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A Rare Case of Invasive Mucormycosis in a Diabetic Patient Treated with a Short Course of Dexamethasone

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Data Interpretation D
Manuscript Preparation E
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Patient: Female, 74-year-old
Final Diagnosis: Mucormycosis
Symptoms: Altered mental status
Medication: —
Clinical Procedure: Central venous catheterization • debridement
Specialty: Infectious Diseases • General and Internal Medicine • Otolaryngology

Objective: Unusual clinical course
Background: Invasive mucormycosis is a rare, life-threatening infection that requires urgent medical management. Here we describe a patient who developed invasive mucormycosis after receiving only a short course of dexamethasone. The purpose is to highlight this atypical presentation of a rare disease.
Case Report: A 74-year-old woman with a medical history of diabetes mellitus (DM), hypertension, hyperlipidemia, and small cell lung cancer with metastasis to the brain presented to the Emergency Department with altered mental status and a hyperosmolar hyperglycemic state. Three weeks before, she had been diagnosed with DM (hemoglobin A1c [HbA1c] 6.5%) and was started on dexamethasone to treat cerebral edema. On admission, her HbA1c was 10.8%, although she had received only a short course of dexamethasone. Her physical exam was concerning for left eyelid swelling and ophthalmoplegia. Computed tomography of the head and neck revealed signs of left ocular proptosis and invasive rhinomaxillary fungal disease. The patient underwent urgent surgical debridement; subsequent magnetic resonance imaging revealed extensive fungal disease extending into her left inferior frontal lobe. A surgical pathology report was positive for *Rhizopus oryzae* and *Stenotrophomonas maltophilia*. Her blood cultures were positive for methicillin-susceptible *Staphylococcus aureus*. She was treated with antibiotics and amphotericin B. Her clinical course was complicated by hypokalemia. She eventually recovered and was discharged from the hospital.
Conclusions: This case highlights an atypical presentation of mucormycosis. Clinicians should remain vigilant for this rare complication of dexamethasone use even when the therapy is given for a short time.


Keywords: Amphotericin B • Dexamethasone • Diabetes Mellitus • Mucormycosis

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/932129>

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Background

Mucormycosis is an infection caused by fungi of the order Mucorales. Fungi of the family *Mucoraceae* and the genus *Rhizopus* are the most common causes of infection, although the genera *Absidia*, *Apophysomyces*, *Mucor*, and *Rhizomucor* all contain species that are isolated less frequently [1-3]. Humans most frequently acquire the infection by inhaling sporangiospores, but oral ingestion and traumatic inoculation also are possible [3]. The global incidence of mucormycosis is rising, primarily in patients with uncontrolled diabetes mellitus (DM), hematologic cancer, and who have received transplants [4]. The rhinocerebral form of mucormycosis is the most common disease seen in patients with DM [4]. Steroids are commonly-prescribed immunosuppressive medications and short courses of these drugs rarely are associated with the development of invasive mucormycosis [5,6].

Case Report

A 74-year-old woman with newly diagnosed DM and a history of hypertension, hyperlipidemia, and small cell lung cancer (SCLC) metastatic to the brain presented to the Emergency Department (ED) with lethargy and weakness that had significantly worsened over the past 2 days. Her cancer had been diagnosed 3 weeks before admission and was treated with gamma knife radiation therapy 1 week after that. She was taking 4 mg of dexamethasone twice a day to treat cerebral edema. Three weeks before admission, she had been diagnosed with DM and her hemoglobin A1c (HbA1C) was 6.5%. When she was admitted, however, her initial blood glucose level was >799 mg/dL and her HbA1c was 10.8% – a significant change

in a matter of weeks (Table 1). During a follow-up appointment with her oncologist several days before presenting to the ED, the patient's blood glucose level was noted to be elevated. She had no symptoms at that time and was advised to follow up with her primary care provider for optimization of her DM regimen. Before she could do that, however, she started to feel ill and went to the ED instead. She was admitted with an initial diagnosis of a hyperosmolar hyperglycemic state.

The patient's physical exam was significant for left eyelid swelling and erythema, which was concerning for preseptal cellulitis. She developed ophthalmoplegia and visual impairment in her left eye. Her mental status worsened and she had difficulty following commands. She received aggressive hydration with i.v. fluids and insulin to control her blood glucose levels. Then, she went into septic shock and was started on broad-spectrum antibiotics and vasopressors through a central venous catheter (Table 1).

