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Case Report
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Rhinocerebral and Pulmonary Mucormycosis Secondary to Uncontrolled Type II Diabetes Mellitus

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Abstract

Mucormycosis (zygomycosis) is a fungal infection in humans that can present insidiously, advance quickly and cause rapid death. Poorly controlled diabetes is one of the major risk factors. We present the case of a 60-year-old male with uncontrolled diabetes who presented at a community hospital with right facial swelling, sudden vision loss in left eye and recent outpatient treatment of bacterial sinusitis. Physical examination and imaging were consistent with rhinocerebral and pulmonary mucormycosis. Patient received broad spectrum antimicrobials. Ophthalmologist, ENT and ID specialists were consulted. Transfer process to Higher Level of Care (HLOC) was initiated however it was delayed due to lack of bed availability. Following transfer to HLOC and after undergoing continued medical treatment and multiple surgical debridements, patient subsequently was transitioned to comfort-care and on day 37, patient expired. These findings demonstrate the importance of timely diagnosis and treatment of mucormycosis to improve associated high morbidity and mortality.

Introduction

Mucormycosis (zygomycosis) is a type of infection in humans that is caused by fungi of the class zygomycetes (orders Mucorales and Entomophthorales) and has a high mortality rate [1]. Cases of mucormycosis infections are rarely reported in community hospitals in the United States. Mucormycosis infection is contracted through inhaling sporangiospores, ingesting contaminated foods or invasion of the organism via trauma [2,3]. Most common clinical manifestation of mucormycosis is angioinvasion leading to thrombosis and ultimately tissue necrosis [4]. Invasive mucormycosis is categorized as one of the following: Rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated and uncommon rare forms [5-7]. Major risk factors include uncontrolled diabetes mellitus, diabetic ketoacidosis, glucocorticoid dependence, blood related malignancies, hematopoietic cell as well as solid transplantations, iron overload, intravenous drug use, immunocompromised status, major trauma such as burn injuries and malnutrition status [8-10]. Mucormycosis can be rapidly progressive and thus it is important to correctly recognize the symptoms and diagnose at early stage to ensure timely medical treatment. In this case report, we will discuss rhinocerebral and pulmonary mucormycosis in a patient with poorly controlled Type II Diabetes.

Case Presentation

A 60-year old Caucasian male with a past medical history of uncontrolled type II diabetes mellitus, atrial fibrillation presented to the emergency department for a month history of right facial swelling and pain. The patient also endorsed left eye blindness and epistaxis. The patient initially was seen by his primary care physician two-week prior to the admission where he was treated with a two-week course of augment in for acute sinusitis, however, the symptoms had progressively worsened. The pain was mainly located in the bilateral frontal and maxillary sinus regions. Patient denied fever, chills, chest pain, shortness of breath, or palpitation. On examination, vital signs were significant for hypertension with blood pressure of 155/85, otherwise unremarkable. The patient was in acute distress. He had blindness in the left eye with ptosis, and normal vision in the right eye. Pupils were reactive. Eye movements were intact. There was no extraocular motion tenderness. Conjunctivae were normal. Patient had swelling, erythema, and tenderness over the right maxillary sinus region. Examination of the oral cavity showed a 2 cm × 1 cm dark black mucosa over the hard palate, posterior to the incisors. A complete blood cell count was within normal limits. The results of basic metabolic panel were significant for glucose of 265 and Hemoglobin A1c of 14. Computed Tomography (CT) scan of the maxillofacial area showed mild soft tissue swelling and subcutaneous

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stranding right facial soft tissues compatible with cellulitis. CT head showed extensive fluid and mucosal thickening seen in the paranasal sinuses. MRI orbits was concerning for mild enhancement of the inferior right orbit and clinoid segment of the left ophthalmic nerve. MRA confirmed no flow signal in left ophthalmic artery, consistent with ophthalmic artery occlusion. CT chest showed lingula nodule and a dense rim with a central ground-glass opacity in the reverse halo sign consistent with pulmonary mucormycosis. Amphotericin B was empirically started for suspected pulmonary and rhinocerebral mucormycosis. Urgent bilateral endoscopic sinus surgery with image guidance, tubectomy, and septectomy followed by video-assisted thoracoscopic surgery left upper lobectomy were performed. Nasal endoscopy showed diffuse left sided edema with extensive secretions obscuring full visualization and right nasal cavity with necrosis of side wall extending up to middle turbinate. Pathology from sinuses and pulmonary lesion were consistent with mucormycosis. Culture from palata and left sinus sphenoid lesion was positive for *Rhizopus*, *Candida glabrata*, *Acinetobacter baumannii*, and *Aspergillus niger*. Micafungin was added to amphotericin B for *Aspergillus* and *Candida glabrata*. Despite the treatment, patient developed septic shock and acute respiratory failure, and eventually deceased.

