Annals of Clinical Case Reports

Case Series
Published: 18 Oct, 2023

# Rhino-Orbital Mucormycosis in Patients with Diabetes Infected with COVID-19 in Babol, Iran: Report of Six Cases

*Jafarzadeh J[1], Tavakoli M[2], Zabihzadeh A[3], Omran SM[4], Bayani M[4], Javanian M[4], Haghani I[5], Abastabar M[5], Bach H[6]* and Armaki MT[4]**

[1]Department of Medical Mycology and Parasitology, School of Medicine, Babol University of Medical Sciences, Babol, Iran

[2]Departments of Mycology, Tarbiat Modares University, Tehran, Iran

[3]Student Research Committee, Babol University of Medical Sciences, Babol, Iran

[4]Infectious Diseases and Tropical Medicine Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

[5]Invasive Fungi Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Babol, Iran

[6]Division of Infectious Diseases, University of British Columbia, Canada

## Abstract

Mucormycosis is an aggressive, opportunistic fungal infection that has emerged as a possible complication of COVID-19. Invasive fungal infections cause significant disability, mortality, and increased cost of care in patients with disease states causing underlying immunosuppression. We report six cases of patients with diabetes diagnosed with rhino-orbital mucormycosis after COVID-19 treatment with corticosteroids. The diagnosis of mucormycosis was performed by radiologic findings and histopathological, microbiological, and molecular evidence. Admitted patients received systemic antifungal therapy with liposomal amphotericin B and extensive surgical treatment. Out of six patients, one patient died, and the others recovered, of whom one patient lost her vision in one eye. Steroid use, diabetes, and the broad use of antibiotics were considered the main risk factors.

**Keywords: Mucormycosis; Mucorales; Diabetes; COVID-19; Antifungal; Steroid**

**OPEN ACCESS**

***Correspondence:***
*Horacio Bach, Division of Infectious Diseases, University of British Columbia, 2660 Oak Street, Vancouver, V6H3Z6, Canada, Tel: +1 604 875 4111 (x: 62107)*
*Armaki MT, Infectious Diseases and Tropical Medicine Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran, Tel: +98 911 314 0571*

**Received Date**: *26 Sep 2023*
**Accepted Date:** *13 Oct 2023*
**Published Date:** *18 Oct 2023*

***Citation:***
*Jafarzadeh J, Tavakoli M, Zabihzadeh A, Omran SM, Bayani M, Javanian M, et al. Rhino-Orbital Mucormycosis in Patients with Diabetes Infected with COVID-19 in Babol, Iran: Report of Six Cases. Ann Clin Case Rep. 2023; 8: 2502.*

***ISSN: 2474-1655.***



## Introduction

The world has witnessed a devastating global pandemic in the 21st century caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), resulting in over 238 million confirmed cases and nearly 5 million deaths globally [1]. Clinical deterioration is dependently associated with underlying comorbidities such as hypertension, diabetes, cancer, chronic kidney disease, heart failure, and mental disorders leading to a high rate of mortality. The lack of access to safe and effective antimicrobials during the management of individuals hospitalized with COVID-19 significantly among critically ill COVID-19 patients, heavy use of steroids and supportive care equipment such as oxygen ventilators, central venous and urinary catheterization, and prolonged ICU stay has raised significant concerns over co-infections or secondary infections [2,3]. Amid the COVID-19 pandemic, many patients have suffered bacterial or fungal infections, including aspergillosis, mucormycosis, and candidiasis, that may complicate the clinical course of COVID-19 [3,4]. During the second wave of COVID-19 in early 2021, there has been an alarming increase in the number of cases and deaths of opportunistic fungal infections, especially mucormycosis worldwide [5]. As mucormycosis is a rare but opportunistic fulminant fungal infection of the mucosa with a rapid and lethal progression, early diagnosis and prompt treatment are essential to reduce preventable mortality [6]. This infection is caused by ubiquitous molds belonging to the fungal order Mucorales and most frequently occurs in individuals with underlying diseases, such as diabetes [7]. Diabetes showed significant comorbidity in previous epidemics and pandemics such as influenza (H1N1), SARS-CoV, and MERS-CoV. It has also been considered a major cause of severity and mortality of COVID-19 infection [8]. In the ongoing COVID-19 pandemic, more attention should be paid to administering corticosteroids to severe patients with diabetes, as these drugs deteriorate glycemic control and the induction of hyperglycemia [9]. In the present study, we describe six patients with