The patient next was evaluated in the Medical Intensive Care Unit (ICU); however, because of her poor prognosis, she was not a candidate for ICU-level care. She was medically managed on the Inpatient Medicine Service for the duration of her admission.

A computed tomography scan of the patient's head and neck revealed signs of left ocular proptosis and invasive rhinomaxillary fungal disease (Figures 1, 2). She was started on amphotericin B and underwent urgent surgical debridement to remove the necrotic tissue. Magnetic resonance imaging of the head and neck subsequently was performed (Table 1) and revealed invasive fungal disease extending into the left inferior frontal lobe (Figure 3). After a multidisciplinary meeting with

Table 1. Clinical course.

Day	Event	Vital signs					BG	K	Mg	Ca	WBC
		T	HR	BP	RR	SpO ₂					
1	Admission	36.7	88	126/56	14	96	799	4.2	2.2	8.8	18.4
4	Vasopressors started (ICU consulted)	37	89	79/53	26	97	219	3.3	2.3	6.6	14.8
5	Debridement and amphotericin b started	37	90	99/63	25	94	116	3.3	2.2	7.0	15.5
19	Vasopressors stopped	37	77	121/69	19	93	93	3.2	2.0	6.5	10.2
25	Amphotericin B completed	36.8	102	134/70	17	94	91	3.1	1.6	7.1	13.1
26	Discharge	36.7	102	125/71	18	96	127	3.9	1.9	7.2	12.4

T – temperature in degrees Celsius; HR – heart rate per minute; BP – blood pressure in mm Hg; RR – respiratory rate per minute; SpO₂ – oxygen saturation in ambient air; BG – blood glucose in mg/dL (reference: 74-200 mg/dL); K – serum potassium in mmol/L (reference: 3.4-4.8 mmol/L); Mg – serum magnesium in mg/dL (reference: 1.6-2.2 mg/dL); Ca – serum calcium in mg/dL (reference: 8.2-10.1 mg/dL); WBC – white blood cells in K/ μ L (reference: 4.8-10.8 K/ μ L); ICU – Intensive Care Unit.



Figure 1. Axial computed tomography scan shows erosion of the medial wall of the left maxillary sinus and middle turbinate as well as asymmetric thickening and sclerosis of the left maxillary sinus walls.



Figure 2. Coronal computed tomography scan shows fluid levels in the left maxillary sinus, sinus cavity, and ethmoid air cells.

the patient's family, her healthcare agent declined further surgery, given the patient's current illness. Orbital exenteration and skull base surgery were offered, but the healthcare agent preferred conservative medical management instead because of the patient's poor long-term prognosis.

The surgical pathology report confirmed the presence of invasive mucormycosis (*R. oryzae*) as well as a concomitant infection with *S. maltophilia* (Figures 4-7) [7]. Her blood cultures grew methicillin-susceptible *S. aureus* (MSSA). She was treated

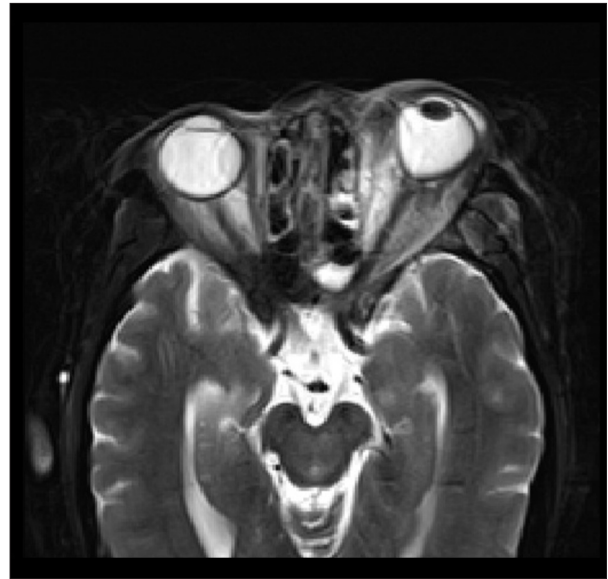


Figure 3. Axial magnetic resonance image performed after left inferior, middle, and superior turbinectomy; partial internal ethmoidectomy; and antrostomy. In the left globe, proptosis is visible and the posterior aspects are deformed because of tension from the optic nerve. The edema in the left orbit and the left inferior frontal lobe is compatible with extension of invasive fungal disease.

