Pharma

COVID-19 associated pulmonary mucormycosis: case report and systematic literature review

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Abstract

Systemic glucocorticoids, widely used in the management of severe COVID-19, are known to increase susceptibility to opportunistic fungal infections. While COVID-19–associated pulmonary aspergillosis is well documented, mucormycosis remains comparatively rare. We report a probable case of pulmonary mucormycosis in a 55-year-old man with diabetes, end-stage kidney disease, and severe COVID-19. The infection developed 21 days after hospitalization, and the patient was successfully treated with liposomal amphotericin B, completing a total dose of 5 g, and was discharged after 54 days.

A systematic literature review identified seven additional cases of COVID-19–associated mucormycosis (CAM). Diabetes mellitus emerged as the most frequent predisposing condition; however, three patients had no identifiable risk factor other than glucocorticoid therapy. In most cases, CAM developed 10–14 days after admission. Except for our case, all reported patients had fatal outcomes, with two diagnoses made postmortem.

Although uncommon, mucormycosis represents a serious and life-threatening complication of severe COVID-19. Patients with diabetes or multiple predisposing conditions appear particularly vulnerable, and glucocorticoid exposure may further elevate this risk. Early recognition and prompt, aggressive antifungal treatment are critical to improving survival.

Keywords: COVID-19, Pulmonary mucormycosis, Glucocorticoids, Diabetes mellitus

Introduction

Coronavirus disease 2019 (COVID-19) continues to present a major global health challenge. Among the various therapeutic strategies evaluated, only systemic glucocorticoids have consistently demonstrated a survival benefit in patients with severe disease. However, their increasing use has been associated with a heightened risk of secondary bacterial and fungal infections. While COVID-19–associated pulmonary aspergillosis (CAPA) is well recognized, mucormycosis remains an underdiagnosed and less frequently suspected complication.

This article reports a case of pulmonary mucormycosis in a patient with severe COVID-19 and summarizes a systematic review of the literature describing COVID-19–associated mucormycosis (CAM), highlighting its clinical characteristics, risk factors, and outcomes.

Case presentation

A 55-year-old man with long-standing type 2 diabetes mellitus, hypertension, ischemic cardiomyopathy, and end-stage renal disease on maintenance haemodialysis presented with a three-day history of fever, dry cough, and progressive dyspnoea. His diabetes had been poorly controlled due to irregular use of oral hypoglycaemic agents and infrequent glucose monitoring. He denied smoking and substance use.

On admission, his respiratory rate was 26 breaths/min, blood pressure 110/80 mmHg, pulse 90 beats/min, and oxygen saturation 84% on room air, improving to 95% with a venturi mask (FiO_2 0.5). Chest radiography revealed bilateral diffuse interstitial infiltrates and cardiomegaly. RT-PCR from a nasopharyngeal swab confirmed SARS-CoV-2 infection. Initial investigations showed haemoglobin 7.8 g/dL and HbA1c 5.3%.

He was treated with intravenous dexamethasone (6 mg daily for 14 days) and remdesivir (200 mg on day 1, followed by 100 mg daily for 4 days), along with supportive care. His blood glucose, initially 140 mg/dL, peaked at 300 mg/dL during steroid therapy. After 14 days, his respiratory symptoms and radiological findings improved.

On day 18, the patient developed cough, sputum production, and dysuria. Urine culture grew *Escherichia coli*, and he was treated with dose-adjusted intravenous meropenem for 10 days.

A repeat chest radiograph on day 21 showed a thick-walled cavity in the right upper lung zone, confirmed on CT as a right upper lobe cavity with minimal pleural effusion.

Sputum microscopy (Gram stain, AFB stain, and fungal smear) was negative; however, culture on Sabouraud dextrose agar grew a cottony, grayish-white colony after 6 days. Lactophenol cotton blue mount demonstrated aseptate hyphae with nodal

rhizoids and short sporangiophores bearing spherical sporangia, consistent with *Rhizopus microsporus*. MALDI-TOF confirmed the identification, and the isolate was deposited in the National Culture Collection of Pathogenic Fungi (NCCPF 710,496). Antifungal susceptibility testing revealed MICs of amphotericin B 0.5 µg/mL, itraconazole 0.03 µg/mL, and posaconazole 2.0 µg/mL.

