Case Report

Airway-destructive pulmonary mucormycosis in a diabetic patient

Kerim Göktürk[1], Burcu Yormaz[2], Özge Göktürk[3]

ORCID:
Kerim Göktürk: 0000-0002-3324-1957
Burcu Yormaz: 0000-0001-6563-8337
Özge Göktürk: 0000-0003-0892-6898

Abstract:

Mucormycosis is a severe fungal infection, primarily caused by organisms from the order Mucorales. This life-threatening condition predominantly affects immunocompromised individuals, particularly those with uncontrolled diabetes mellitus. Here, we present a case of a 32-year-old patient diagnosed with diabetes mellitus who developed pulmonary mucormycosis. The patient exhibited classic symptoms, including fever, respiratory distress, and expectoration of dark sputum. Both chest Computed Tomography (CT) and flexible bronchoscopy demonstrated an adherent, friable endobronchial lesion accompanied by bronchial wall necrosis and an adjacent thick-walled cavitary lesion. Initial antifungal therapy with liposomal amphotericin B and oral posaconazole was initiated; during therapy the patient developed massive hemoptysis, and surgical resection was performed for hemorrhage control. This case highlights the importance of a multidisciplinary approach in the management of mucormycosis, integrating antifungal therapy with surgical intervention to optimize treatment outcomes. Furthermore, it underscores the critical role of early diagnosis and proactive management in patients with predisposing conditions, such as uncontrolled diabetes mellitus, to mitigate severe complications associated with mucormycosis.

Keywords:

Endobronchial lesions, invasive fungal infections, pulmonary mucormycosis,

[1]Department of Chest Diseases, Ankara 29 Mayıs State Hospital, Ankara, Türkiye,
[2]Department of Chest Diseases, Konya Selçuk University Faculty of Medicine, Ankara, Türkiye,
[3]Department of Allergy Immunology, Ankara Kecioren Sanatorium Atatürk Training and Research Hospital, Ankara, Türkiye

Address for correspondence:
Dr. Kerim Göktürk, Department of Chest Diseases, Ankara 29 Mayıs State Hospital, Ankara, Türkiye.
E-mail: kgokturk94@gmail.com

Introduction

Mucormycosis, also known as zygomycosis, is a severe fungal infection primarily caused by fungi in the genera *Mucor, Rhizopus, Rhizomucor*, and *Absidia*, which belong to the order Mucorales of the class Zygomycetes.[1] This invasive infection is characterized by rapid progression and can affect multiple organs and tissues, leading to high morbidity and mortality rates. The pathogenesis of mucormycosis is complex and is largely influenced by the host's immune status and environmental factors.

Risk factors for mucormycosis include uncontrolled diabetes mellitus, hematologic malignancies, prolonged use of corticosteroids and immunosuppressive therapy, and conditions such as acquired immunodeficiency syndrome (AIDS) or

organ transplantation that compromise host defenses.[2,3] Notably, mucormycosis has also been reported in patients without any discernible immunodeficiencies, although such cases are exceedingly rare.[2]

The clinical presentation of mucormycosis can vary significantly depending on the affected site. The most common forms include rhinocerebral, pulmonary, cutaneous, gastrointestinal, and disseminated mucormycosis.[3] Each clinical form is associated with specific predisposing factors. For instance, the rhinocerebral form is most prevalent among patients with diabetes mellitus, whereas pulmonary mucormycosis frequently occurs in patients with neutropenia resulting from bone marrow transplantation or leukemia.[4]

Given the severe and often rapid progression of mucormycosis, early recognition and prompt initiation of treatment are crucial for improving survival rates. This case report discusses the presentation, diagnosis, and management of a diabetic patient with pulmonary mucormycosis, emphasizing the challenges and considerations in treating this severe infection.

Case Report

A 32-year-old female patient with a history of poorly controlled type 1 diabetes mellitus (glycated hemoglobin [HbA1c] 8.2%) presented to the outpatient clinic with symptoms of fever, chills, shortness of breath, cough, and expectoration of dark sputum for one week. On physical examination, her body temperature was 37°C, pulse rate was 85 beats/ minute, and arterial blood pressure was 110/70 mmHg. Her oxygen saturation was 94% on room air. Pulmonary auscultation revealed coarse rales in the left lower pulmonary zone.

