JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Case Report

Fungal sinusitis due to mucormycosis in a diabetic immunosuppressed patient with acute myeloid leukemia (AML)

Gulfem Ece[1], Ejder Ciger[2], Celal Acar[3], Seckin Cagirgan[3], Ogulcan Cetin[4]

[1] *Department of Medical Microbiology, Izmir City Hospital, Izmir, Turkiye*
[2] *Department of Ear Nose and Throat, Tepecik Education and Research Hospital, Izmir, Turkiye*
[3] *Department of Hematology, Izmir University of Economics School of Medicine, Medical Point Izmir Hospital, Izmir, Turkiye*
[4] *Izmir City Hospital, Izmir, Turkiye*

Abstract

Introduction: Mucormycosis is an acute onset, invasive, fungal infection, characterized by organ involvement, and caused by *Mucor*, *Rhizopus*, or *Absidia*. Our aim was to present a case of mucormycotic infection and emphasize its importance in a diabetic immunosuppressed patient with acute myeloid leukemia (AML).

Case presentation: A 68-year-old hypertensive and diabetic male patient with a diagnosis of AML developed respiratory failure and exhibited diffuse bilateral consolidation in high-resolution computed tomography (HRCT). The treatment plan involved chemotherapy with cytarabine (200 mg/m^2/day for 7 days) and daunorubicin (60 mg/m^2/day for 3 days) starting on 20 July 2022. Posaconazole prophylactic treatment was initiated on 23 July 2022, to prevent fungal infections. Five days later there was a black necrotic appearance on the left wing of the nose. The patient underwent excision of the left wing of the nose. *Mucor* was detected in the excision tissue both histopathologically and in culture. A culture under lactophenol cotton blue (LFCB) staining displaying hyphal structures of *Mucor* was obtained. The patient died of progressive pneumonia and sepsis.

Conclusions: Mucormycosis is an infection with high mortality, and should be considered in the early stages of diagnosis when dealing with immunosuppression patients.

Key words: fungal sinusitis; diabetes mellitus; AML; *Mucor*.

J Infect Dev Ctries 2024; 18(10):1636-1639. doi:10.3855/jidc.19742

(Received 19 December 2023 – Accepted 13 June 2024)

Introduction

Mucormycosis is caused by mould fungi belonging to the *Mucor*, *Rhizopus*, *Rhizomucor*, and *Absidia* genera, and it is an invasive fungal infection characterized by organ and tissue involvement [1]. The disease was first described in 1876 in Germany from a patient who died of cancer and in whom the right lung showed a hemorrhagic infarct with fungal hyphae and a few sporangia [2]. Prominently uncontrolled diabetes, haematological malignancies, long-term immunosuppressive therapy, and transplantations constitute its main predisposing factors [3].

Early recognition and treatment of the disease are paramount to increasing survival [4]. It is imperative to consider clinical mucormycosis in the differential diagnosis of susceptible patient groups. The Mucorales are common environmental fungi to which humans are constantly exposed. These fungi cause infection primarily in patients with uncontrolled diabetes, defects in phagocytic function, and/or elevated levels of free iron which supports fungal growth in serum and tissues. In the past, iron overloaded patients with end stage renal failure who were treated with deferoxamine had a high risk of developing rapidly fatal disseminated mucormycosis. Deferoxamine is an iron chelator for the human host, but it serves as a fungal siderophore, directly delivering iron to the Mucorales. Besides, patients with diabetic ketoacidosis are at high risk of developing rhinocerebral mucormycosis. The acidosis causes dissociation of iron from sequestering proteins, resulting in enhanced fungal survival and virulence [5].

Diagnosis consists of recognition of risk factors; assessment of clinical manifestations; early use of imaging; and prompt initiation of diagnostic methods based on histopathology, cultures, and advanced molecular techniques [2,6].