COVID-19-associated rhino cerebral mucormycosis admitted to Ayatollah Rouhani Hospital in Babol due to COVID-19 from July 2021 to August 2021.

## Materials and Methods

This study was conducted at the Department of Pathology and Mycology, Babol University of Medical Sciences, Iran, and approved by the research ethics committee of Babol University College of Medicine (IR.MUBABOL.HRI.REC.1401.191). Informed consent was obtained orally in the presence of the attending physician from all subjects involved in the study. According to EORTC/MSG criteria, six cases of proven mucormycosis were studied by radiologic findings, histopathological, microbiological, and molecular evidence [10,11].

A biopsy sample was sent to the pathology lab for processing and staining with Hematoxylin and Eosin (H&E). Samples were examined under a microscope, revealing broad aseptate and ribbon-like hyphae and evidence of associated tissue damage. Mycological evidence was obtained by the biopsy specimen's direct smear and culture.

The identification was performed based on macroscopic and microscopic evaluation of the culture growing on Sabouraud dextrose agar (CONDA, Madrid, Spain) supplemented with 0.05 g/L chloramphenicol (Merck, Darmstadt, Germany) and Internal Transcribed Spacer (ITS) sequence analysis (ITS1 = 5' - T C C G T A G G T G A A C C T G C G G -`3, ITS4= 5' - T C C T C C G C T T A T T G A T A T G C - `3) on ABI sequencer (Bioneer, Daejeon, South Korea) [12]. The sequences were subjected to the Basic Local Alignment Search Tool (BLAST) program (http://www.blast.ncbi.nlm.nih.gov/Blast). Data were compared to the NCBI nucleotide database and deposited in GeneBank (for case 1, accession number: MZ736586.1, *Rhizopus arrhizus*; for case 2, accession number: MZ541992.1, *R. arrhizus*; for case 3, accession number: OQ473381, *Lichtheimia corymbifera*; for case 4; accession number: OQ473382, *R. arrhizus*; for case 5, accession number: OQ473383, *R. arrhizus*; and for case 6, accession number: OQ473384, *R. arrhizus*).

In addition, we tested the *in vitro* activity of amphotericin B (Sigma-Aldrich, Saint Louis, MO, USA), itraconazole (Sigma-Aldrich, Gillingham, UK), voriconazole (Sigma-Aldrich, UK), and posaconazole (Sigma-Aldrich, UK) against the six fungal isolates. The microdilution susceptibility test was performed according to the guidelines of the Clinical and Laboratory Standards Institute M38-A2 [13,14]. Overall, the MICs of amphotericin B, posaconazole, itraconazole and voriconazole were for all the strains, 0.032 µg/mL, 0.032 µg/mL, 0.064 µg/mL, and 1 µg/mL, respectively.

## Case Series

### Case 1

A 48-year-old female who presented with diabetes and COVID-19 was treated with an ambulatory 21-day course of remdesivir. After five days of the treatment, the patient started swelling, a purulent (Figure 1A), and a painful left eye with loss of vision, fever, and neurological symptoms. Computed Tomography (CT) scan of the Paranasal Sinuses (PNS CT scan) showed mucosal thickening in the maxillary sinuses, sphenoid sinuses, ethmoid sinuses, and Unilateral Osteomeatal Complex (UOMC) obstruction (Figure 1B). There was a strong suspicion of rhino-orbital mucormycosis, and this patient underwent surgery to drain the sinuses. The final diagnosis confirmed mucormycosis by tissue culture (Figure 1C) and PCR. This patient was treated with Liposomal Amphotericin B (LAMB) at a dose ranging from 3 mg/kg/day to 5 mg/kg/day. The outcome improved significantly 30 days after hospital discharge, but unfortunately, the patient lost vision in the left eye.