The laboratory analysis indicated significant hyperglycemia, with glucose levels at 289 mg/dL (normal range: 74–106 mg/dL), an elevated HbA1c of 8.2% (normal range: 4–6%), and a markedly elevated C-reactive protein (CRP) level of 256 mg/L (normal range: 0–5 mg/L). Renal and liver function tests were within normal limits A complete blood count revealed a slight leukocytosis at 12,000 cells/μL (normal range: 4,000–11,000 cells/μL), with a predominance of neutrophils (80%). A chest X-ray revealed a cavitary lesion with an air-fluid level in the left lower lung zone [Fig. 1a]. A subsequent thoracic computed tomography (CT) scan demonstrated the cavitary lesion in the posterobasal segment of the left lower lobe. [Fig. 1b], leading to the patient's hospitalization for advanced care.

Upon admission, microbiological assessments were conducted, including sputum and blood cultures, a respiratory fungal culture and testing for acid-fast- bacilli (AFB), all of which returned negative results. Empirical treatment was initiated with linezolid and meropenem. Bronchoscopic examination revealed a yellow-white, mobile,
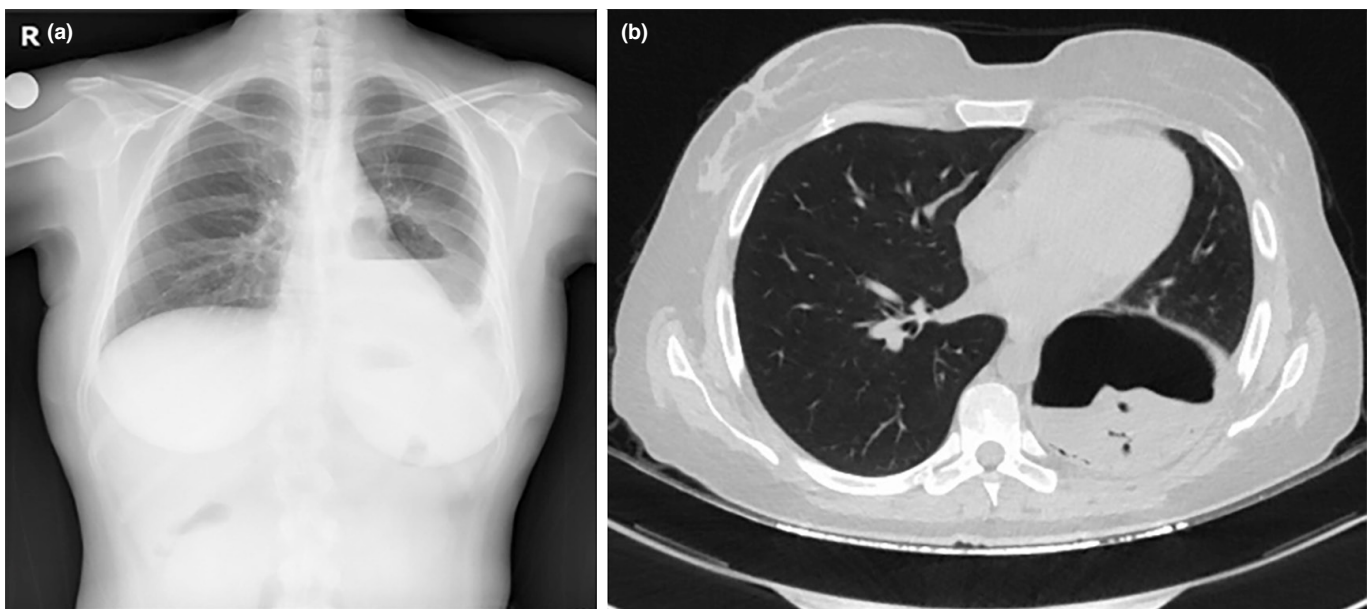
Figure 1: Cavitary lesion with an air-fluid level in the left lower lung zone. (a) Chest X-ray. (b) Thoracic computed tomography (CT)

