JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

A fatal post-COVID-19 sino-orbital mucormycosis in an adult patient with diabetes mellitus: a case report and review of the literature

Yousef Moghdam[1], Bahareh Arghavan[2], Firoozeh Kermani[3], Seyed Ali Jeddi[4], Shaghayegh Khojasteh[5], Tahereh Shokohi[6,7], Narges Aslani[8], Abolghasem Ebrahimi[1], Javad Javidnia[6,7]

[1] Khatam al-Anbia Hospital, Golestan Social Security Management, Golestan Province, Gonbad Kavus, Iran
[2] Department of Basic Medical Sciences, School of Medicine, Abadan University of Medical Sciences, Abadan, Iran
[3] Department of Parasitology and Medical Mycology, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran
[4] Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran
[5] Molecular Medicine Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
[6] Invasive Fungi Research Center, Communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran
[7] Department of Medical Mycology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
[8] Department of Parasitology and Mycology, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

Abstract

Introduction: COVID-19 is associated with a broad spectrum of bacterial and fungal superinfections.

Case Presentation: We present a case of mucormycosis developing during post-COVID-19 therapeutic management. A 63-year-old diabetic female presented with COVID-19 and received combination therapy per institutional protocol, including dexamethasone, remdesivir, and ivermectin. Seven days post-discharge, the patient was readmitted with dyspnea and lethargy. On day 3 of readmission, the patient reported unilateral facial and orbital pain. Subsequent histopathological and mycological examination confirmed mucormycosis. Despite surgical debridement and treatment with amphotericin B (3 mg/kg/day), the patient succumbed to the infection.

Results: Based on ITS rDNA sequencing, the fungus was identified as *Rhizopus arrhizus*. Antifungal susceptibility testing was performed according to the CLSI M38-A2 guideline, yielding minimum inhibitory concentration (MIC) values of 0.016 µg/mL for amphotericin B, 0.031 µg/mL for posaconazole, 0.25 µg/mL for isavuconazole, 1 µg/mL for itraconazole, and 8 µg/mL for voriconazole.

Conclusions: Early diagnosis, prompt antifungal therapy, and appropriate surgical intervention are critical for improving mucormycosis outcomes, especially in COVID-19 patients.

Key words: mucormycosis; zygomycosis; sino-orbital; COVID-19; diabetes mellitus; corticosteroids.

J Infect Dev Ctries 2025; 19(5):661-668. doi:10.3855/jidc.16526

(Received 01 March 2022 – Accepted 30 October 2022)

Introduction

The COVID-19 pandemic has increased susceptibility to bacterial and fungal coinfections due to prolonged hospitalization and widespread use of immunosuppressive therapies [1]. Corticosteroids and immunomodulators (e.g., tocilizumab) are utilized in the management of immune-mediated pulmonary injury in COVID-19 patients. However, their use may increase susceptibility to secondary infections, thereby exacerbating morbidity and mortality rates [2]. Numerous studies have established consensus that COVID-19 increases susceptibility to fungal and bacterial coinfections [1,3,4]. Secondary fungal infections- including candidiasis, aspergillosis, mucormycosis, and cryptococcosis- have been frequently documented in COVID-19 patients [3,4].

Mucormycosis is a potentially life-threatening fungal infection that primarily occurs in immunocompromised patients, especially those with diabetes mellitus (DM), hematologic malignancies, or prior organ transplantation [5,6]. Emerging evidence highlights an increasing incidence of COVID-19-associated mucormycosis (CAM), as documented in numerous recent reports [7-16].

This infection is characterized by angioinvasion, tissue necrosis, and thrombus formation, contributing to its high mortality rate [5]. Therefore, COVID-19 patients with suspected invasive mucormycosis require both highly accurate early diagnosis and prompt

therapeutic intervention. This report describes a case of sino-orbital mucormycosis in a post-COVID-19 patient with prior systemic corticosteroid exposure. We also provide a systematic review of documented sino-orbital mucormycosis cases in COVID-19-affected adults.

