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Case Report

Rhinocerebral Mucormycosis Case Report and Brief Review of the Literature

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Abstract

The purpose of this paper is to present a case report of rhinocerebral mucormycosis in the setting of uncontrolled diabetes mellitus in which the patient underwent aggressive surgical and medical treatment. The outcome of the case was a success with the patient surviving despite having intracranial involvement which was left untouched. In addition to presenting the case, we will review the literature in regards to invasive fungal infections of the maxillofacial region, its various presentations, therapeutic modalities, and outcomes of treatment. Our goal is to share our experience and provide a review of literature to help provide a foundation of knowledge upon which clinicians can identify and rapidly treat maxillofacial cases of mucormycosis.

Introduction

Mucormycosis is a rapidly progressing fungal infection caused by filamentous fungi in the Mucoraceae family and is frequently seen in diabetic and immunocompromised patients. Mucormycosis is categorized as rhinocerebral, pulmonary, cutaneous, gastrointestinal or disseminated, depending on organ involvement; the most common form is rhinocerebral (39%). This form may be divided into subtypes based on which tissues are affected: rhinonasal, rhinoorbital or rhinoorbitocerebral [1]. Mucorales with 7 genera: *Rhizopus*, *Mucor*, *Absidia*, *Saksenaea*, *Rhizomucor*, *Apophysomyces*, and *Cunninghamella* are documented to be pathogenic organisms that produce invasive disease in humans, with the most common causative agent being of the *rhizopus* species [2]. Patients with poorly controlled diabetes and ketoacidosis are at high risk of developing rhinocerebral mucormycosis, with systemic acidosis creating an ideal environment for the growth of *Rhizopus*. However initial presentation of rhinocerebral mucormycosis infection can often appear non-specific making correct diagnosis extremely difficult until the disease has caused significant morbidity since it is an aggressive fungal invasion of the paranasal sinuses, orbit, hard palate and brain [3, 4]. Economopoulou et al. cited the following signs and symptoms of rhinocerebral mucormycosis: clinical signs include bloody nasal secretion; facial pain; perinasal swelling; black necrotic eschar in the nasal septum and turbinate bones, with perforations; oral ulcers with bone denudation. Radiographic signs include sinus opacification without the presence of fluid; nodular thickening of the sinus lining; focal bone destruction of the sinus walls. The picture initially resembles sinusitis, a reason for concern about sinusitis occurring in diabetic or immunosuppressed patients [5].

A thorough knowledge of changes in trends of epidemiology and behavior of this invasive fungal infection is particularly important while devising effective diagnostic and therapeutic strategies [6]. The early diagnosis and treatment of rhinocerebral mucormycosis is paramount to decreasing morbidity and mortality. The treatment of rhinocerebral mucormycosis commonly involves aggressive surgical debridement and systemic antifungal therapy, along with correction of underlying metabolic abnormalities and reversion of immunocompromised states, when possible [7]. It is paramount that any surgical specialist managing maladies of the head and neck region have a clear understanding of this disease with mindfulness for early detection and aggressive intervention. Immunocompromised individuals, especially those who are diabetic, with signs of progressive sinus disease must be treated expeditiously with a "surgery first and medication second" approach.Traditional teaching encourages aggressive surgical resection until viable, bleeding tissue is encountered. This has often lead to orbital exenteration, skull base resection, and cerebral debridement due to the characteristically rapid involvement of these structures [8]. We present a successfully treated case of rhinocerebral mucormycosis that was treated aggressively with surgical and medical therapy. The case at hand, interestingly, demonstrated intracranial involvement of the dura mater, yet despite this finding the patient survived.