(a)

(b)
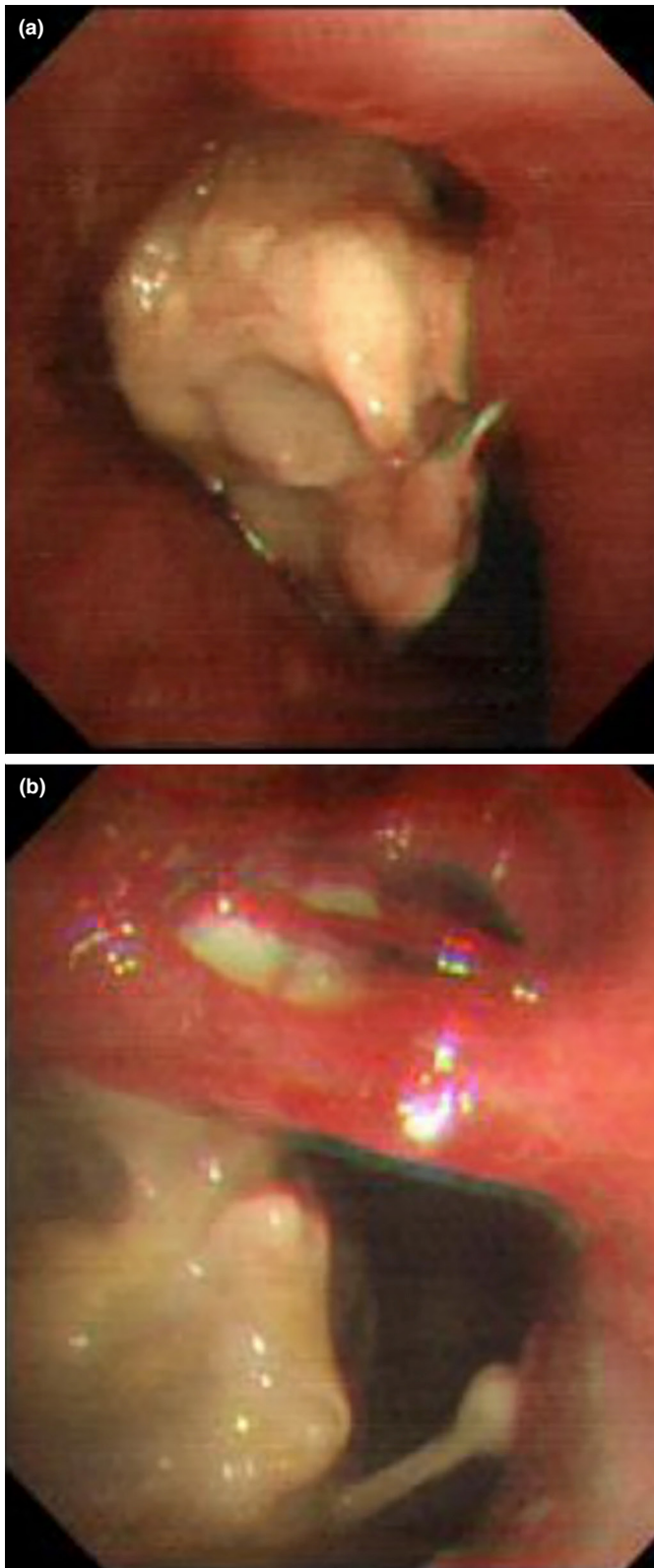
Figure 2: Bronchoscopic images. (a) Bronchoscopic view of the yellow-white, mobile, adhesive endobronchial lesion obstructing the left main bronchus. (b) Bronchoscopic examination showed bronchial wall necrosis and a fistulous opening at the orifice of the left lower lobe bronchus
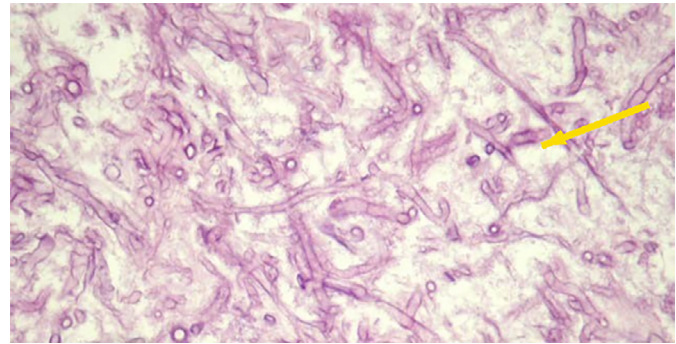
Figure 3: Pulmonary mucormycosis histopathology image (Periodic acid–Schiff (PAS), original magnification ×400: broad, non-septate hyphae with right-angle branching)