Discussion

The true incidence of mucormycosis infections is not known as it is not a reportable disease; however, approximately 500 cases occur in the Unites States every year [11]. The incidence of mucormycosis has been rising due to increase in the number of patients with immunocompromised status [12,13]. It is also alarming that in 2021, mucormycosis or "black fungus" infections have been increasingly reported among diabetic and immunocompromised patients recovering from COVID-19 infections in countries including India, Pakistan and Russia [14]. Among diabetics, such as our patient, rhinocerebral mucormycosis is the most common form [15]. It manifests in a susceptible host when inhaled spores germinate in the nasal sinuses and rapidly multiply as a septate or with few septate hypha leading to invasion of blood vessels, tissue, cartilage and bones and eventually leading its way up to the eye orbits or ethmoid sinuses then to the meninges and brain [16]. This can eventually lead to hemorrhage, thrombosis and infarcts as was evident in this patient. In early stage of the disease, physical examination may reveal facial/ocular pain and nasal blockage with or without discharge whereas later manifestations of the disease often include proptosis and necrotic lesions or eschar on the hard palate, nasal mucosa and/or nasal turbinates as well as ophthalmoplegia, vision loss and even hemiparesis if carotid artery or jugular vein is thrombosed [17]. Differential diagnosis includes periorbital or orbital cellulitis, orbital tumor, cavernous sinus thrombosis, aspergillosis, Anthrax and Wegener granulomatosis. Suspicion of rhinocerebral mucormycosis should initially prompt obtaining biopsy and culture of the necrotic tissue and diagnostic imaging such as CT or MRI imaging with contrast of the paranasal sinuses to evaluate extension into orbit, cavernous sinus and central nervous system [18]. Tissue biopsy may show hypha with right angle branching, commonly irregularly shaped near blood vessels [18]. Cultures may remain negative even with microscopic evidence of the fungus [16,18]. CT scan shows mucosa with edema, fluid accumulation in ethmoid sinuses, periorbital tissue, and bone destruction. MRI shows intradural/intracranial invasion, cavernous sinus thrombosis or involvement of the internal carotid artery [19]. Empiric therapy with intravenous amphotericin B should be started while waiting for results, underlying ketoacidosis if present should be corrected and surgical debridement of infected tissues and drainage of the sinuses involved are required to achieve disease control [18,19]. If orbital involvement is evident, lamina papyracea of the eye must be removed and if intracranial tissue is involved, treatment includes burr hole and aspiration of cerebral abscess and possible craniofacial resection or debulking [19]. In addition to rhinocerebral mucormycosis, our patient was also found to have pulmonary involvement. Unfortunately, the mortality rate of pulmonary mucormycosis is approximately 90% and higher than that of rhinocerebral mucormycosis [20]. Pulmonary mucormycosis is more common among neutropenic patients with malignancy undergoing chemotherapy treatment and patients who underwent Hematopoietic Stem Cell Transplantation (HSCT) and developed graft versus host disease [21]. Clinical features of pulmonary mucormycosis are often unclear and similar to that of pulmonary aspergillosis [21]. Common symptoms include persistent high-grade fever that does not respond to broad spectrum antibiotics and dry cough, and later in the process, development of malaise, pleuritic chest pain and hemoptysis [4,21]. Differential diagnoses include lung abscess, pulmonary embolism, pulmonary aspergillosis or candidiasis, tuberculosis, neoplasm, and echinococcal cysts [21]. Choice of diagnostic modality is CT chest with contrast which often reveals a "halo" sign (opacification around pulmonary mass) and "air crescent" sign (air between parenchymal lesion and normal tissue of lung) [22]. Diagnosis is confirmed by evaluation of trans-bronchial biopsy *via* bronchoscopy [22]. Other techniques that can also be employed include surgical removal, open lung biopsy, transthoracic needle aspiration or bronchoalveolar lavage [22]. If presence of pulmonary lesion is localized, surgical debridement or lobectomy is an option [21,23]. However, pulmonary mucormycosis often manifests as multifocal lesions and surgery is not feasible [24]. Similar to other forms of mucormycosis, treatment of choice is the antifungal, amphotericin B, however, other antifungals such as isavuconazole and less preferably posaconazole can be used in patients who cannot tolerate amphotericin B [24].

Conclusion

In this case report, our patient was initially misdiagnosed with acute bacterial sinusitis in an outpatient setting leading to delay in presenting to the hospital and correct diagnosis. Despite initiation of appropriate treatment at the community hospital setting, transfer to higher level of care and multiple surgeries, patient eventually expired. It is thus important to timely diagnose rhinocerebral and pulmonary mucormycosis. Sinusitis symptoms in a poorly controlled diabetic patient should raise strong suspicion for possible mucormycosis and requires thorough history and physical examination and if diagnosed, prompt hospitalization. In conclusion, it is important for health care providers to educate patients about complications of uncontrolled diabetes and optimize diabetes treatment to avoid this devastating disease.

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