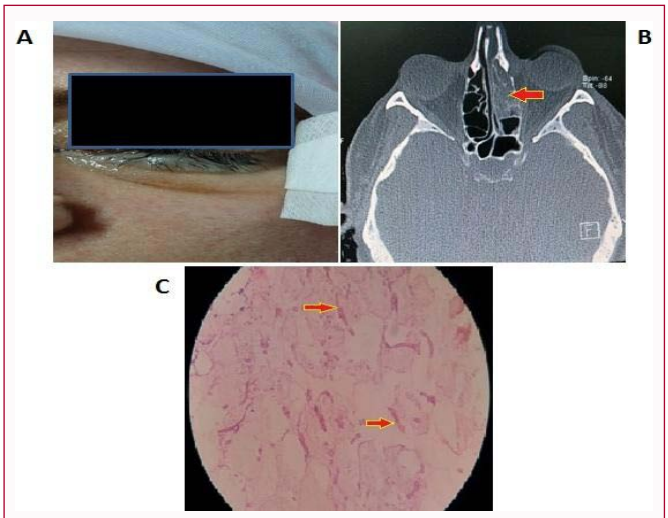


**Figure 1:** Examinations of Case 1. (A) Clinical photo showing a left eye with purulent discharge. (B) CT scan showing total opacification of the left frontal, ethmoid, and maxillary sinus. (C) Histopathological examination showing aseptate hyphae (H&E stain, magnification: x100).

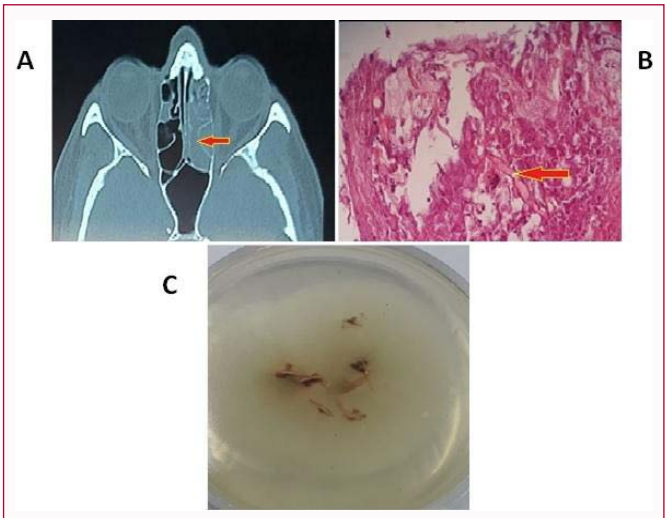


**Figure 2:** Examinations of Case 2. (A) CT scan showing mucosal thickening of all paranasal sinuses and air-fluid level at both sphenoidal sinuses. (B) Histopathological examination showing aseptate hyphae (H&E stain, magnification: x100). (C) A positive culture of nasal sinus biopsy samples on SDA medium.

### Case 2

A 44-year-old male was hospitalized because of COVID-19 and a severe headache. The patient had a history of diabetes and hepatitis B. PNS CT scan showed mucosal thickening in the paranasal sinuses and UOMC obstruction (Figure 2A). Histopathological examination of the sinus excision material, including a cream-gray elastic tissue with a typical size of 1.5 mm, revealed vascular invasion and the presence of broad and ribbon-like aseptate hyphae (Figure 2B, 2C). Clinical, radiographic, and histological findings indicated the diagnosis of mucormycosis. The patient received 20 days of treatment with LAMB at a dose ranging from 3 mg/kg/day to 5 mg/kg/day and recovered.

