A disfiguring and fatal case of mucormycosis after dexamethasone treatment for a COVID-19 infection

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Abstract

This case report describes a patient with uncontrolled type 2 diabetes mellitus who received steroids for an outpatient infection of COVID-19. The steroid course combined with his acute illness likely contributed to his development of extremely high blood sugar levels (790 mg/dL) and subsequent hyperosmolar hyperglycemic syndrome. In this compromised state, he contracted invasive mucormycosis of the right sinuses and right orbit. This fungal infection caused him to lose his eye and, later, his life. Prescribing systemic steroids has many potential risks. Providers must be careful to use them only when absolutely indicated, especially in patients who are vulnerable to complications, such as those with uncontrolled type 2 diabetes. This case is a grim example of the dangers that can occur with systemic steroid use.

Keywords: Mucormycosis, SARS-COV-2, *Rhizopus*, diabetic ketoacidosis, dexamethasone

Introduction

Mucormycosis is a type of acute invasive fungal rhinosinusitis (AIFR) and is a potentially devastating and deadly infection.[1] Caused by molds found naturally in the environment, this disease is classically found in people who are immunocompromised, such as diabetics with poor glucose control or those in diabetic ketoacidosis (DKA).[1,2] The fungus *Rhizopus oryzae* is the most common cause of mucormycosis, accounting for about 70% of cases.[3] The fungus invades through neural and vascular tissue, causing thrombosis of blood vessels. A sino-orbital infection rapidly spreads, invading into sinuses, the orbit, and the brain. Treatment includes surgical intervention, antifungal medications, and treatment of any underlying predisposing conditions.[1]

Treatment for symptomatic COVID-19 infections often includes steroids, such as dexamethasone, which have been shown to increase ventilator-free days.[4] However, no benefit has been shown in patients who are not hospitalized and don't require supplemental oxygen.[5] We present a case in which a diabetic patient had a SARS-CoV-2 infection and unnecessary treatment with dexamethasone, which led to a *Rhizopus* infection, a disfiguring case of AIFR, and eventual death.

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Case

A 60-year-old man with a past medical history that included type 2 diabetes mellitus and stage IV chronic kidney disease presented to an urgent care clinic with a SARS-COV-2 infection. He was prescribed doxycycline, dexamethasone, inhaled budesonide, and molnupiravir. A week later, he presented to the Emergency Department with altered mental status and decreased vision in the right eye. His blood glucose was 790 mg/dL, and he had negative ketones, suggesting hyperosmolar hyperglycemic syndrome (HHS). His right eye was swollen, painful, and unable to open. He was admitted to the ICU for stabilization.

On hospital day 3, computed tomography (CT) of his orbits showed pre-septal cellulitis of the right eye,

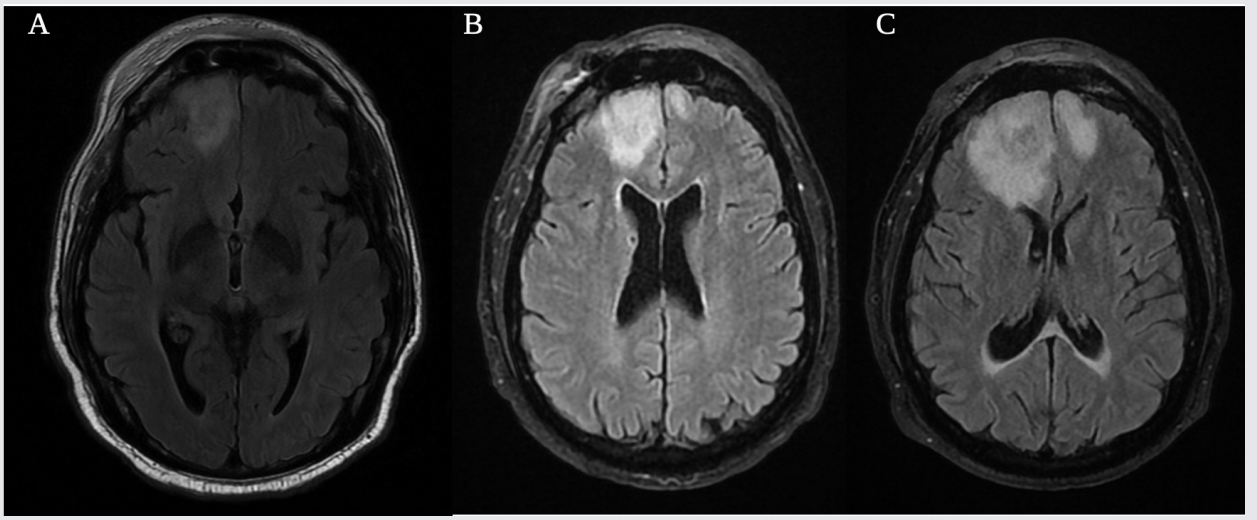

Figure 1. MRI images showing progression of the frontal lobe lesion. A: Right frontal lobe lesion on initial MRI. **B:** (7 days after A) Left frontal lobe extension and right frontal lobe progression. **C:** (22 days after B) Continued progression of right and left frontal lobe lesions.