adhesive endobronchial lesion obstructing the entrance to the left main bronchus [Fig. 2a]. Bronchoscopy demonstrated bronchial wall necrosis and fistulous opening at the left lower lobe bronchial orifice. [Fig. 2b].

Bronchial lavage and subsequent tests for galactomannan, AFB, and aerobic pathogens yielded negative results. Histopathological examination of the biopsied specimen confirmed the diagnosis of pulmonary mucormycosis [Fig. 3].

A comprehensive evaluation to exclude additional causes of immunosuppression demonstrated normal HIV serology and quantitative serum immunoglobulins; there was no history of immunosuppressive medication use, and no other predisposing condition was identified beyond uncontrolled diabetes mellitus. The patient was started on an antifungal regimen of liposomal amphotericin B, administered at 5 mg/kg for four weeks, followed by a loading dose of oral posaconazole (300 mg twice daily) and then a maintenance dose of 300 mg daily.

At the time of diagnosis, the patient was considered at high surgical risk, and the procedure was postponed. After four weeks of stabilization with amphotericin B, the patient was deemed fit for surgery. On the 35th day of treatment, the patient developed massive hemoptysis, with an estimated blood loss of 200 mL. Despite the administration of 1 g of intravenous tranexamic acid, the bleeding persisted, necessitating urgent surgical intervention. A left pneumonectomy was performed, involving the complete removal of the left lung via a standard posterolateral thoracotomy. Postoperatively, the patient remained hospitalized for 14 days for close monitoring and recovery. Posaconazole therapy was continued for an additional four months. Upon reassessment, with no

evidence of new lesion development, posaconazole therapy was discontinued. At a follow-up visit three months after cessation of therapy, the patient had achieved full recovery, with no signs of recurrence or residual disease.

Discussion

Mucormycosis is rare in healthy individuals and is typically observed in patients with predisposing risk factors. Due to its rapidly progressive and often devastating nature, mucormycosis requires urgent intervention. Delayed initiation of treatment is associated with increased mortality.[5] All-cause mortality rates for mucormycosis range from 40% to 80%, depending on the underlying conditions and sites of infection.[6]

In a meta-analysis evaluating 851 cases of mucormycosis, hematopoietic stem cell transplantation was identified as a risk factor in 11% of cases, organ transplantation in 14%, hematologic malignancy in 32%, corticosteroid use in 33%, and diabetes mellitus in 40%.[7] The overall incidence of mucormycosis is estimated to be between 1.7 and 3.4 cases per million people annually. In the literature, endobronchial mucormycosis has been reported to account for less than 5% of all mucormycosis cases. Diabetes mellitus reduces natural killer cell and T-cell activity and suppresses cellular immunity, while uncontrolled diabetes leads to decreased phagocytic function and impaired neutrophil activity, making patients more susceptible to mucormycosis.[8]

The clinical manifestations of pulmonary mucormycosis can be difficult to distinguish from those of other fungal or bacterial pulmonary infections. Patients may present with symptoms such as fever, cough, hemoptysis, and pleuritic chest pain. Consequently, when imaging findings strongly suggest an invasive fungal infection, a tissue biopsy is imperative for definitive diagnosis.

