprednisolone 8mg once daily. On evaluation, he was febrile, tachypneic, hypoxic requiring supplemental oxygen.

CT thorax revealed COVID pneumonia in resolution with cavitating consolidation in left lingular lobe.

Sputum analysis revealed mucor.

A provisional diagnosis of pulmonary mucormycosis was made and he was started on iv amphotericin and then switched over to oral posaconazole. His glycaemic level was managed with insulin and steroid was tapered and stopped.

Patient improved symptomatically and was discharged on oral antifungal drugs. Follow up CT thorax done after three months of antifungal therapy revealed minimal residual pneumonia in resolution phase following which duration of oral antifungal therapy was extended to six months and follow up advice was given.

This was a case of post COVID fungal pneumonia occurring in a diabetic patient who received steroids for COVID-19 pneumonia.

#### 2.4. Case: 4

A 47-years-old male who was a diabetic and was treated for severe COVID-19 two weeks earlier and discharged with oral steroids and domiciliary oxygen presented with complaints of pus discharge near maxillary molar region on the right side. On examination, mobility of maxillary molars was elicited. Pus was sent for microbiological analysis and bone scraping was done and sent for microbiological and HPE examination which revealed mucormycosis involving maxillary sinus.

MRI brain with contrast revealed no intracranial extension and there was pansinusitis with bony erosion involving alveolar recess of maxilla on right side and medial aspect of hard palate right side.

Patient underwent total maxillectomy and he was treated with iv amphotericin B and then switched over to oral posaconazole. Steroids were tapered and stopped and blood sugar level was controlled with insulin.

This was a case of post COVID fungal mucormycosis involving maxilla occurring in a diabetic patient who received steroids for COVID-19 pneumonia. He was treated with surgery and antifungal therapy.

#### 2.5. Case: 5

A 63-years-old female who was diabetic, hypertensive presented with features of severe COVID-19 pneumonia. She was treated with oxygen, therapeutic anticoagulation, convalescent plasma transfusion, steroids, insulin and other supportive medications. With treatment, her oxygen requirements decreased and oxygen was tapered off.

During hospital stay, there was acute worsening in clinical status requiring increasing oxygen requirements. Secondary sepsis was considered and investigations were sent. Total count was elevated. Procalcitonin was normal. Blood culture (central and peripheral) grew *Candida famata*/*Candida guilliermondi* with rapid differential time to positivity in central line. (Central 12 h < peripheral 22 h). CLABSI (central line associated blood stream infection) was considered and central line was changed. She was started on intravenous anidulafungin as per sensitivity reports and steroids were tapered. She recovered completely with treatment.

This was a case of fungal blood stream infection - central line associated due to *Candida* sp. – non albicans species resistant to azoles and amphotericin B and required intravenous echinocandins.

It occurred in a diabetic patient who received steroids for COVID-19 pneumonia during hospital stay.

### 3. Conclusions

Fortunately, four patients recovered and one patient succumbed to infection and thrombotic complication despite best efforts from the team of physicians, ENT and ophthalmologic surgeon during the difficult restrictions faced due to COVID-19.

Prolonged antifungal therapy and cost of treatment made treatment challenging for the patients and physicians.

Prevention of fungal infections should be considered in all patients who become hyperglycemic after COVID-19.

Meticulous glycemic monitoring, insulin therapy, minimizing antibiotic use and very safe handling of Intravenous lines should be practiced to prevent these serious infections.

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### Authors' contributions

Supervised by Dr. G. Dominic Rodriguez. Report written by Dr. Ivan A Jones and drafted by Dr. G. Dominic Rodriguez.

### Competing Interest

The authors have no competing interests to declare.

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