Mucormycosis is an angioinvasive fungal infection caused by fungi of the order Mucorales and can be seen in various forms. Depending on the clinical presentation it is classified as rhinocerebral; pulmonary; cutaneous;

gastrointestinal; disseminated; or other, which includes uncommon rare forms, such as endocarditis, osteomyelitis, peritonitis, and renal [2]. The signs and symptoms of rhinocerebral mucormycosis are usually headaches, rhinorrhea, intranasal or intraoral black necrotic areas, and epistaxis [7]. As the disease progresses there may be involvement of orbital cellulitis, orbital apex syndrome, cavernous sinus syndrome, and central nervous system [8].

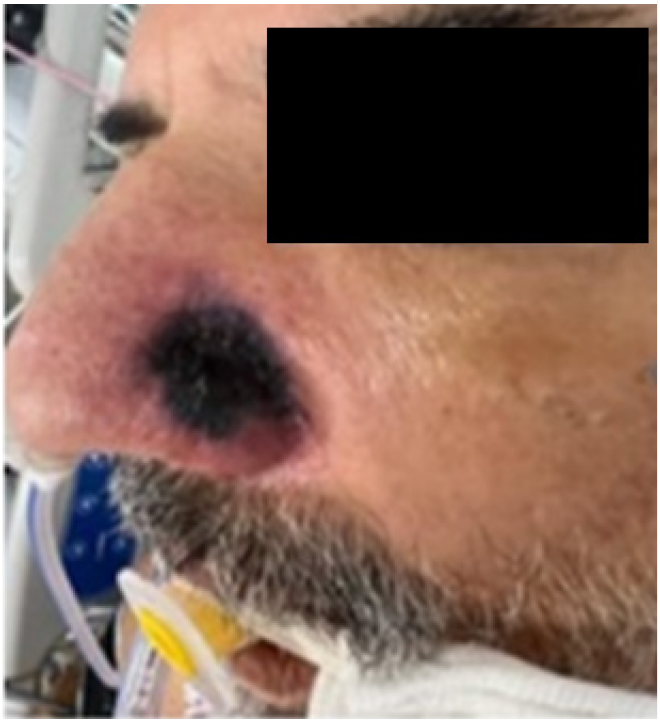
Optimizing the chances for successful treatment of mucormycosis requires early initiation of therapy, surgical debridement, rapid reversal of underlying predisposing risk factors (when possible), and treatment of underlying malignancy [9].

Our aim was to present a case of mucormycosis infection, and emphasize its importance in a diabetic immunosuppressed patient with acute myeloid leukaemia (AML).

Case presentation

A 68-year-old male patient with a history of diabetes mellitus type II and hypertension, and taking oral anti-diabetic medication, had complaints of weakness, fatigue, palpitation on exertion, sore throat, and abdominal distension that lasted about 3 weeks. Based on the laboratory results, the patient's blood counts were as follows: leukocytes 19,600/mm^3, hemoglobin (Hb) 6.7 g/dL, platelets (Tr) 23,000/mm^3, and neutrophils (neut) 7,800/mm^3. On admission (day 0), petechiae and purpura were present in the extremities and hard palate. The patient was diagnosed with AML by bone marrow examination on 19 July 2022. The patient also had disseminated intravascular coagulation (DIC) syndrome.

Figure 1. A black necrotic appearance on the left wing of the nose.



The treatment plan involved chemotherapy with cytarabine (200 mg/m^2/day for 7 days) and daunorubicin (60 mg/m^2/day for 3 days), starting on 20 July 2022 (day + 2). Posaconazole prophylactic treatment was initiated on 23 July 2022 to prevent fungal infections. Diffuse bilateral consolidation was observed in the high-resolution computed tomography (HRCT) and the patient developed respiratory failure during the follow-up. Meropenem treatment was started. Oxygen saturation gradually deteriorated, and the patient was intubated on the same day. Rasburicase and haemodialysis treatments were applied as the patient developed tumour lysis syndrome. Due to intense haemoptysis, 1 mg/kg methylprednisolone was administered. In the follow-up, an increase in blood sugar after steroids, up to 302 mg/dL, was observed. Posaconazole prophylaxis had to be interrupted after 5 days as the patient developed hyperbilirubinemia. Fever developed on the next day, and empirical caspofungin and teicoplanin were added to his treatment. No growth was detected in the tracheal specimens of the intubated patient.