Thoracic computed tomography is essential for evaluating patients with suspected pulmonary mucormycosis. On CT angiography, consolidation and the inverted halo sign are frequently observed.[9] The radiographic manifestations of pulmonary mucormycosis are diverse and may include pulmonary infiltrates, cavities, consolidation, pleural effusion, fistula formation, or pneumothorax. In certain cases, the disease may present with airway obstruction due to fungal invasion of the bronchi, resulting in intrabronchial lesions similar to those described in this report. Bronchoscopy has proven to be an effective diagnostic modality in mucormycosis with airway involvement, often revealing granulation tissue and gray-white mucoid material obstructing the airway. The affected airways are typically edematous and necrotic.[10]

Endobronchial mucormycosis can only be definitively diagnosed through a biopsy, as its appearance can closely resemble that of a malignancy or bacterial abscess. Although sputum culture is commonly used as an initial diagnostic method, it often fails to yield positive results. Histopathologically, mucormycosis is characterized by thick, non-septate hyphae branching at right angles with vascular proliferation.[11] The appearance of *Mucor* hyphae in tissue differs from that of *Aspergillus, Fusarium,* or *Pseudallescheria spp*. These latter hyphae are narrowly angled, thin, more regular, and septate. Class and species identification is based on the morphological characteristics of fungal elements grown in culture. However, fungal growth in culture may not always be observed.

Pulmonary mucormycosis is characterized by its pronounced angioinvasive nature. Cases of fatal hemorrhage have been documented in patients with endobronchial mucormycosis following standard endobronchial forceps biopsy.[12] To mitigate the risk of bleeding while obtaining adequately sized biopsy specimens, cryobiopsy should be considered whenever feasible.[13] The bronchoscopic management of endobronchial mucormycosis and other endobronchial fungal infections remains insufficiently defined.

Current therapeutic strategies advocate for a combination of medical and surgical interventions, as antifungal agents often demonstrate limited penetration at the infection site, and the disease typically progresses rapidly with a poor prognosis.[13,14] Liposomal amphotericin B remains the gold standard antifungal therapy for mucormycosis. While effective, its use is constrained by considerable toxicity, particularly at the doses and duration required for treatment. Amphotericin B should be administered systemically at a dose of 1–10 mg/kg. It is recommended to adjust the duration of treatment based on the clinical response, typically requiring at least 6 to 10 weeks. Isavuconazole, a triazole antifungal drug, is recommended for mucormycosis. Its efficacy has been shown to be similar to that of amphotericin B. Isavuconazole rescue therapy should be considered when other first-line agents have failed due to refractory mucormy-

cosis or drug-related toxicity.[15] However, isavuconazole is not available in Türkiye. Oral posaconazole is another recommended option for treating mucormycosis,[16] whereas voriconazole has been shown to be ineffective against this infection.[17] The exact duration of treatment is not well established and is typically continued until both clinical and radiological improvements are evident. In the present case, the patient was initially treated with amphotericin B, followed by oral posaconazole. Early surgical resection is critical to prevent vascular invasion and subsequent erosion, which could result in life-threatening massive hemoptysis. Studies have reported that surgical interventions, such as lobectomy or pneumonectomy, in combination with antifungal therapy, are associated with reduced mortality rates.[18]

Conclusion

Pulmonary mucormycosis is a rare but aggressive angioinvasive fungal infection that is often challenging to diagnose due to its nonspecific clinical presentation. It should be suspected in immunocompromised patients presenting with persistent fever and respiratory symptoms that do not respond to antibiotic treatment. Among immunocompromised hosts, diabetes mellitus, particularly when poorly controlled, is the leading predisposing condition and should prompt heightened clinical vigilance in diabetic patients with respiratory symptoms unresponsive to antibiotics. Early recognition is critical, as prompt initiation of antifungal therapy combined with surgical intervention can significantly improve patient outcomes and survival rates.

Ethics Committee Approval
This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent
This case report includes the clinical data and treatment process of the patient. The patient's personal information has been kept confidential, and her identity has not been disclosed. The patient has been informed that her medical information may be used and published for academic and scientific purposes, and written consent has been obtained. The patient understands that sharing this information may contribute to the treatment of other patients with similar health conditions and has consented to this purpose.

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References

1. Willke Topçu A, Söyletir G, Doğanay M, eds. Enfeksiyon Hastalıkları ve Mikrobiyolojisi: Sistemlere Göre Enfeksiyonlar. İstanbul: Nobel Tıp Kitabevleri; 2002.