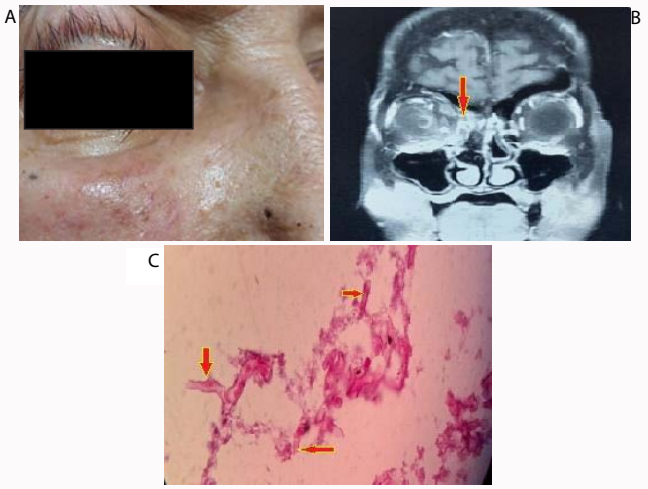


**Figure 3:** Examinations of Case 3. (A) Clinical photo showing a right eye with swelling and redness. (B) CT scan showing right ethmoidal sinus consolidation and bilateral sphenoid sinuses. (C) Histopathological examination showing non-septate hyphae (H&E stain, magnification: x100).

## Case 3

An 81-year-old female with diabetes and Ischemic Heart Disease (IHD) presented after COVID-19. Signs were evaluated by clinical examination and included fever, chills, swollen purulent eye swelling with redness (Figure 3A), and facial paralysis. It was suspected that this infection was mucormycosis because of the typical clinical signs. Following CT scan findings, the most commonly involved sinus was the ethmoid sinuses (Figure 3B), and the patient underwent surgical debridement of the sinuses. Broad aseptate hyphae were well observed on histologic biopsy examination (Figure 3C). Clinical, radiographic, and histological findings indicated the diagnosis of mucormycosis. This patient died three weeks after starting antifungal therapy with LAMB at a dose ranging from 3 mg/kg/day to 5 mg/kg/day.

## Case 4

A 46-year-old male with diabetes and COVID-19 presented with pain, ptosis (Figure 4A), impaired movements, and reduced vision in the right eye. PNS CT scan provided detailed information on sinus involvement (Figure 4B). A sample was taken from the ethmoid sinus, analyzed in the pathobiology lab, and confirmed the presence of broad aseptate hyphae (Figure 4C) by the direct smear of tissue samples and culture. After one week of treatment with LAMB, the patient was discharged at a dose ranging from 3 mg/kg/day to 5 mg/kg/day.

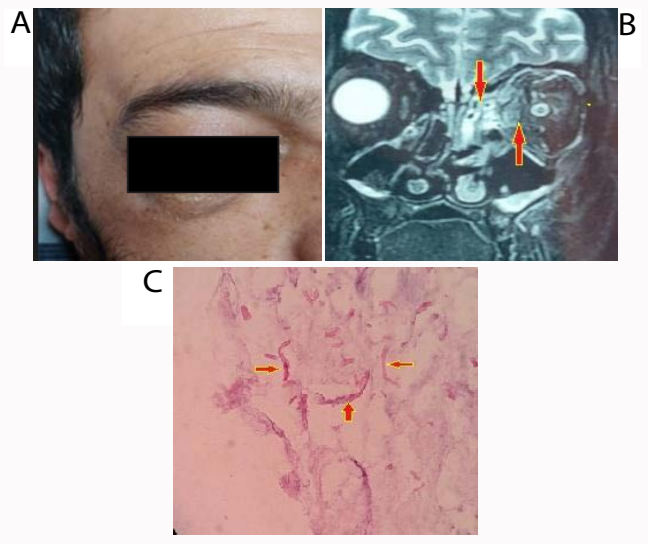


**Figure 4:** Examination of Case 4. (A) Clinical photo showing a right eye with swelling and ptosis. (B) CT scan showing air-fluid level in the right sphenoid and maxillary sinuses (acute sinusitis). (C) Histopathological examination showing non-septate hyphae (H&E stain, magnification: x100).