Case Details

45 y.o. hispanic male with medical history of uncontrolled type 2 diabetes who presented to our hospital (Community Regional Medical Center in Fresno, CA) with chief complaint of right eye swelling and pain of approximately 1-week in duration and subsequently found to be in Diabetic Ketoacidosis (DKA). The patient reported recent upper respiratory infection a week prior to eye swelling. The patient went to be seen, by an outpatient clinic, after he developed eye swelling where he was prescribed Keflex (500mg, 4 times a day) and Tobramycin eye drops (0.3%,1 drop every 4 hours). According to his report there was resolution of respiratory infection, however his eye swelling remained unchanged. No COVID-19 testing was performed because this case occurred in 2017 and predates the COVID-19 pandemic which saw wide spread PCR testing become standard of care with upper respiratory infections. With the continued right eye swelling, progressively worsening vision, and mild bleeding from the right nasal cavity, our patient decided to seek further medical attention at the hospital. On physical exam, the patient was noted to have significant right mid-facial swelling with severe induration and erythema over cheek and malar region. He was noted to have a proptotic right eye with severe periorbital edema and 1x1 inch gray patch of necrotic appearing skin along medial upper/lower eyelid (Figure 1). Mild oozing of exudate from the region was also documented. Further orbital examination showed the patient was unable to open the right eye and ophthalmoplegia was evident. Although light perception from the right eye was intact there was complete loss of visual acuity. The left eye was noted to have 20/200 vision. Dried heme present in the right nasal cavity resulted in partial obstruction of airflow.

Additionally, the right upper lip was swollen. Intraorally a necrotic appearing 1x1 inch of tissue in the right posterior palate could be appreciated (Figure 2).

Figure 1: Patient initial presentation to CRMC ED.

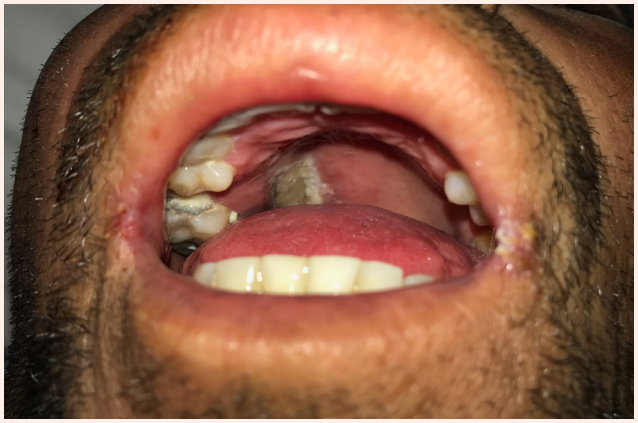

Figure 2: Necrotic palatal region.

Laboratory results on admission (day 0) showed an elevated white cell count 16.3 x 10^9/uL, B-Hydroxybutyrate level of 57.9 (0.2 - 2.8 mg/dL), blood glucose of 460 mg/dL, hemoglobin A1C greater than 15%, and anion gap of 27. Our patient was immediately started on DKA protocol with IV fluids and supplemental dosing of potassium (K) prior to insulin drip. An urgent computed tomography scan (CT) of the sinus (figure 3) showed findings compatible with pre- and post-septal cellulitis of the right orbit with marked proptosis, as well as tenting in the posterior globe with straightened appearance of the right optic nerve in addition to extensive paranasal sinus disease on the right side.

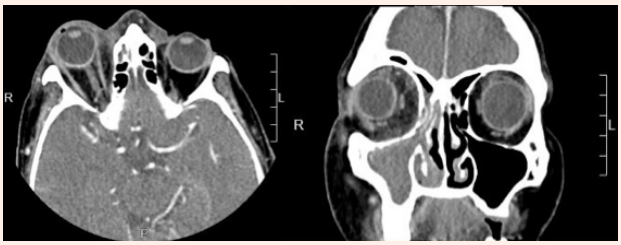

Figure 3: CT sinus on initial presentation.