The patient's fever had not improved 5 days after caspofungin treatment, and now there was a progressively advancing skin lesion on the left wing of the nose which was 8 × 6 cm and had a black necrotic appearance (Figure 1). A sampling of necrotic tissue was performed by the ear nose throat (ENT) department. Facial magnetic resonance imaging (MRI) revealed a density in the left wing of the nose that partially spread towards the front side of the face and was comprised of thickness of the soft tissue. No bone destruction was observed. Maxillofacial computed tomography (CT) showed borders that started on the side of the left nasal wing extending towards the front of the face, with a depth of up to 3 cm; and that invaded into the subcutaneous adipose tissue and cartilaginous tissue, also invading the maxillary bone process distally, including the frontal prominence of the maxillary sinus. Limited T1 and T2W hypointense mass lesions were observed in the region. Caspofungin treatment was replaced with amphotericin B liposomal complex, which was given at the rate of 3 mg/kg/day on the first day and 5 mg/kg/day on the following days. The patient underwent excision of the left wing of the nose with the support of the blood products provided.

Mucor was detected in the excision tissue using both pathological and microbiological investigation methods. Growth in the culture of the nasal biopsy specimen revealed mucor hyphal structures after lactophenol cotton blue (LPCB) staining (Figure 2). The patient died of progressive pneumonia and sepsis on the third post-operative day, and on the 18th day of chemotherapy.

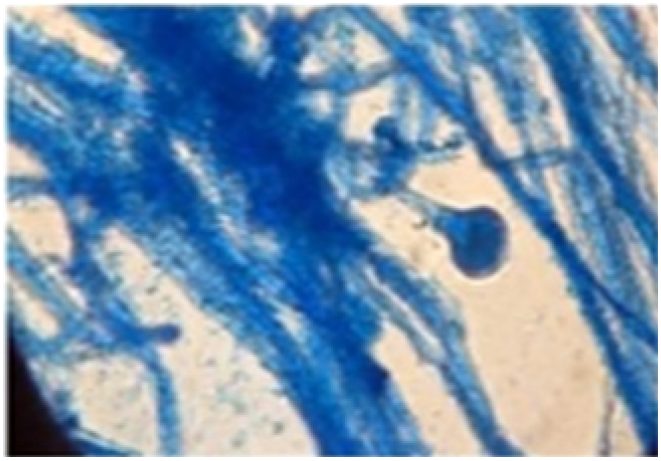
Discussion

Patients with diabetes mellitus, solid organ transplantation or hematopoietic stem cell transplantation, prolonged neutropenia, corticosteroid use, or malignancy, have a higher likelihood of developing mucormycosis. This is an invasive and opportunistic fungal infection with all-cause mortality rates between 40% and 80% depending on underlying conditions and the origin of the infection [10]. In developed countries, the most common underlying condition is hematological malignancies whereas in developing countries, the disease affects mostly diabetic or trauma patients [11]. In our case, the patient had both AML and diabetes, which are known risk factors for mucormycosis. When Mucorales spores enter the body through inhalation, they encounter the mono and polynuclear phagocytes which are the body's first defence mechanism. In healthy humans, mucor spores are killed by the phagocytes [12]. Histopathologically, thrombosis and tissue necrosis occur in the involvement of the internal elastic lamina of blood vessels. Local ischemia and susceptibility to infection begin due to peripheral vascular disease. Mucor spores may lead to thrombosis of the internal maxillary artery or descending palatine arteries, which then result in palatal and maxillary necrosis [13].

Davis *et al*. reported a case of a 46-year-old female with undiagnosed diabetes, coronavirus disease 2019 (COVID-19), and mucormycosis. The patient initially presented at two outside ophthalmology clinics due to right eye pain and was prescribed steroids. Laboratory results demonstrated leukocytosis, hyperglycemia, and a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test. Magnetic resonance imaging confirmed a diagnosis of mucormycosis, and the patient underwent surgery and began intravenous antifungal therapy [10].