2. Bottone EJ, Weitzman I, Hanna BA. Rhizopus rhizopodiformis: emerging etiological agent of mucormycosis. J Clin Microbiol 1979;9(4):530–7. [CrossRef]

3. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis 2005;41(5):634–53. [CrossRef]

4. Shi BY, Lan L, Guo H, Tan YF. Concomitant diabetic ketoacidosis and rhinocerebral mucormycosis: Report of a case. Chin Med J (Engl) 2004;117(7):1113–5.

5. Vaughan C, Bartolo A, Vallabh N, Leong SC. A meta-analysis of survival factors in rhino-orbital-cerebral mucormycosis-has anything changed in the past 20 years? Clin Otolaryngol 2018;43(6):1454–64. [CrossRef]

6. Marty FM, Ostrosky-Zeichner L, Cornely OA, Mullane KM, Perfect JR, Thompson GR 3rd, et al.; VITAL and FungiScope Mucormycosis Investigators. Isavuconazole treatment for mucormycosis: a single-arm open-label trial and case-control analysis. Lancet Infect Dis 2016;16(7):828–37. [CrossRef]

7. Jeong W, Keighley C, Wolfe R, Lee WL, Slavin MA, Kong DCM, et al. The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. Clin Microbiol Infect 2019;25(1):26–34. [CrossRef]

8. Gupta R, Kesavadev J, Krishnan G, Agarwal S, Saboo B, Shah M, et al. COVID-19 associated mucormycosis: a descriptive multisite study from India. Diabetes Metab Syndr 2021;15(6):102322. [CrossRef]

9. Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, et al.; Mucormycosis ECMM MSG Global Guideline Writing Group. 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 2019;19(12):e405–e421.

10. Husari AW, Jensen WA, Kirsch CM, Campagna AC, Kagawa FT, Hamed KA, et al. Pulmonary mucormycosis presenting as an endobronchial lesion. Chest 1994;106(6):1889–91. [CrossRef]

11. Kung VL, Chernock RD, Burnham CD. Diagnostic accuracy of fungal identification in histopathology and cytopathology specimens. Eur J Clin Microbiol Infect Dis 2018;37(1):157–65. [CrossRef]

12. Di Carlo P, Cabibi D, La Rocca AM, De Luca D, La Licata F, Sacco E. Post-bronchoscopy fatal endobronchial hemorrhage in a woman with bronchopulmonary mucormycosis: a case report. J Med Case Rep 2010;4:398. [CrossRef]

13. Zuil M, Villegas F, Jareño J, Martos–Peregrin J, Llobregat N, Gómez Terreros FJ, et al. Cryotherapy in the diagnosis of endobronchial mucormycosis. J Bronchol 2001;8(2):107–9. [CrossRef]

14. Brunet K, Rammaert B. Mucormycosis treatment: Recommendations, latest advances, and perspectives. J Mycol Med 2020;30(3):101007. [CrossRef]

15. Marty FM, Cornely OA, Mullane KM, Ostrosky-Zeichner L, Maher RM, Croos-Dabrera R, et al. Isavuconazole for treatment of invasive fungal diseases caused by more than one fungal species. Mycoses 2018;61(7):485–97. [CrossRef]

16. Greenberg RN, Mullane K, Van Burik JAH, Raad I, Abzug MJ, Anstead G, et al. Posaconazole as salvage therapy for zygomycosis. Antimicrob Agents Chemother 2006;50(1):126–33. [CrossRef]

17. Fanci R, Pecile P, Di Lollo S, Dini C, Bosi A. Pulmonary mucormycosis with cervical lymph node involvement in a patient with acute myeloid leukaemia: a case report. Mycoses 2008;51(4):354–6. [CrossRef]

18. Serio B, Rosamilio R, Giudice V, Zeppa P, Esposito S, Fontana R, et al. Successful management of pulmonary mucormycosis with liposomal amphotericin B and surgery treatment: a case report. Infez Med 2012;20 Suppl 2:43–7.