right maxillary sinusitis, and a 2.5 cm lesion in the right frontal lobe of the brain. Magnetic resonance imaging (MRI) (Figure 1A) suggested a possible infarct, abscess, or mass. The next day, an infectious disease specialist noted that the patient had a dusky, early necrotic appearance of the tissues near the right medial canthus in addition to severe edema, erythema, and pain surrounding the right eye. He was started on isavuconazole due to concern about amphotericin's nephrotoxicity. The otolaryngology (ENT) surgeon collected sputum cultures and performed an anterior rhinoscopy, which showed only purulent mucous and no black eschars. At that time, there was no destruction nor necrosis of the maxillary, ethmoid, sphenoid, or frontal sinuses. The ophthalmology service was consulted for evaluation of his presumed pre-septal cellulitis.

Initial ophthalmic exam of the right eye (Figure 2A) showed a visual acuity (VA) of light perception (LP), a closed erythematous lid with a darker medial canthal area, minimal movement from primary gaze, no relative afferent pupillary defect, 360 bulbar chemosis, nerve pallor, and a yellow-white spherical shape in the vitreous near the superior arcade. Two days after the original orbital CT, repeat CT imaging showed worsening right orbital cellulitis with post-septal extension of the inflammation, right maxillary and ethmoid sinusitis, and the persistent lesion in the right frontal lobe of the brain. That same day, the patient was taken to the operating room with ENT for sinus lavage, where he was found to have large eschars in the right middle meatus and right maxillary sinus. Samples were sent to pathology, which showed angioinvasive fungal hyphae with morphological features consistent with mucormycosis. The culture grew *Rhizopus oryzae.*

The oculoplastics service took the patient back to the OR to debride the orbit. His VA was no light perception (NLP), and the medial canthus was necrotic (Figure 2B). The medial canthus and medial 1/3 of the eyelid were debrided. These specimens were sent as frozen sections to pathology and were confirmed as active mucormycosis. The medial orbital tissue of the right eye was gray, avascular, and necrotic, indicating that the infection extended into the globe. After obtaining consent from the medical power of attorney, a right orbital exenteration was performed (Figure 2C). The ENT service performed right frontal sinusotomy, right maxillary sinusotomy, right total ethmoidectomy, right inferior turbinectomy, and right nasal cavity debridement. Unfortunately, the final biopsy of the most proximal apex orbital tissue was positive for mucormycosis. All other external tissue margins were clear of active disease before closing.