Ophthalmology and Oral Maxillofacial Surgery (OMFS) teams were consulted (day 1) for surgical interventions. Patient was taken to operating room by OMFS for an open and endoscopic surgical debridement of right periorbital skin, nasal cavity, maxillary sinus, and palatal lesion (Figures 4 & 5). He was then empirically started on intravenous liposomal Amphotericin B (5mg/kg daily) coupled with Vancomycin (initial dose 1g) and Zosyn (piperacillin-tazobactam ; initial dose 3.375g) for both fungal and bacterial coverage. Vancomycin remained a part of treatment for 30 days (total dose of 28.25g), while Zosyn was discontinued after 16 days (total dose 60.75g). In regards to his DKA, his anion gap had closed and acidosis improved. He was started on 20u of Lantus and placed on a sliding scale of regular insulin with an initial goal of 180-220mg/dL. The patient was taken to the operating room (day 2) for further debridement of necrotic margins following the histopatholgic confirmation, using GMS (Gomori Methanamine Silver) stains, of fungal hyphae consistent with that of invasive mucormycosis (Figures 6 & 7). Vision continued to worsen in the left eye (now 20/400) while the right eye continued to deteriorate further.

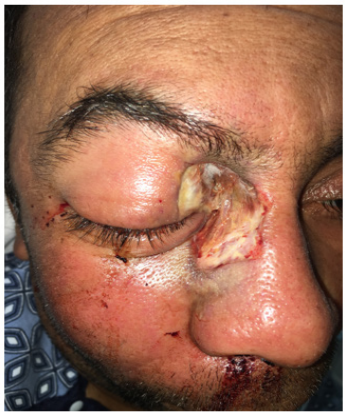

Figure 4: Initial layer of necrotic skin removed prior to surgery.

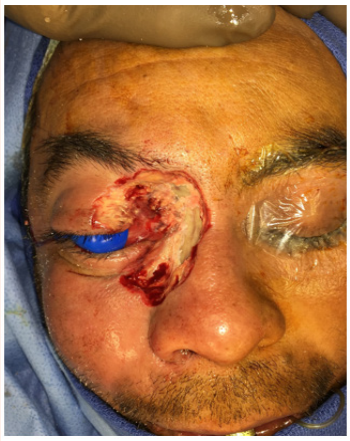

Figure 5: Day 1 surgical debridement.

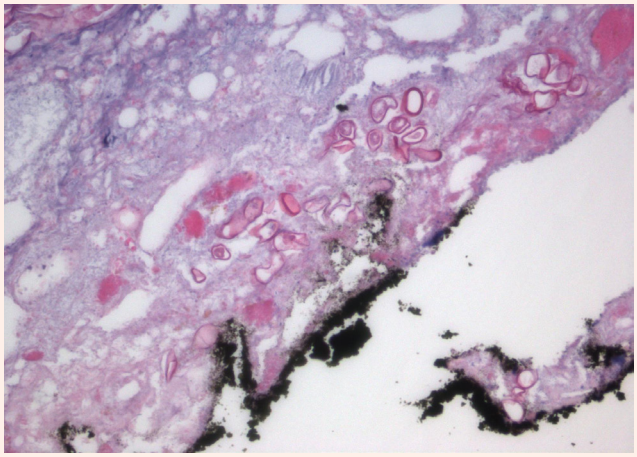

Figure 6: Mucormycosis fungal hyphae elements seen on GMS stain.

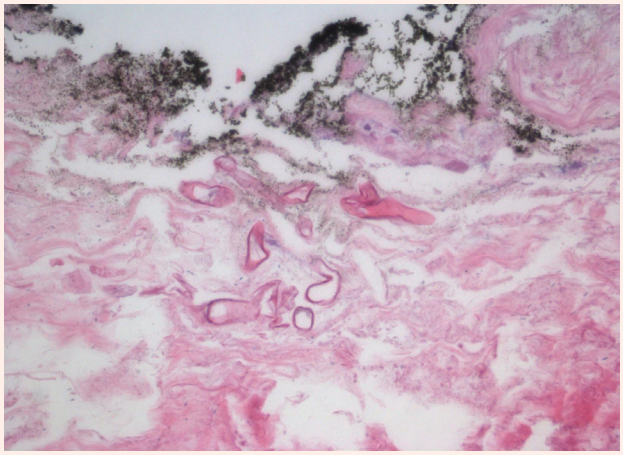

Figure 7: Mucormycosis fungal hyphae elements, detailed view, seen on GMS stain.