with liposomal amphotericin B for invasive fungal disease, ceftazolin for MSSA infection, and levofloxacin for *S. maltophilia*. The patient also developed a herpetic lesion, which resolved with valacyclovir. She remained on vasopressor support until hospital day 19. Her clinical course was complicated by the presence of electrolyte abnormalities – namely, hypokalemia – which were more pronounced after liposomal amphotericin B was started on hospital day 5. Her potassium level was 4.2 mmol/L, but after starting liposomal amphotericin B, her hypokalemia persisted (despite potassium supplementation and spironolactone once she was off vasopressor support) until she completed her course on hospital day 25. She was discharged the following day (Table 1). The patient was lost to follow-up because she declined appointments with her oncologist and the Infectious Disease Clinic.

Discussion

Invasive mucormycosis is a life-threatening condition that is associated with significant morbidity and mortality. Risk factors for acquiring it include uncontrolled DM (especially leading to diabetic ketoacidosis), use of corticosteroids, immunosuppressive therapy (such as for bone marrow and organ transplantation), neutropenia, cancer (especially hematological), and trauma and burns [2]. Mucormycosis is difficult to

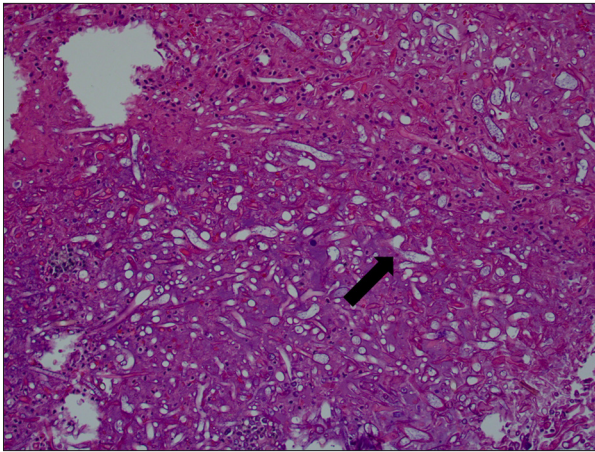


Figure 4. Slide stained with hematoxylin and eosin. Broad, disordered hyphae (arrow) are penetrating through the cell wall and but not into the structures [7].

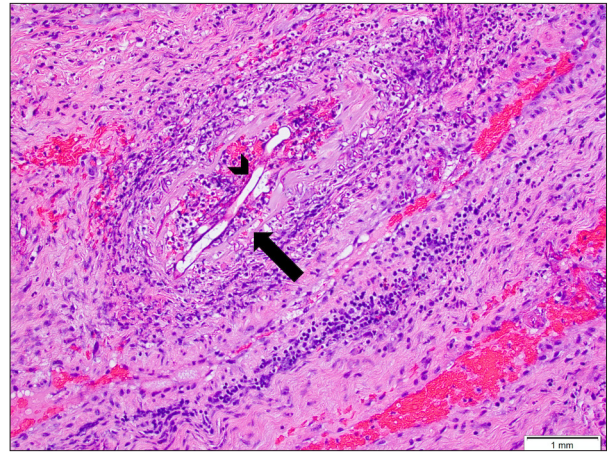


Figure 6. Slide stained with hematoxylin and eosin stain that shows angioinvasion of mucormycosis. Hyphae are seen invading the blood vessel wall (arrow) and the inside of the vessel lumen (arrowhead).

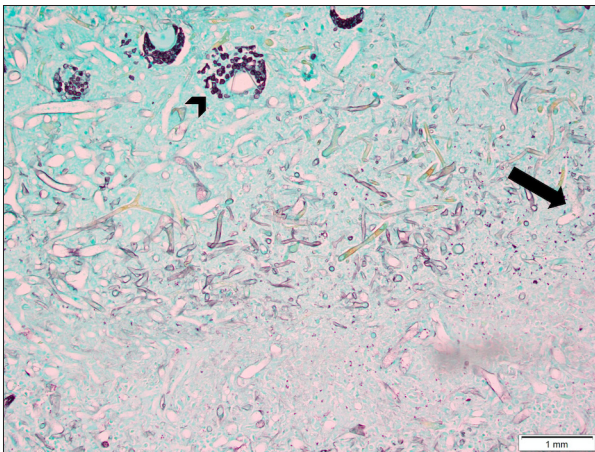


Figure 5. Slide stained with Grocott/Gomori methenamine silver (GMS). The spores (arrowhead) have a black color. Hyphae (arrow) often stain poorly with GMS and here they have a characteristic 90-degree branching pattern [7].