Case report

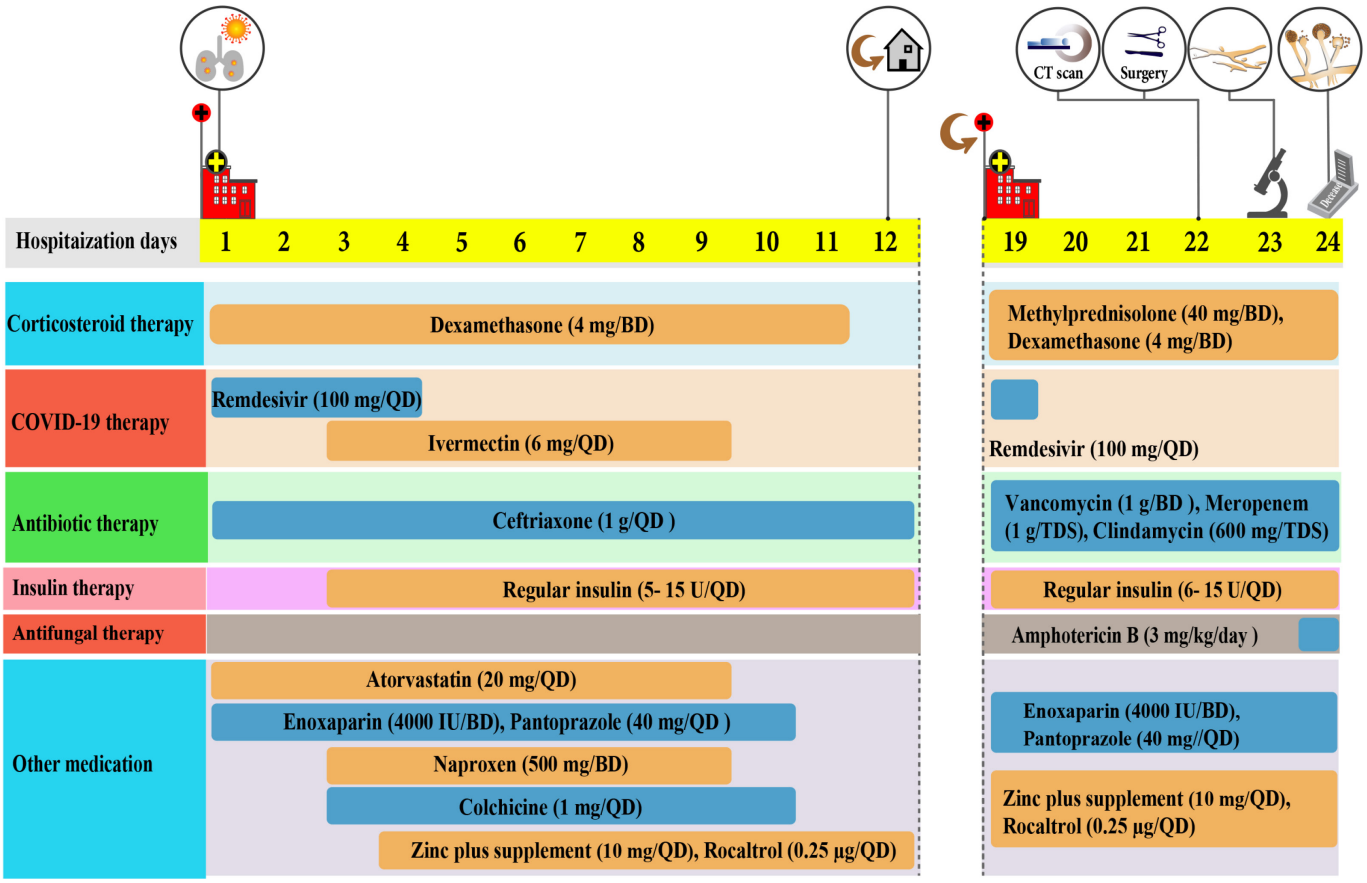
A 63-year-old female was admitted to Khatam Al-Anbia Hospital in Gonbad Kavus, Iran, with a 4-day history of cough, dyspnea, fever, and fatigue. She had a past medical history of arterial hypertension and insulin-dependent type I DM. On examination, the patient's vital signs were as follows: blood pressure of 120/80 mmHg, body temperature of 37 °C, resting pulse rate of 80 beats per minute, respiratory rate of 20 breaths per minute, and peripheral oxygen saturation of 89% on room air.

COVID-19 diagnosis was confirmed via reverse transcriptase-polymerase chain reaction analysis of her nasopharyngeal swab specimen. She was administered an 11-day regimen of dexamethasone (4 mg twice daily), a 4-day of course remdesivir (100 mg daily), and a 7-day treatment of ivermectin (6 mg daily) as part of the COVID-19 management protocol.

Empiric ceftriaxone (1g daily IV) was prescribed for the treatment of healthcare-associated pneumonia bacterial pneumonia. Insulin therapy was initiated to manage the patient's comorbidities. Additionally, zinc and calcitriol (Rocaltrol) supplements were added to the treatment regimen. Figure 1 summarizes all medications administered, including dosages and treatment durations. During her hospitalization, the patient required non-invasive ventilation and urinary catheterization. After 12 days of hospitalization, she was discharged with overall clinical improvement.

Seven days after discharge, the patient was readmitted with lethargy, fatigue, and dyspnea. The patient's vital signs were: temperature 36.9°C, blood pressure 105/60 mmHg, and oxygen saturation 87% on room air. Laboratory results showed hemoglobin of 12.1 g/dL, marked leukocytosis (21.5 × 10^9/L with 96% neutrophils), hyperglycemia (fasting glucose 288 mg/dL), and elevated ESR (59 mm/hour). Table 1 presents the patient's laboratory findings from both initial and subsequent hospital admissions. During the second admission, the patient was treated with remdesivir, clindamycin, vancomycin, meropenem, methylprednisolone, and dexamethasone (Figure 1).

Figure 1. Patient's timeline of treatment events.