Follow up Magnetic Resonance Imaging (MRI) on day three showed ongoing inflammatory process persistently seen within the intra and extraconal space with tenting of the posterior choroid, deformity of the optic globe, straightening of the optic nerve, and some meningeal enhancement within the right middle cranial fossa without definite collection (Figure 8). With those findings on day three, Ophthalmology service recommended immediate exenteration of the right orbit to avoid mortality for patient. Knowing that our patient would need to be taken to the operating room for sequential debridements an elective tracheostomy was planned. As planned the patient was taken to operating room by OMFS team for tracheostomy, exenteration of the right orbit, and surgical debridement of the right paranasal sinuses (Figure 9). For next few days, the patient underwent daily debridements of the right orbit and paranasal sinuses with washout of the wound using a mixture of betadine/hydrogen peroxide solution. Packing of the right orbital region was done with kerlix soaked in Vashe solution (hypochlorous acid-HClO). To help maintain nutrition during this time, the patient also had an open gastrostomy tube placement by general surgery.

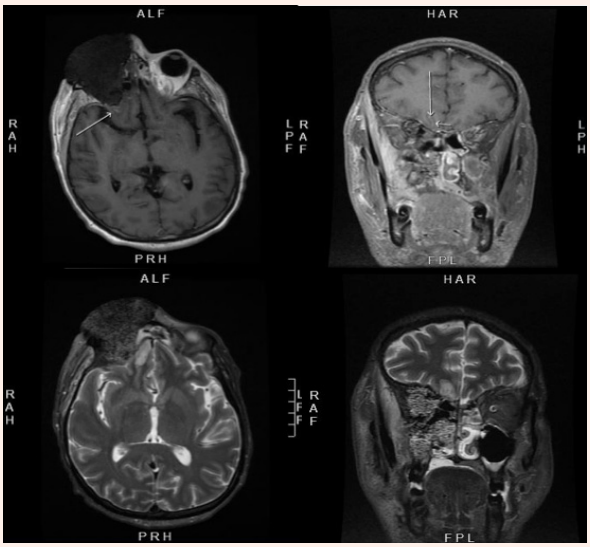

Figure 8: Day 3 MRI with contrast T1 (top) and T2 (bottom).

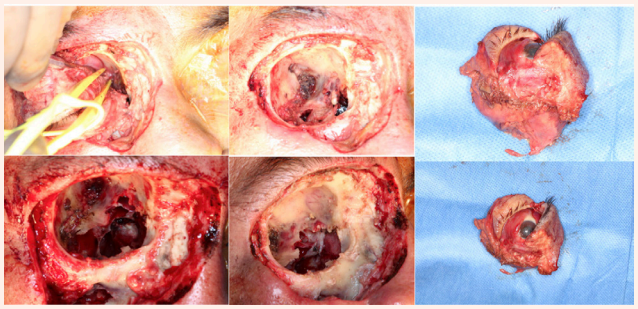

Figure 9: Exenteration and debridement of right eye.

Figure 10: One day status post exenteration and debridement hyphae growth can be seen.

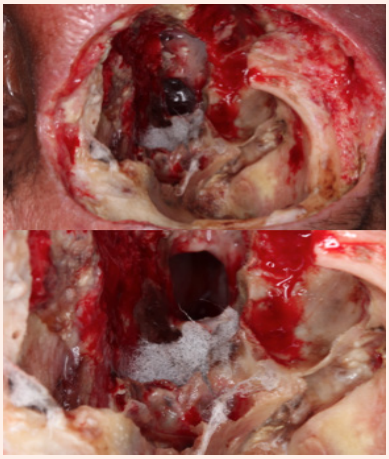

Figure 11: Hyphae growth.