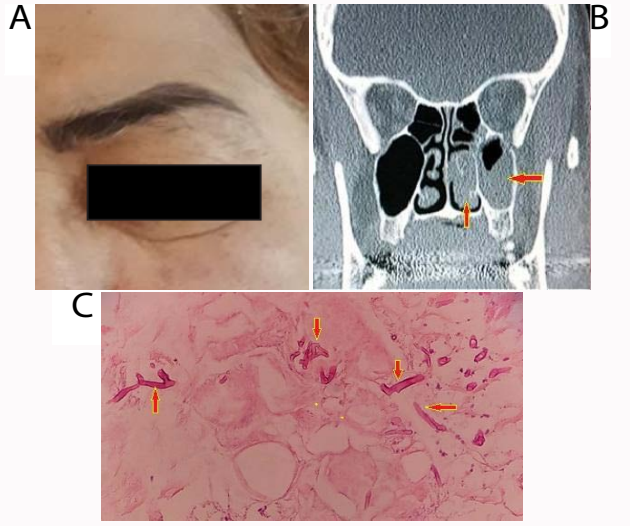


**Figure 5:** Examinations of Case 5. (A) Clinical photo showing the left eye with swelling and discharge. (B) CT scan showing left ethmoidal, sphenoid, maxillary, and frontal sinus consolidation. (C) Histopathological examination showing non-septate hyphae (H&E stain, magnification: x100).

## Case 5

A 65-year-old female with a previous history of diabetes, hypertension, sinusitis, and appendectomy was hospitalized for five days because of COVID-19. Two days after discharge, she was readmitted with headache, dizziness, ear pain, diplopia, and gingivitis (Figure 5A). A color Doppler ultrasonography showed that carotid and bilateral temporal arteries were normal. CT scan, however, showed paranasal sinus abnormalities (Figure 5B), and this patient underwent surgical debridement of the involved sinuses followed by


**Figure 6:** Examinations of Case 6. (A) Clinical photo showing a left eye with swelling. (B) The left side of the hard palate shows a deep necrotic ulcer. (C) CT scan showing left nasal thickening in the ethmoidal, sphenoid, maxillary, and frontal sinus. (D) Histopathological examination showing non-septate hyphae (H&E stain, magnification: x100).

antifungal therapy with LAMB. Broad aseptate hyphae indicative of mucormycosis were found on histopathology (Figure 5C). Clinical, radiographic, and histological findings indicated the diagnosis of mucormycosis. Within two weeks of beginning treatment with LAMB at a dose ranging from 3 mg/kg/day to 5 mg/kg/day, the patient was discharged after full recovery.

### Case 6

A 53-year-old female presented with COVID-19 having a history of diabetes, hypertension, and hyperlipidemia. The patient started having fever, chest pain, and dyspnea symptoms. PNS CT scan showed mucosal thickening in the maxillary sinuses and UOMC obstruction. A diagnosis of mucormycosis was suspected, so the patient underwent sinus surgery to drain the sinuses and take a sample. Histopathological examination of the tissue biopsy accompanied by a positive culture confirmed the diagnosis of mucormycosis. The patient was treated for two weeks with LAMB at a dose ranging from 3 mg/kg/day to 5 mg/kg/day. However, the fungus spread to invade adjacent tissues, evident in oral signs in the palate, mandible, and maxilla regions. The involved areas of the tissues were removed by surgery, and the patient outcome improved (Figure 6 and Table 1).