On day 3 of the second admission, the patient reported unilateral facial and orbital pain. Physical examination revealed facial swelling, chemosis, and periorbital cellulitis. Computed tomography (CT) scan identified heterogeneously attenuating soft tissue with poorly defined margins, accompanied by mucosal thickening in all bilateral paranasal (maxillary, ethmoid, and frontal) sinuses (Figure 2A-C). Functional endoscopic sinus surgery was performed for debridement, which identified necrotic tissue. Surgical specimens obtained during debridement were sent for histopathological examination and microbiological analysis. Direct microscopy with 10% potassium hydroxide demonstrated broad, non-septate hyphae (Figure 1D).

Additionally, the presence of granulomatous inflammation with necrosis and wide, non-septate hyphae was observed in hematoxylin and eosin staining (Figure 1. E), confirming invasive mucormycosis. Due to the scarcity of liposomal amphotericin B in the hospital, there was a three-day delay before she received the medication (3 mg/kg/day) on the sixth day of hospitalization. Given orbital involvement, the patient was transferred to a tertiary care center for ophthalmologic evaluation and potential orbital exenteration. Despite antifungal therapy, the patient expired on hospital day 6 post-readmission following a myocardial infarction.

Figure 2A. Computed tomography (CT) scan of involvement bilateral maxillary sinuses; **B.** CT scan of involvement bilateral ethmoid; **C.** CT scan of involvement bilateral frontal; **D.** Broad aseptate hyphae in tissue after surgical debridement in direct microscopy (wet mount with KOH); **E.** Broad non-septate hyphae on hematoxylin and eosin stain; **F.** Broad hyaline aseptate hyphae, rhizoids, and sporangiophores with lactophenol aniline blue stain in slide culture.

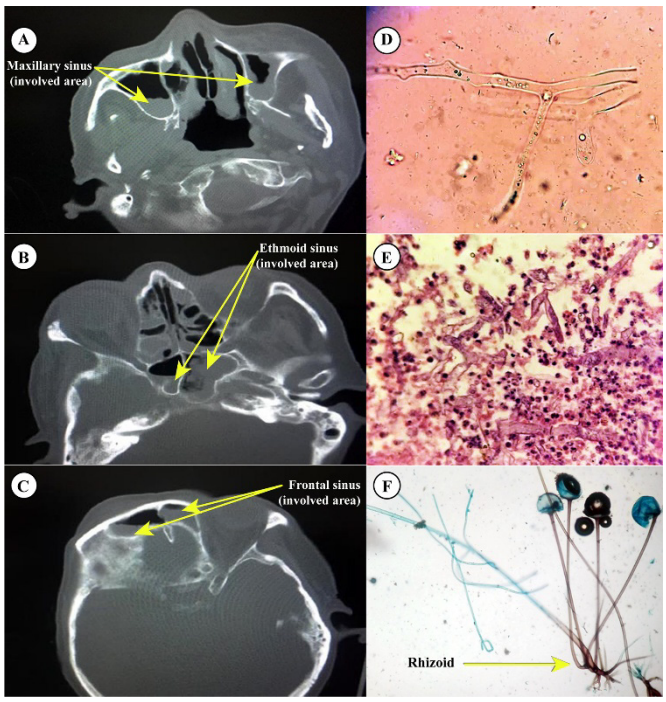


Table 1. Laboratory parameters of the patient at the time of admission for COVID-19 and mucormycosis.

Parameters	COVID-19	Mucormycosis
Red Blood Cell Count (RBC), million/µL	4.04	4.35
White Blood Cell (WBC) Count, µL	3600	21500
Hemoglobin (Hb), mg/dL	11	12.1
Platelets, µL	114000	297000
Neutrophil count, %	74%	96%
Lymphocyte count, %	24 %	4%
Qualitative C-Reactive Protein (CRP)	+++	++
ESR, mm/hour	59	91
Blood Urea Nitrogen (BUN), mg/dL	10	22
Serum creatinine, mg/dL	0.8	0.7
Sodium Blood, mEq/L	128	124
Potassium Blood, mEq/L	2.6	4.8
Creatine Kinase-MB (CK-MB), IU/L	-	36
Lactate Dehydrogenase (LDH), U/L	-	577
Fasting Blood Sugar, mg/dl	288	479