Despite MRI studies which continued to show abnormal enhancement along the right middle cranial fossa along the right cavernous sinus (week 1) (Figure 12) and abnormal enhancement involving the right middle and anterior cranial fossae with nodular enhancement and involvement of the right inferior frontal lobe measuring up to 18 mm in craniocaudal dimension and right anterior temporal lobe (week 2), our patient continued to remain stable without any deterioration of Glasgow Coma Scale (GCS). Surgical debridement by OMFS had continued to the base of skull, orbital apex, and posterior wall of frontal sinus and further debridement required the expertise of neurosurgery. Neurosurgery was consulted and they recommended continual medical management of the patient as the debridement and resection of the temporal lobe involved would be a terminal surgery for the patient. Infectious disease recommended continuing IV amphotericin B with addition of Caspofungin (50 mg daily).

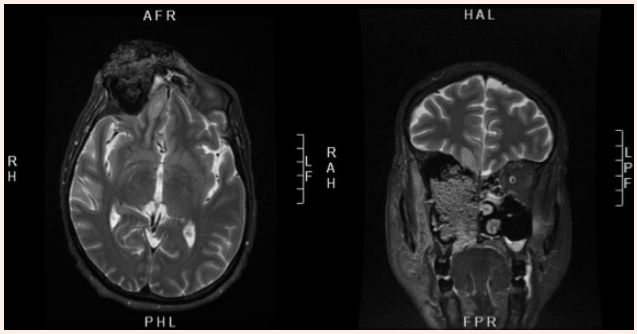

Figure 12: Week 1 MR Oribts w contrast T2 showing hyperintense regions in the right frontal lobe.

At week 2, our patient did not appear to have any necrotic bone or soft tissue. Daily dressing changes, were carried out by the OMFS team, of the right orbital/facial defect with amphotericin B soaked kerlix for one week followed by a transition to Vashe solution. Week 3 MRI study showed interval development of a well-defined abscess involving the right frontal lobe measuring 1.4 x 1.7 x 2.1 cm (Figure 13). Neurosurgical intervention was still terminal for having unresectable intracranial involvement of the middle temporal fossa, cavernous sinus, and Meckel's cave (dura mater pouch containing cerebrospinal fluid-CSF). Any drainage of right frontal abscess would lead to a CSF leak and meningitis due to an inability to reconstruct the surgical defect.

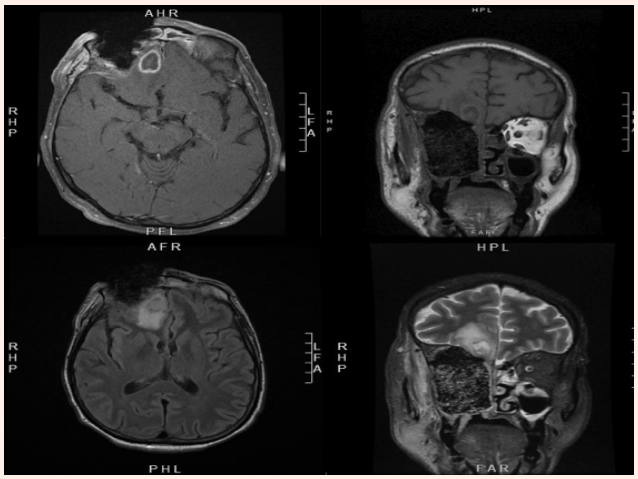

Figure 13: MR orbits with contrast T1 (top) and T2 (bottom), shows definite intracranial abscess of the right frontal lobe.