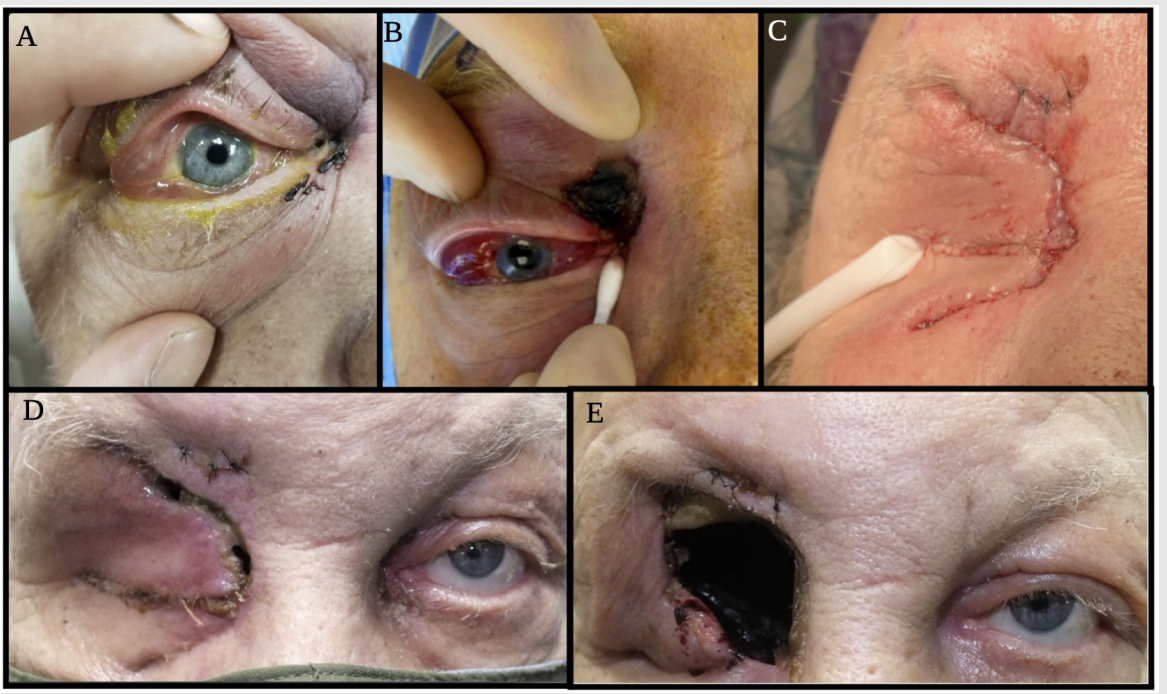

Figure 2. Progression of mucormycosis infection of the right orbit. A: Early necrotic appearance of the right medial canthus. **B:** Eschar of the right medial canthus prior to exenteration. **C:** Right orbit after exenteration (lateral drain in place). **D:** Partial medial dehiscence of the right orbital skin closure with mucopurulent discharge. **E:** Near-complete dehiscence of the right orbital skin closure with black eschar filling the orbit.

The patient was started on IV amphotericin B in addition to isavuconazole; however, the amphotericin was discontinued after four days due to decreasing kidney function. A repeat MRI showed progression of the right frontal lobe lesion and extension into the left frontal lobe (Figure 1B). The patient refused further interventions and asked to be discharged on isavuconazole. It was explained that mucormycosis needs aggressive debridement, but he was firm in his decision.

The patient presented to clinic 11 days later. Due to lack of insurance coverage, he had never started isavuconazole. He had two areas of dehiscence of his right orbit with mucopurulent discharge (Figure 2D). He was re-admitted and restarted on Amphotericin B. An MRI showed further progression of right and left frontal lobe lesions (Figure 1C). Again, he refused surgical intervention and asked to be discharged on posaconazole.

Two weeks after discharge, the patient returned to clinic. The view through the partial dehiscence of the right orbit showed that it was filled with black eschar (Figure 2E). Five months after initial presentation, the patient died of complications from his fungal infection.

Discussion

Phagocytes have been implicated in preventing a pathogenic infection. If phagocytic function is impaired, then there is an increased risk for a pathogenic mucormycosis infection.[3] Corticosteroids are known immunosuppressors, and they affect the function of phagocytes.[6] In addition, almost one third of patients who receive glucocorticoid therapy will develop hyperglycemia.[6] Phagocytes become dysfunctional with hyperglycemia and acidosis, which causes a deficit in chemotaxis, oxidative intracellular killing, and non-oxidative intracellular killing.[3]

While early studies indicated that an ambulatory multi-drug therapy of antibiotics, corticosteroids, and an antiviral for COVID-19 was safe,[7] the CDC now recommends against the use of systemic corticosteroids, such as dexamethasone, for COVID-19 patients who do not require hospitalization or supplemental oxygen.[5] This case underlines that recommendation by illustrating the inherent risk of using these drugs, especially when other risk factors for phagocytic suppression exist.

Treatment for mucormycosis involves intravenous antifungal therapy, treatment of any pre-disposing state, and aggressive surgical debridement.[1] This patient may have had a poorer prognosis due to the inadequate duration of antifungal therapy he received. Liposomal amphotericin B therapy improves survival,[1] and first-line antifungal treatment involves IV liposomal amphotericin B for a minimum of 6–8 weeks, until complete resolution of the infection occurs on imaging and clinical exam.[8] Posaconazole has been successfully used to complete therapy after initial amphotericin treatment, and isavuconazole has been shown to be comparable to liposomal amphotericin B.[8] However, both alternatives have only been studied when given continuously after diagnosis.

Surgical debridement is another crucial part of management that improves survival,[1] and in combination with amphotericin B therapy is more effective than amphotericin therapy alone.[8] This case shows the unfortunate natural progression of mucormycosis when subsequent surgical debridement is not performed. It is important to note that Turner et al. demonstrated that orbital exenteration does not correlate with decreased mortality. While it may be necessary for patients with NLP and clearly necrotic orbital tissue, patients who still have visual potential should be counseled that exenteration may not improve their rate of survival.[9]

Patient consent

Patient's surviving spouse consented to this case study on 10/24/22 in writing.

Acknowledgment and Disclosure

We would like to acknowledge the family of the patient described above who so graciously gave their consent to share this case.

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