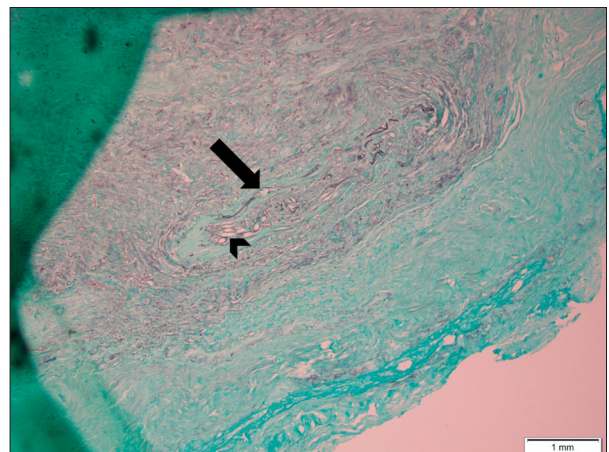


Figure 7. Slide stained with Grocott/Gomori methenamine silver that shows angioinvasion of mucormycosis. Hyphae are seen in the blood vessel wall (arrow) and inside the lumen (arrowhead).

diagnose, but early diagnosis and treatment are critical to patient outcome [8]. One study demonstrated that delaying treatment for 6 days from symptom onset is associated with an increase in 30-day mortality from 35% to 66% [8].

The mortality rate with localized cutaneous mucormycosis is 10% to 30%, whereas disseminated mucormycosis carries a much higher rate (50% to 90%), depending upon organ involvement [9-11]. One study comparing treatment modalities indicated that the lowest mortality rate was associated with amphotericin B plus surgery (18.8% to 43.7%) [12]. This was in comparison to surgery alone (38.5% to 60.9%) and amphotericin B alone (50% to 61.3%) [12]. As a result, early, aggressive surgical excision combined with systemic antifungal therapy is the mainstay of treatment [9,11,13,14]. Ideally, surgery

should be performed before fungus dissemination, although it is beneficial even after fungus spread [9,11,13,14]. Recently, endoscopic sinus surgery for radical resection has been found to result in better local control of the disease (with reduced operative morbidity) compared to the classical transcranial approach [15,16].

Our patient received dexamethasone therapy for cerebral edema caused by metastatic SCLC, but it was given for only 3 weeks before her HbA1c level rapidly increased (6.5% to 10.8%). That presentation is rare, as most cases of invasive mucormycosis are in patients who have received steroids for a longer time [5,6]. Steroid use in conjunction with the hyperglycemic and acidic state found in uncontrolled DM causes phagocytic impairment – the primary defense mechanism against

mucormycosis [2]. Mucormycosis causes angioinvasion, which leads to tissue necrosis, thrombosis, and a disseminated infection (Figures 6, 7) [2]. Thrombosis and tissue necrosis subsequently prevent leukocytes and other immune-regulating cells from arriving via the bloodstream to control the infection [2]. Heme supplied by red blood cells is thought to be a substrate leading to increased pathogenicity [2]. The rich blood supply to the head and neck allows the fungus to cause rhinocerebral mucormycosis – the most common site of infection [17].

Treatment of invasive mucormycosis involves the use of antifungals, with liposomal amphotericin B being the drug of choice [18]. It is well-known to cause renal impairment and electrolyte abnormalities such as the hypokalemia, which developed in our patient [19]. Early potassium supplementation (within 2 days of the initiation of liposomal amphotericin B) reduces the risk of liposomal amphotericin B-induced hypokalemia [19].

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Conclusions

In summary, invasive mucormycosis is a rare, life-threatening infection most commonly seen in patients with depressed immunity. Our patient's history of DM, cancer, and dexamethasone use put her at risk for it because of immunosuppression; however, her presentation is rare, as she only received dexamethasone for a brief time. Liposomal amphotericin B is the mainstay of therapy for invasive mucormycosis, along with surgical intervention, and clinicians should remain vigilant for complications associated with it. A multidisciplinary approach is suggested for successful treatment of this devastating disease.

Conflict of Interest

None.

Declaration of Figures Authenticity

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