Infectious disease further recommended continuing IV amphotericin B at high dose of 600mg daily, Caspofungin (50mg daily), and starting Posaconazole (300 mg daily). Without any further surgical debridement from OMFS and Neurosurgery, hyperbaric team was consulted at week 4. Their recommendation consisted of 20 hyperbaric oxygen (HBO) dives at a pressure of 2 atmosphere absolute. Our patient tolerated a total of 12 sessions of HBO therapy prior to refusing any further treatments. He remained in hospital for additional 3 weeks (Weeks 4, 5, and 6) receiving both daily dressing changes of kerlix soaked in vashe solution and antifungal therapy as recommended by infectious disease. During this period of time the surgical site progressively granulated in such that the initially exposed bone became covered in a bed of healthy tissue (Figure 14). Finally, on week 7 our patient was discharged to hospice with oral posaconazole therapy and dressing changes. Unfortunately, our patient failed to followed up with any outpatient speciality clinics over next few months. A follow up call to hospice was made and according to them the patient had gone on to live in Los Angeles, CA with a relative. 10 months since the original hospital admission, we were finally able to contact the relative our patient was staying with and we were informed that patient had moved back to his native country of Guatemala and was continuing to live normal life without any neurological deficits. According to the relative our patient continued to adhere to his oral diabetic medications and has not had any surgical reconstructive treatments since being discharged (Figure 15).

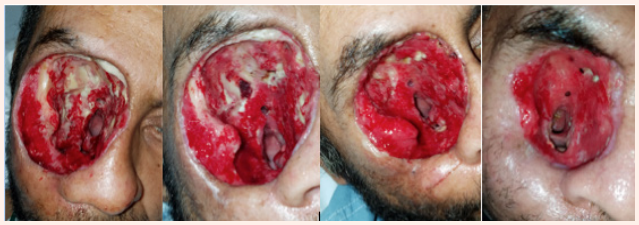

Figure 14: Starting from left a progression of granulating surgical site is shown over a period of 20 days. With the final image (far right) 7 weeks after the third image.

Figure 15: A photograph taken of the patient 10 months after discharge.

Discussion

Rhinocerebral mucormycosis is an opportunistic infection caused by inhalation of the airborne fungal spores. In an immunocompetent individual, spores land on the upper respiratory tract mucosa and get contained by phagocytic response. In an immunocompromised patient, phagocytes become dysfunctional or impaired leading to failure of phagocytosis of spores, which go onto germination and hyphae formation. Polymorphonuclear leukocytes are less effective in clearing hyphae in such individuals as a result infection develops [6]. Angioinvasion is a hallmark characteristic of mucormycosis infections. Organisms proliferate within the internal elastic lamina, dissecting it away from the media layer. Hyphae penetrating the endothelium results in thrombosis, infarction, and subsequent tissue necrosis [9,10]. This results in vicious cycle - vessel occlusion causes a decrease in tissue oxygenation, thus propagating further acidosis, which assists fungi to continue through the proliferative stage resulting in more angioinvasion and tissue necrosis [11].

Mucormycosis usually begins in the paranasal sinuses and progresses to the orbit, brain and oral cavity. Factors contributing to the spread into the orbit include thinness of the lamina papyracea, congenital or traumatic dehiscence along the medial orbital wall, and the foramina of the arteries/veins. Spread to intra-crainal regions may occur via invasion of the retro-orbital, ethmoid and sphenoid sinus regions. Cranial nerves III, IV, and VI tend to be increasingly affected by disease progression. Brain involvement may lead to patient becoming confused, obtunded and comatose state. Fungal invasion of the globe or retinal artery leads to the blindness [6]. Early visual loss would favor a diagnosis of rhinocerebral mucormycosis over bacterial cavernous sinus thrombosis [12,13]. On review of the initial CT scan of our patient, no signs of cavernous sinus thrombosis was appreciated and so the suspicion for mucormycosis was elevated since patient's blindness had occurred rapidly. Invasion, by Mucor species, of the sphenopalatine and greater palatine arteries from maxillary sinus leads to palatal tissue necrosis and subsequent perforation, which was noted on initial exam in our patient [14]. Common local clinical features may include black nasal secretions, orbital pain, periorbital cellulitis, sudden loss of vision, ophthalmoplegia, proptosis, ptosis, loss of sensation in the trigeminal nerve territory, which were all observed in our patient on presentation.