## Discussion

Post-COVID-19 opportunistic fungal infections, such as aspergillosis, candidiasis, and mucormycosis, are steeply rising [3,4]. Uncontrolled diabetes mellitus exacerbated by COVID-19–induced

**Table 1:** Demographic and clinical data, treatment, and follow-up in 6 cases of mucormycosis.

| Case | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Age (y)/gender | 48/F | 44/M | 81/F | 46/M | 65/F | 53/F |
| Anamnesis | HTN/HLP/DM | HTN/HLP/DM Appendectomy | DM | DM/HTN/IHD/ eyes surgery | DM | HTN/DM |
| Hospitalization Time | 2021-08-24 | 2021-08-16 | 2021-08-25 | 2021-08-28 | 2021-06-23 | 2021-07-28 |
| BS | 180 | 128 | 308 | 204 | 231 | 172 |
| Vaccinated | No | No | No | No | No | No |
| COVID-19 Symptoms | Fever/dyspnea/cough | Fever/cough/ weakness | Fever/dyspnea/cough | Fever/dyspnea/ill/ weakness | Fever/dyspnea/cough | Fever/dyspnea/cough |
| COVID-19 Treatment | Remdesivir/ Vancomycin/Imipenem/ Apotel/ Heparin/ Salbutamol sulfate | Remdesivir/ Vancomycin/ Imipenem/ Apotel/ Heparin/ Salbutamol sulfate | Remdesivir/ Vancomycin/Imipenem/ Apotel/ Heparin/ Salbutamol sulfate | Remdesivir/ Vancomycin/Ceftriaxone/ Imipenem/ Apotel/ Heparin/ Salbutamol sulfate | Remdesivir/ Vancomycin/ Imipenem/ Apotel/ Heparin/ Salbutamol sulfate | Remdesivir/ Vancomycin/ Imipenem/ Apotel/ Heparin/ Salbutamol sulfate |
| Onset | After 2 weeks | After 1 week | After 2 weeks | After 7 weeks | After 1 week | After 3 weeks |
| Clinical features | Fever/Left Maxillary swelling and inflammation/ Weakness | Fever/Ear pain/ Headache/ Double vision/ Left eye glob deviation/ Gum and mouth swelling/ Mouth ulcer/ Mastoid tenderness/ Temporomandibular joint | Fever/Right orbit pain/ Eye weakness/ Periorbital swelling/ without orbit movement/ Ptosis/ Headache/ Blindness | Fever/Periorbital swelling/ Ear pain/ Frozen eye weakness | Fever/Nose pain and headache | Fever/Periorbital swelling |
| Neurologic symptoms | Unilateral facial palsy | Change voice | ND | Unilateral facial palsy | ND | Unilateral facial palsy |
| Mucormycosis | None | None | None | None | None | None |
| Radiographic features | CT: * inflammation and edema with fat stranding on left maxillary and infraorbital (Cellulite) *Mucosal thickening right maxillary sinus and left frontal sinus *Left deviated nose septal with 3mm nasal spur on right space *Close left OMC | CT: Mucosal thickening of all paranasal sinuses *Some secretin with air-fluid level at both sphenoidal sinuses | CT: *Right etmoidal sinus consolidation and bilateral sphenoid sinuses *Mucosal thickening bilateral maxillary sinuses/ open OMC Orbit MRI: diffuse mucosal thickening all paranasal sinuses (pansinusitis) | CT: *Air-fluid level in right sphenoid and maxillary sinuses (Acute sinusitis) *Right etmoidal sinus consolidation *Skull bony cortex hypertrophy with dipole space widening *Fat stranding posterior space of right glob with some ptosis on right eye *Derm thickening on right pre-septal and right maxillary | CT: Left etmoidal / sphenoid /maxillary and frontal sinus consolidation/ At least 3 polyp/ retention cyst in right maxillary/ close left OMC | CT: left nasal thickening left etmoidal / sphenoid/ maxillary and frontal sinus hypertrophied/ close OMC Oral lesion: ulcero-necrotic lesion over the hard palate |
| Microbiologic Feature | non-septate hyphae | non-septate hyphae | non-septate hyphae | non-septate hyphae | non-septate hyphae | non-septate hyphae |
| Treatment | Hospitalization: LAmB (3-5 mg/kg/day):and surgical debridement | Hospitalization: LAmB (3-5 mg/kg/ day): and surgical debridement | Hospitalization: LAmB (3-5 mg/kg/day): and surgical debridement | Hospitalization: LAmB (3-5 mg/kg/day): and surgical debridement | Hospitalization: LAmB (3-5 mg/kg/ day): and surgical debridement | Hospitalization: LAmB (3-5 mg/kg/ day): and surgical debridement |
| Follow up | 2 weeks | 2 weeks | 1 week | 3 weeks | 5 weeks | 2 weeks |
| Outcome | Stable | Stable | Improved | Death | Stable | Stable |