Yong *et al.* reported four cases of mucormycosis precipitated by classical as well as atypical risk factors, with common sites of infection such as pulmonary and rhino-orbital, to rare manifestations such as peritoneal mucormycosis. Diagnoses were confirmed by either a histopathological sample or a positive culture. One of the four cases had concomitant positive culture and histopathology results [14].

Figure 2. A biopsy culture sample showing fungal hyphal structures stained with lactophenol cotton blue.



In our case, the patient with risk factors such as AML and diabetes mellitus died despite debridement and antifungal treatment.

Conclusions

Mucormycosis is a serious infection with high mortality. Therefore, it should be considered in the early stages of diagnosis of immunosuppressive patients with underlying disorders.

References

1. Walther G, Wagner L, Kurzai O (2019) Updates on the taxonomy of Mucorales with an emphasis on clinically important taxa. J Fungi (Basel) 5: 106. doi: 10.3390/jof5040106.
2. Skiada A, Pavleas I, Drogari-Apiranthitou M (2020) Epidemiology and diagnosis of mucormycosis: an update. J Fungi 6: 265. doi: 10.3390/jof6040265.
3. Jeong W, Keighley C, Wolfe R, Lee WL, Slavin MA, Kong DCM, Chen S C-A (2019) The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. Clin Microbiol Infect 25: 26–34. doi: 10.1016/j.cmi.2018.07.011.
4. Steinbrink JM, Miceli MH (2021) Mucormycosis. Infect Dis Clin North Am 35: 435–452. doi: 10.1016/j.idc.2021.03.009.
5. Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson JL (2022) Chapter 218. Mucormycosis. In Harrison's Principles of Internal Medicine, 21st edition. McGraw-Hill Education. 1680–1685.
6. Cag Y, Vahaboglu H (2020) Mucomycosis. Turkiye Klinikleri Infectious Diseases — Special Topics: Opportunisitc Fungal Infections. 13: 58–63.
7. Sun HY, Forrest G, Gupta KL, AguadoJM, Lortholary O, Julia MB, Safdar N, Patel R, Kusne S, Singh N (2010) Rhino-orbital-cerebral zygomycosis in solid organ transplant recipients. Transplantation 90: 85–92. doi: 10.1097/TP.0b013e3181dde8fc.

8. Akagun F, Sekercan O, Batmaz T, Bora F, Inci A, Fincancı M (2011) Rhinoorbital mucormycosis: palatal necrosis. Istanbul Med J 12: 96–100. [Article in Turkish]. doi: 10.5505/1304.8503.2011.32032.
9. Centers for Disease Control and Prevention (nd) Treatment of mucormycosis. Available: https://www.cdc.gov/mucormycosis/treatment/index.html#:. Accessed: 8 October 2024.
10. Davis K, Almog R, Peleg Y, Spiegelman L (2023) Case report of invasive mucormycosis in a COVID-19 positive and newly-diagnosed diabetic patient. J Educ Teach Emerg Med 8: V10–V13.
11. Skiada A, Lass-Floerl C, Klimko N, Ibrahim A, Roilides E, Petrikkos G (2018) Challenges in the diagnosis and treatment of mucormycosis. Med Mycol 56 Suppl 1: S93–S101. doi: 10.1093/mmy/myx101.
12. Theoharides CT (2018) Mold and immunity. Clin Ther 40: 882–884. doi: 10.1016/j.clinthera.2018.05.005.
13. Bouza E, Munoz P, Guinea J (2006) Mucormycosis: an emerging disease? Clin Microbiol Infect 12 Suppl 7: 7–23. doi: 10.1111/j.1469-0691.2006.01604.x.
14. Yong J, Chong KL, Gan WF, Zaidan NZ (2023) Mucormycosis: a case series. Cureus 15: e41375. doi: 10.7759/cureus.41375.

Corresponding author
Gulfem Ece, MD.
Izmir City Hospital, Department of Medical Microbiology, Izmir, Turkiye
Tel: 902329550500
Fax: 902329550500
Email:gulfem.ece@gmail.com

Conflict of interests: No conflict of interests is declared.