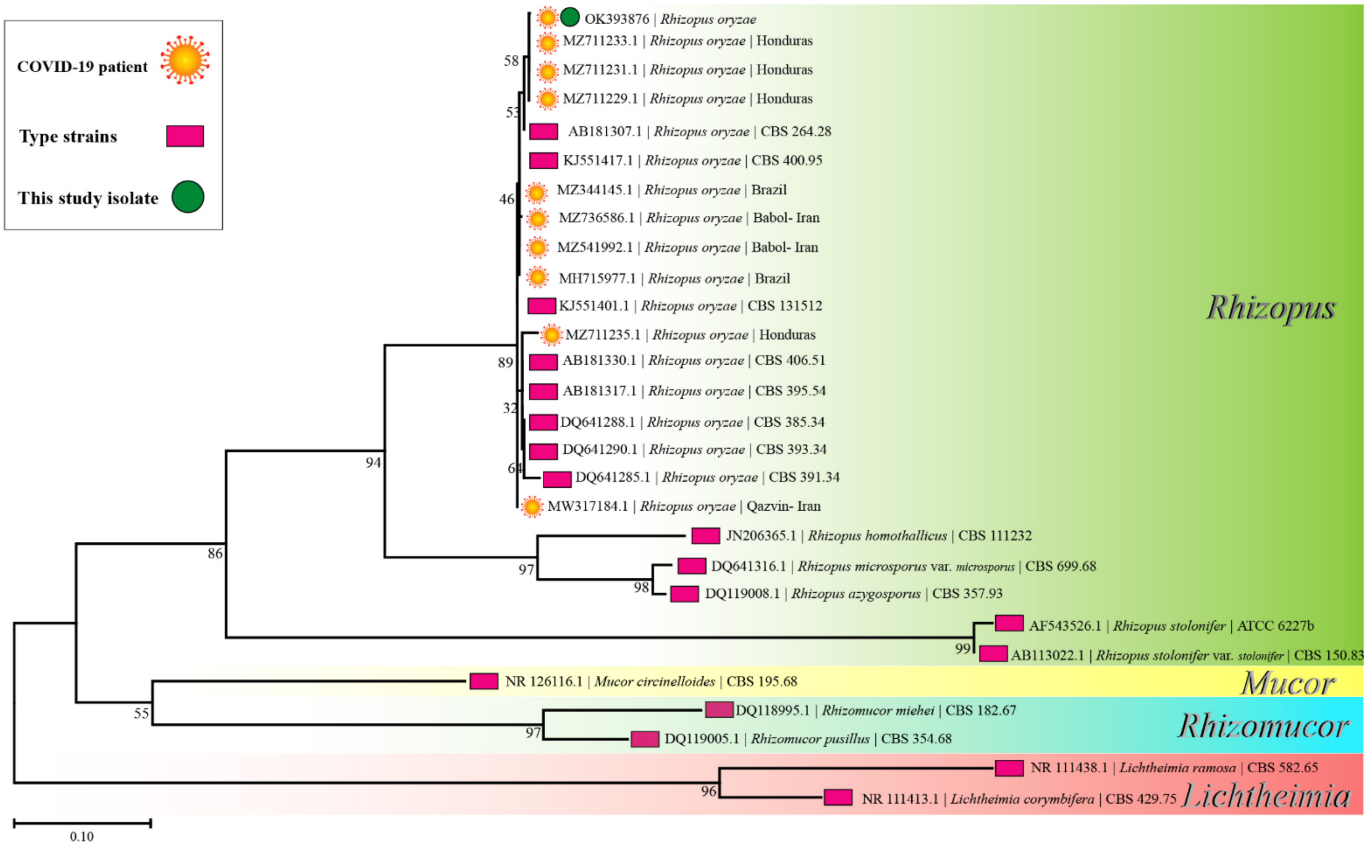
On the sixth day, cottony fungal colonies with fluffy morphology were observed on Sabouraud dextrose agar. Microscopic examination revealed broad, hyaline, pauciseptate hyphae with rhizoids and sporangiophores (Figure 2F), consistent with Mucorales fungi. Genomic DNA was extracted using a glass bead-phenol-chloroform protocol, as previously described [17]. Fungal species identification was performed by amplifying the internal transcribed spacer (ITS) ribosomal DNA region with ITS1 and ITS4 primers [17]. The ITS rDNA sequence showed 100% identity with *Rhizopus arrhizus* (syn. *R. oryzae*) and was submitted to GenBank under accession number OK393876.

Molecular diversity within this strain was assessed through phylogenetic analysis performed using MEGA 11 software. This analysis involved comparing the sequence with existing sequences of invasive mucormycosis in COVID-19 patients, as well as type strains obtained from the GenBank database.

Phylogenetic analysis was conducted using the maximum-likelihood method with the Tamura-Nei evolutionary model and 1000 bootstrap replicates. Figure 3 illustrates the phylogenetic similarity between this isolate and *R. arrhizus* strains from COVID-19 patients in Honduras (GenBank accessions: MZ711233.1, MZ711231.1, MZ711229.1).

Antifungal susceptibility was determined following the Clinical and Laboratory Standards Institute (CLSI) document M38-A2 protocols [18]. The minimum inhibitory concentrations (MICs) were determined as follows: amphotericin B 0.016 µg/mL, posaconazole 0.031 µg/mL, isavuconazole 0.25 µg/mL, itraconazole

Figure 3. Phylogenetic tree of *Rhizopus arrhizus* (*R. oryzae*) and other genera of mucormycetes isolated from COVID-19 patients, based on ITS rDNA region sequencing, using the maximum-likelihood method analysis based on 1,000 bootstrap replicates.



1 µg/mL, and voriconazole 8 µg/mL. The isolate showed the highest susceptibility to amphotericin B, followed by posaconazole and isavuconazole.