HTN: Hypertension; HLP: Hyperlipidemia; DM: Diabetes Mellitus; IHD: Ischemic Heart Disease; CT: Computerized Tomography; OMC: Ostiomeatal Complex; MRI: Magnetic Resonance Imaging; LamB: Liposomal amphotericin B; ND: Not Determined

inflammation and systemic corticosteroids is established as the strongest and most well-known risk factor for COVID-19–associated rhino-orbital-cerebral mucormycosis [15]. Of note, rhino-orbital-cerebral mucormycosis occurs mainly in uncontrolled diabetes with earlier development than well-controlled diabetes [15]. Our findings are significant in at least two major aspects; uncontrolled diabetes and systemic corticosteroid treatment. Steroids and related immunosuppressant therapies are integral in managing inflammatory responses and immune-mediated function. Still, long-term administration of high doses of corticosteroids can also increase the risk of contracting infections [16]. Furthermore, hyperglycemia triggers an inflammatory state and may be potentiated by activating the antiviral immunity [15]. In addition, diverse Mucorales species also produce a wide range of cytokines and chemokines during infection [17]. Therefore, the interplay of COVID-19 and an inflammatory environment, in which multiple inflammatory pathways are recruited, may play a crucial role in developing the COVID-19-associated mucormycosis [15]. In the present study, LAMB and surgery were the predominant treatment strategies. Out of six cases presented, one patient died, and five patients recovered, of whom one case (Case 1) lost the vision in one eye. This patient resulted in LAMB treatment failure. An important cause of treatment failure can be related to drug-drug interaction. Accordingly, it was suggested that a possible interaction mechanism might be the direct binding of corticosteroids to amphotericin B, leading to decreased antifungal effects [18]. First, LAMB was administered in Case 1, but due to its lack of efficacy and vascular and tissue invasion by the fungal hyphae, LAMB was subsequently replaced by posaconazole. However, this patient had to discontinue posaconazole mainly due to the difficulties in providing and the much higher daily drug costs of the posaconazole tablets. To the best of our knowledge, among many current therapeutic options for the treatment of mucormycosis, posaconazole or isavuconazole remains the treatment of choice for COVID-19-associated mucormycosis [19].

## Conclusion

Increasing published evidence should warn health professionals about the association between SARS-CoV-2, secondary invasive fungal infections, and diabetes and about appropriate management of drugs that decrease blood glucose levels, the susceptibility of SARS-CoV-2, and the risk of drug-drug interactions.