Serum beta-D-glucan was 189 pg/mL, and galactomannan index was 0.18. The patient was diagnosed with probable pulmonary mucormycosis and treated with liposomal amphotericin B (3 mg/kg/day). After clinical improvement, he was discharged on day 54, having received a cumulative amphotericin dose of 5 g. Outpatient amphotericin therapy was continued for 25 days. A right upper lobectomy is planned. Post-treatment imaging showed marked improvement of the lung cavity.

Overview of mucormycosis and covid-19 context

Mucormycosis is a life-threatening fungal infection caused by fungi of the order *Mucorales*, most commonly *Rhizopus*, *Mucor*, *Absidia*, and *Cunninghamella*. Infection occurs through inhalation or inoculation of spores, often from soil or decaying organic matter. In COVID-19, the disease gained public attention as “black fungus.”

Mucormycosis is characterized by rapidly progressive angio-invasion leading to vessel thrombosis and tissue necrosis. It commonly affects the sinuses, brain, lungs, skin, and gastrointestinal tract. Clinical manifestations depend on the site, ranging from facial swelling, headache, black eschars, and ocular pain in rhinocerebral disease to fever, cough, chest pain, and hemoptysis in pulmonary involvement.

Risk factors include uncontrolled diabetes mellitus, corticosteroid use, hematologic malignancies, transplantation, renal failure, malnutrition, and immunosuppressive therapy. In COVID-19 patients, steroid-induced hyperglycemia and immune dysregulation further elevate risk.

Diagnosis relies on direct microscopy and biopsy, as routine swabs are often non-diagnostic. Treatment requires early initiation of amphotericin B (liposomal formulation preferred), surgical debridement when feasible, and reversal of underlying risk factors. Despite aggressive treatment, mortality remains high, particularly in disseminated disease.

Discussion

With more than a million global deaths, COVID-19 continues to impose significant clinical challenges. Glucocorticoids remain essential for managing hypoxemic COVID-19 but simultaneously predispose patients to opportunistic fungal infections. Additional immunomodulators such as tocilizumab may further compromise host defences.

A systematic review of PubMed and Embase up to January 9, 2021, identified seven published reports of CAM. Including the present case, eight cases were documented: three from the USA, two from India, and one each from Brazil, Italy, and the UK. The median age was 57.5 years, and 87.5% were male. Diabetes mellitus was present in half the patients; three had no identifiable risk factors aside from COVID-19 treatment. ARDS was documented in seven cases, and renal dysfunction in at least five.

Mucormycosis typically developed between 10 and 14 days after hospitalization for COVID-19. Sites of infection included rhino-orbito-cerebral (n=3), pulmonary (n=3), gastric (n=1), and disseminated (n=1). Except for the present case, all patients died.

CAM poses substantial diagnostic difficulty because of overlapping risk factors and imaging features shared with CAPA. Unlike aspergillosis, biomarkers such as galactomannan and beta-D-glucan are unreliable for mucormycosis, leading to frequent delays in diagnosis. Two of the eight reviewed cases were diagnosed only at autopsy.

The favourable outcome in the present case may be attributed to controlled hyperglycaemia, vigilant monitoring, and early initiation of amphotericin B. Although standard guidelines recommend liposomal amphotericin B at 5–10 mg/kg/day, our patient responded well to a 3 mg/kg/day regimen, likely due to early intervention.

COVID-19 has created circumstances that impair optimal management of mucormycosis:

- Steroid therapy exacerbates hyperglycemia.
- Severe respiratory failure limits timely imaging.
- Overburdened healthcare systems restrict surgical and diagnostic services.

These factors may contribute to the high mortality observed in CAM (87.5% in this review).

Notably, CAM occurred even in patients without classical risk factors, suggesting that indiscriminate corticosteroid use—especially in non-hypoxemic or mild cases—should be avoided. Immunomodulatory agents without proven mortality benefit should also be used cautiously.

Conclusion

Clinicians managing critically ill COVID-19 patients must maintain a high index of suspicion for invasive fungal infections such as mucormycosis. Early recognition and prompt treatment with liposomal amphotericin B are vital to improving survival. Judicious use of glucocorticoids and close monitoring of glycemic control are essential to reducing the risk of CAM. As COVID-19 continues to evolve, heightened awareness and timely diagnosis of mucormycosis can significantly impact patient outcomes.

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