Currently, no species-specific interpretive breakpoints or epidemiological cutoff values exist for Mucorales. Therefore, MIC interpretation relies on clinical efficacy data from *Aspergillus fumigatus* [19]. The MIC values fell within the susceptibility range established for *A. fumigatus*. Notably, the elevated voriconazole MIC (8 µg/mL) corroborates its known lack of activity against Mucorales [19].

We performed a systematic literature review of sino-orbital mucormycosis in COVID-19 patients, including studies published up to February 28, 2022. The review findings are summarized in Table 2 [8-16]. Twenty-three cases were reported up until the aforementioned date, including the present case. Twenty cases (86.9%) were male. The mean patient age was 50.22 years (range: 23-71 years). Eighteen patients (78.2%) had pre-existing DM. Systemic corticosteroids were administered to 60.8% of patients, compared to 30.4% receiving remdesivir and 4.3% treated with tocilizumab. Fungal species were identified in only 4 cases (17.3%), all of which were *R. arrhizus*. The mean interval between COVID-19 diagnosis and onset of invasive mucormycosis symptoms was 17.92 ± 12.48 days. Ten patients (43.4%) died. Antifungal treatment was administered to 19 patients (82.6%), while 17 (73.9%) underwent surgical debridement.

Discussion

COVID-19 has demonstrated rapid global spread, causing a wide clinical spectrum from mild to severe disease in adults. The inappropriate use of systemic corticosteroids and broad-spectrum antibiotics in COVID-19 management significantly increases the risk of invasive fungal infections [5].

Invasive mucormycosis represents a life-threatening opportunistic fungal infection caused by the order Mucorales [5]. While invasive mucormycosis shows an approximate 50% mortality rate overall, this varies substantially by disease manifestation, infecting species, and patient comorbidities. Disseminated infections prove most fatal, with > 90% mortality [6].

In high-risk patients (e.g., those with uncontrolled DM, malignancy, organ transplantation, or immunosuppressive therapy), Mucorales fungi exhibit angioinvasive potential, directly penetrating vascular

Table 2. Characteristics of sino-orbital mucormycosis in COVID-19 patients reported in the literature.

Reference	Sex/age	Underlying diseases	Treatment for COVID-19	Corticosteroid therapy	Antifungal therapy	Surgical Debridement	Fungal species	CAM diagnosis	Outcome
Mehta *et al.* India [8]	M/ 60	DM	Oseltamivir, tocilizumab	MPS	AMB	No	ND	10	Died
Pakdel *et al.* Iran [9]	M/ 32	AML, Chemotherapy, Neutropenia	ND	ND	AMB	Yes	ND	7	Died
	M/ 71	DM, HTN, Cardiovascular disease	ND	DXM	AMB, POS	Yes	ND	14	Survived
	M/ 55	DM, HTN, Hepatic cirrhosis	ND	ND	AMB	Yes	ND	1	Died
	M/ 44	DM	ND	ND	AMB	Yes	ND	2	Died
	M/ 66	DM	ND	DXM	AMB	Yes	ND	18	Died
Maini *et al.* India [10]	M/ 38	None	Remdesivir	MPS, DXM	FLC, AMB	Yes	*R. oryzae*	18	Survived
Patil *et al.* India [11]	M/ 45	None	ND	ND	ND	Yes	ND	ND	ND
Singh *et al.* India [12]	M/ 53	DM, CAD, post-PTCA	ND	ND	ND	ND	ND	Previously diagnosed	Survived
Bansal *et al.* India [13]	M/ 50	DM	ND	ND	FLC, AMB	Yes	ND	30	ND
Patel *et al.* India [14]	M/ 68	None	ND	ND	AMB, POS	Yes	ND	45	Survived
Garg *et al.* India [15]	M/ 65	Type II DM	ND	ND	ND	ND	*R. oryzae*	25	Survived
	M/ 38	Type II DM	ND	ND	ND	ND	*R. oryzae*	24	Survived
Sarkar *et al.* India [16]	M/ 67	DM	Remdesivir	DXM	AMB	Yes	No growth.	At presentation	Survived
	M/ 49	DM	None	DXM	AMB	No	No growth.	At presentation	Died
	M/ 23	DM	None	DXM	AMB	Yes	*Rhizopus* sp.	During stay	Died
	F/ 59	DM	Remdesivir	DXM	AMB	No	*Mucor* sp.	At presentation	Died
	F/ 27	DM	None	DXM	AMB	Yes	*Rhizopus* sp.	During stay	Survived
	M/ 45	DM	None	DXM	AMB	Yes	*Mucor* sp.	During stay	Survived
	M/ 62	DM	Remdesivir	DXM	AMB	Yes	*Rhizopus* sp.	During stay	Survived
	M/ 43	None	Remdesivir	DXM	AMB	Yes	No growth.	None	Survived
	M/ 32	DM	Remdesivir	DXM	AMB	Yes	No growth	During stay	Died
Current case	F/ 63	Type I DM, HTN	Remdesivir, Ivermectin	MPS, DXM	AMB	Yes	*R. oryzae*	21	Died