## References


1. Li J, Lai S, Gao GF, Shi W. The emergence, genomic diversity and global spread of SARS-CoV-2. Nature. 2021;7889:408-18.
2. Seyedjavadi SS, Bagheri P, Nasiri MJ, Razzaghi-Abyaneh M, Goudarzi M. Fungal infection in co-infected patients with COVID-19: An overview of case reports/case series and systematic review. Front Microbiol. 2022;13:888452.
3. Jithendra C, Sudhindra K, Suprith S, Kumar P, Bansal S, Madhusudan M, et al. Incidence, resistance patterns, and outcomes of secondary bacterial and fungal infections in critically Ill ICU patients in the 2nd wave of the COVID-19 pandemic. Indian J Crit Care Med. 2022;26:S97.
4. Baddley JW, Thompson III GR, Chen SC-A, White PL, Johnson MD, Nguyen MH, et al. Coronavirus disease 2019–Associated invasive fungal infection. Open Forum Infect Dis. 2021;8(12):fab510.
5. Bashar M. Mucormycosis infection in COVID-19 patients in India: An emerging lethal threat. J Clin Ophtalmol. 2021;5(4):433-4.
6. Mahalaxmi I, Jayaramayya K, Venkatesan D, Subramaniam MD, Renu K, Vijayakumar P, et al. Mucormycosis: An opportunistic pathogen during COVID-19. Environ Res. 2021;201:111643.
7. Smith C, Lee SC. Current treatments against mucormycosis and future directions. PLOS Pathog. 2022;18(10):e1010858.
8. Hussain H, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: Knowledge in progress. Diabetes Res Clin Pract. 2020;162:108142.
9. Apicella M, Campopiano MC, Mantuano M, Mazoni L, Coppelli A, Del Prato S. COVID-19 in people with diabetes: Understanding the reasons for worse outcomes. Lancet Diabetes Endocrinol. 2020;8(9):782-92.
10. De Pauw B, Walsh TJ, Donnelly JP, Stevens DA, Edwards JE, Calandra T, et al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses study group (EORTC/MSG) Consensus Group. Clin Infect Dis. 2008;46(12):1813-21.
11. Donnelly JP, Chen SC, Kauffman CA, Steinbach WJ, Baddley JW, Verweij PE, et al. Revision and update of the consensus definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clin Infect Dis. 2020;71(6):1367-76.
12. Irinyi L, Serena C, Garcia-Hermoso D, Arabatzis M, Desnos-Ollivier M, Vu D, et al. International Society of Human and Animal Mycology (ISHAM)-ITS reference DNA barcoding database—the quality controlled standard tool for routine identification of human and animal pathogenic fungi. Med Mycol. 2015;53(4):313-7.
13. Badali H, Cañete-Gibas C, McCarthy D, Patterson H, Sanders C, David MP, et al. Epidemiology and antifungal susceptibilities of mucoralean fungi in clinical Samples from the United States. J Clin Microbiol. 2021;59(9):e0123021.
14. Jafarian H, Amanati A, Badiee P. Antifungal activity of taurolidine against Mucorales: An *in vitro* study on clinical isolates. Curr Med Mycol. 2022;8(1):26-31.
15. Hoenigl M, Seidel D, Carvalho A, Rudramurthy SM, Arastehfar A, Gangneux J-P, et al. The emergence of COVID-19 associated mucormycosis: a review of cases from 18 countries. Lancet Microbe. 2022;3(7):e543-e52.
16. Tavakoli M, Shokohi T, Lass Flörl C, Hedayati MT, Hoenigl M. Immunological response to COVID-19 and its role as a predisposing factor in invasive aspergillosis. Curr Med Mycol. 2020;6(4):75-9.
17. Wurster S, Thielen V, Weis P, Walther P, Elias J, Waaga-Gasser AM, et al. Mucorales spores induce a proinflammatory cytokine response in human mononuclear phagocytes and harbor no rodlet hydrophobins. Virulence. 2017;8(8):1708-18.
18. Hodge G, Cohen SH, Thompson III GR. *In vitro* interactions between amphotericin B and hydrocortisone: Potential implications for intrathecal therapy. Med. Mycol. 2015;53(7):749-53.
19. Soman R, Chakraborty S, Joe G. Posaconazole or isavuconazole as sole or predominant antifungal therapy for COVID-19-associated mucormycosis. A retrospective observational case series. Int J Infect Dis. 2022;120:177-8.