M: male; F: Female; DM: Diabetes mellitus; HTN: Hypertension; AML: Acute myeloid leukemia; CAM: COVID-19-associated mucormycosis; DXM: Dexamethasone; MPS: Methylprednisolone; ND: Not determined; FLC: Fluconazole; AMB: Amphotericin B; POS: Posaconazole; FESS: functional endoscopic sinus surgery; PTCA: Percutaneous coronary angiography; CAD: Coronary artery disease.

walls and inducing thrombosis, tissue necrosis, and ischemia [20]. The infection typically originates in the paranasal sinuses and may spread contiguously to orbital and intracranial structures, with potential hematogenous dissemination. Rhino-orbital-cerebral mucormycosis constitutes the most common presentation, though pulmonary, cutaneous, gastrointestinal, and disseminated forms also occur [5].

Current evidence demonstrates that COVID-19 patients show significantly elevated levels of proinflammatory cytokines, including IL-6, IL-2R, IL-10, and TNF-α. Conversely, severe COVID-19 cases are characterized by reduced peripheral CD4+ and CD8+ T lymphocyte counts. Consequently, these immunological alterations significantly increase susceptibility to fungal coinfections [21].

Multiple comorbidities- particularly essential hypertension, cardiovascular diseases, and DM- are established risk factors for severe COVID-19 progression. Notably, DM and uncontrolled hyperglycemia are specifically associated with increased COVID-19 mortality [22]. Therefore, therapeutic strategies for COVID-19 must be carefully selected with consideration of potential hyperglycemic effects, particularly in diabetic patients. While numerous therapeutic approaches have been investigated, many have been discontinued due to limited efficacy or safety concerns.

Remdesivir has received FDA approval as the first antiviral agent authorized for COVID-19 treatment in the United States [23]. While dexamethasone remains a mainstay for severe COVID-19 [2,24], emerging evidence links high-dose corticosteroid and remdesivir regimens to iatrogenic DM across diverse populations [25,26]. Consequently, concerns have emerged about remdesivir's potential hyperglycemic effects. Further investigation is required to elucidate this relationship in COVID-19 patients [27]. In the current case, systemic corticosteroid therapy likely contributed as a risk factor for sino-orbital mucormycosis. Additionally, the

patient's history of insulin-dependent DM represented a significant predisposing factor for fungal infection.

Contrastingly, Muthu *et al*. (2021) reported that zinc supplementation during COVID-19 treatment may promote *in vitro* growth of *R. arrhizus* isolates from CAM cases [28]. The study found no significant differences in serum zinc levels among CAM patients. The authors further highlighted the necessity for additional research to evaluate zinc supplementation as a potential predisposing factor [28].

Mucormycosis diagnosis relies on a triad of clinical presentation, imaging studies, and histopathological examination- all critical for assessing disease invasiveness [29]. In this case, imaging findings were consistent with sino-orbital mucormycosis. Serial clinical examinations and advanced imaging (CT and MRI) are essential for evaluating disease progression and determining the extent of invasion [30]. Classic clinical manifestations of sino-orbital mucormycosis comprise facial pain, headache, proptosis, periorbital swelling, both external and internal ophthalmoplegia, and vision loss [30].

Early initiation of antifungal therapy is critical for reducing mortality in mucormycosis. Although our patient underwent prompt sinus debridement, treatment failure likely resulted from delayed antifungal administration. While controlling predisposing factors remains the cornerstone of invasive mucormycosis management, this proves particularly challenging in COVID-19 patients requiring high-dose corticosteroid therapy.

Mucorales species exhibit distinct antifungal susceptibility patterns, with significant variability in azole responsiveness across different genera [19,31]. Current evidence remains insufficient to support species-level identification of Mucorales for guiding antifungal therapy. However, genus/species determination is strongly recommended for epidemiological surveillance, as it enhances outbreak investigations and advances our understanding of healthcare-associated mucormycosis [32]. Standardized antifungal susceptibility testing of Mucorales, though not routinely recommended for initial treatment selection, may inform therapeutic decisions in cases of non-response to first-line agents [32]. *Rhizopus arrhizus* represents the most prevalent causative agent, accounting for nearly 60% of all mucormycosis cases [5]. Antifungal activity against Mucorales varies significantly among azoles, with posaconazole, isavuconazole, and itraconazole demonstrating species-dependent efficacy, while voriconazole shows no detectable in vitro activity [19].

In vitro susceptibility testing in this study demonstrated that *R. arrhizus* was most sensitive to amphotericin B, followed by posaconazole. Current global guidelines recommend liposomal amphotericin B as first-line therapy for suspected invasive mucormycosis, combined with surgical debridement when feasible [32]. The prognosis of mucormycosis depends on multiple factors, underscoring the critical importance of early intervention. Upon diagnosis, immediate initiation of antifungal therapy is essential. In sino-orbital cases, orbital exenteration presents a significant therapeutic challenge due to its profound functional and cosmetic consequences. While considered a last resort option, this potentially life-saving procedure carries substantial morbidity.

Conclusions

This case report underscores the clinical significance of invasive mucormycosis in COVID-19 patients with comorbidities, particularly diabetes mellitus. Adherence to international guidelines for early diagnosis and prompt treatment initiation, coupled with improved access to first-line antifungals, is essential for reducing disease burden.

Acknowledgements

The authors would like to thank the medical staff of the Khatam Al-Anbia Hospital in Gonbad Kavus, Iran.

Corresponding author

Javad Javidnia, Ph.D.
Invasive Fungi Research Center,
Communicable Diseases Institute,
Mazandaran University of Medical Sciences,
Sari, Iran
Tel: +98-9175570355
E-mail: Javidniaj@gmail.com

Conflict of interests

No conflict of interests is declared.

References

1. Sarkar S, Khanna P, Singh AK (2021) Impact of COVID-19 in patients with concurrent co-infections: A systematic review and meta-analyses. J Med Virol 93: 2385-95. doi: 10.1002/jmv.26740.
2. Group RC (2021) Dexamethasone in hospitalized patients with Covid-19. N Engl J Med 384: 693-704. doi: 10.1056/NEJMoa2021436.
3. Song G, Liang G, Liu W (2020) Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. Mycopathologia 185: 599-606. doi: 10.1007/s11046-020-00462-9.
4. Kottarathil M, Thayanidhi P, P S, Jyoti Kindo A (2023) Rise of mucormycosis during the COVID-19 pandemic and the

challenges faced. Curr Med Mycol 9: 44-55. doi: 10.18502/cmm.2023.345032.1400.
5. Prakash H, Chakrabarti A (2019) Global epidemiology of mucormycosis. J Fungi 5: 26. doi: 10.3390/jof5010026.
6. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, Sein M, Sein T, Chiou CC, Chu JH, Kontoyiannis DP, Walsh TJ (2005) Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis 41: 634-53. doi: 10.1086/432579.
7. Dursun ZB, Sipahioğlu H, Yüksel RC, Sav H, Çelik İ (2022) Risk factors and lethality associated with Candidemia in severe COVID-19 patients. Curr Med Mycol 8: 32–8. doi: 10.18502/cmm.8.1.9212.
8. Mehta S, Pandey A (2020) Rhino-orbital mucormycosis associated with COVID-19. Cureus 12: e10726. doi: 10.7759/cureus.10726.
9. Pakdel F, Ahmadikia K, Salehi M, Tabari A, Jafari R, Mehrparvar G, Rezaie Y, Rajaeih S, Alijani N, Barac A, Abdollahi A, Khodavaisy S (2021) Mucormycosis in patients with COVID-19: A cross-sectional descriptive multicentre study from Iran. Mycoses 64: 1238-52. doi: 10.1111/myc.13334.
10. Maini A, Tomar G, Khanna D, Kini Y, Mehta H, Bhagyasree V (2021) Sino-orbital mucormycosis in a COVID-19 patient: a case report. Int J Surg Case Rep 82: 105957. doi: 10.1016/j.ijscr.2021.105957.
11. Patil S, Sarate D, Chopade S, Khade M, Dhage S, Kangate S (2021) Emerging challenge of mucormycosis in postCOVID patients. IAR Journal of Medical Case Reports 2. doi: 10.47310/iarjmcr.2021.v02i01.022.
12. Singh Y, Ganesh V, Kumar S, Patel N, Aggarwala R, Soni KD, Trikha A (2021) Coronavirus disease-associated mucormycosis from a tertiary care hospital in India: a case series. Cureus 13: e16152. doi: 10.7759/cureus.16152.
13. Bansal S, Kalra H, Soni N (2021) Post- COVID mucormycosis- a case report. International Journal of Advanced Community Medicine 4: 21-3. doi: 10.33545/comed.2021.v4.i2a.191.
14. Patel DJ, Patel PG, Patel PP, Sapariya B, Parmar MB, Diwanji NS (2021) Case series of mucormycosis occurring in patients of COVID-19. Int J Res Med Sci 9: 5. doi: 10.18203/2320-6012.ijrms20212246.
15. Garg R, Bharangar S, Gupta S, Bhardwaj S (2022) Post Covid-19 infection presenting as rhino-orbital mycosis. Indian J Otolaryngol Head Neck Surg 74: 3050-7. doi: 10.1007/s12070-021-02722-6.
16. Sarkar S, Gokhale T, Choudhury SS, Deb AK (2021) COVID-19 and orbital mucormycosis. Indian J Ophthalmol 69: 1002. doi: 10.4103/ijo.IJO_3763_20.
17. Gholinejad-Ghadi N, Shokohi T, Seifi Z, Aghili SR, Roilides E, Nikkhah M, Pormosa R, Karami H, Larjani LV, Ghasemi M, Haghani I (2018) Identification of mucorales in patients with proven invasive mucormycosis by polymerase chain reaction in tissue samples. Mycoses 61: 909-15. doi: 10.1111/myc.12837.
18. Clinical and Laboratory Standards Institute (2008) Reference method for broth dilution antifungal susceptibility testing of filamentous fungi. 2nd ed., Wayne, PA.
19. Borman AM, Fraser M, Patterson Z, Palmer MD, Johnson EM (2021) In Vitro antifungal drug resistance profiles of clinically relevant members of the mucorales (mucoromycota) especially with the newer triazoles. J Fungi 7: 271. doi: 10.3390/jof7040271.
20. Goel S, Palaskar S, Shetty VP, Bhushan A (2009) Rhinomaxillary mucormycosis with cerebral extension. J Oral Maxillofac Pathol 13: 14-7. doi: 10.4103/0973-029X.48743.
21. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, Wang T, Zhang X, Chen H, Yu H, Zhang X, Zhang M, Wu S, Song J, Chen T, Han M, Li S, Luo X, Zhao J, Ning Q (2020) Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest 130: 2620-9. doi: 10.1172/JCI137244.
22. Lim S, Bae JH, Kwon HS, Nauck MA (2021) COVID-19 and diabetes mellitus: from pathophysiology to clinical management. Nat Rev Endocrinol 17: 11-30. doi: 10.1038/s41574-020-00435-4.
23. Lamb YN (2020) Remdesivir: first approval. Drugs 80: 1355-63. doi: 10.1007/s40265-020-01378-w.
24. Owji H, Negahdaripour M, Hajighahramani N (2020) Immunotherapeutic approaches to curtail COVID-19. Int Immunopharmacol 88: 106924. doi: 10.1016/j.intimp.2020.106924.
25. Langarizadeh MA, Ranjbar Tavakoli M, Abiri A, Ghasempour A, Rezaei M, Ameri A (2021) A review on function and side effects of systemic corticosteroids used in high-grade COVID-19 to prevent cytokine storms. EXCLI J 20: 339-65. doi: 10.17179/excli2020-3196.
26. Nabil A, Uto K, Elshemy MM, Soliman R, Hassan AA, Ebara M, Shiha G (2020) Current coronavirus (SARS-CoV-2) epidemiological, diagnostic and therapeutic approaches: An updated review until June 2020. EXCLI J 19: 992-1016. doi: 10.17179/excli2020-2554.
27. Negahdaripour M (2021) Post-COVID-19 hyperglycemia: a concern in selection of therapeutic regimens. Iran J Med Sci 46: 235-6. doi: 10.30476/ijms.2021.47666.
28. Muthu V, Kumar M, Paul RA, Zohmangaihi D, Choudhary H, Rudramurthy SM, Panda NK, Pannu AK, Sharma N, Sharma S (2021) Is there an association between zinc and COVID-19–associated mucormycosis? results of an experimental and clinical study. Mycoses 64: 1291-7. doi: 10.1111/myc.13365.
29. Deutsch PG, Whittaker J, Prasad S (2019) Invasive and non-invasive fungal rhinosinusitis-a review and update of the evidence. Medicina 55: 319. doi: 10.3390/medicina55070319.
30. Mohindra S, Mohindra S, Gupta R, Bakshi J, Gupta SK (2007) Rhinocerebral mucormycosis: the disease spectrum in 27 patients. Mycoses 50: 290-6. doi: 10.1111/j.1439-0507.2007.01364.x.
31. Badali H, Canete-Gibas C, McCarthy D, Patterson H, Sanders C, David MP, Mele J, Fan H, Wiederhold NP (2021) Epidemiology and antifungal susceptibilities of mucoralean fungi in clinical samples from the United States. J Clin Microbiol 59: e0123021. doi: 10.1128/JCM.01230-21.
32. Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, Hoenigl M, Jensen HE, Lagrou K, Lewis RE, Mellinghoff SC, Mer M, Pana ZD, Seidel D, Sheppard DC, Wahba R, Akova M, Alanio A, Al-Hatmi AMS, Arikan-Akdagli S, Badali H, Ben-Ami R, Bonifaz A, Bretagne S, Castagnola E, Chayakulkeeree M, Colombo AL, Corzo-Leon DE, Drgona L, Groll AH, Guinea J, Heussel CP, Ibrahim AS, Kanj SS, Klimko N, Lackner M, Lamoth F, Lanternier F, Lass-Floerl C, Lee DG, Lehrnbecher T, Lmimouni BE, Mares M, Maschmeyer G, Meis JF, Meletiadis J, Morrissey CO, Nucci M, Oladele R, Pagano L, Pasqualotto A, Patel A, Racil Z, Richardson M, Roilides E, Ruhnke M, Seyedmousavi S, Sidharthan N, Singh N, Sinko J, Skiada A, Slavin M, Soman R, Spellberg B, Steinbach W, Tan BH, Ullmann AJ,

Vehreschild JJ, Vehreschild M, Walsh TJ, White PL, Wiederhold NP, Zaoutis T, Chakrabarti A, Mucormycosis EMSGGGWG (2019) Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. Lancet Infect Dis 19: e405-e21. doi: 10.1016/S1473-3099(19)30312-3.