Immunocompromised state of the host is an important factor in progression of the disease. At risk populations include patients with haematological malignancy, bone marrow or organ transplants, diabetes mellitus with or without ketoacidosis, chronic corticosteroid use, end stage renal disease, and deferoxamine therapy for iron overload. Mucormycosis in immunocompetent hosts is rare, and is often related to previous trauma. Human immunodeficiency virus (HIV) infection does not appear to increase the risk of developing mucormycosis probably because neutrophils, as opposed to T lymphocytes, play a major role in defence against Mucorales. New case reports have documented the mucormycosis to be a sequelae of COVID-19 as immune dysfunction, immunosuppressive treatments, and proinflammatory state increase ones risk for this aggressive invasive fungal infection [31]. Our case however, predates the COVID-19 pandemic and as such no PCR testing or screening was done as part of the work up. Additionally, other potential causes such as osteonecrosis of the jaw were unlikely since he did not have a history of head/neck radiation treatment or any known exposure to bisphosphonate medications (intravenous or oral). Diabetics, especially those with ketoacidosis, are predisposed to rhinocerebral mucormycosis, the most common form of the disease. The acidic physiologic environment enhances the angioinvasive capabilities of the fungus, due to increased free iron present which is dissociated from sequestering proteins, and also alters the host immune response by impairing chemotactic function and phagocytic capacity of polymorphonuclear leukocytes (PMNs) [10,15,32,33]. Spellberg in his paper discusses how even when acidosis is absent, hyperglycemia itself can increases the risk of mucormycosis by at least 4 likely mechanisms; 1) hyper-glycation of iron-sequestering proteins, which disrupts the proteins' ability to sequester iron, resulting in increased free iron levels in blood even without acidosis; 2) upregulation of a mammalian epithelial receptor (GRP78) that binds to Mucorales, enabling tissue penetration; 3) upregulation of a fungal protein, CotH, which binds to the mammalian receptor to initiate invasion into host tissue; and 4) inducing poorly characterized defects in phagocytic function. About seventy percent of patients with rhinocerebral mucormycosis have been found to have diabetic ketoacidosis [15]. Our patient in this case was diagnosed with uncontrolled type 2 diabetes mellitus resulting in ketoacidosis on presentation. This uncontrolled immunocompromising condition is the most likely reason for the development of his mucormycosis especially given the setting of his work in the agricultural environment which could have been the source of exposure. Of importance laboratory values were Hemoglobin A1C greater than 15%, blood glucose of 460mg/dL, b-hydroxybutyrate levels of 57.9, arterial bicarbonate levels of 12mmol/L, and anion gap of 27. Management of underlying immunosuppressed state was as important as the surgical treatment and so patient was started on diabetic ketoacidosis protocol consisting of IV fluids and supplemental potassium (K) before insulin drip.

Radioimaging becomes an important tool for evaluating disease progression. In initial stages, radiographic findings often lag behind the clinical progression of the disease by showing very subtle changes or normal features. In the presence of clinical context, evidence of bony erosion on CT is strongly suggestive of the diagnosis. Additionally, Silverman et al. described, presence of retroantral, facial and orbital fat stranding as other indicators of the aggressive nature of the infection [16]. Middlebrooks et al. proposed 7 CT based variables as a screening tool to evaluate and triage patients who may be at risk for acute sinusitis of invasive fungal origin [17]. The variables included periantral fat, bone dehiscence, orbital invasion, septal ulceration, pterygopalatine fossa, nasolacrimal duct and lacrimal sac. While CT serves as a sensitive indicator to determine the extent of any orbital and/or cranial involvement, use of MRI has been more specific given the fungal invasion of the vascular and soft tissue structures. MRI enables early detection of vascular occlusion, often before the patient develops clinical signs. Reports suggest that T2-weighted magnetic resonance images are appropriate for demonstrating intracranial involvement which is consistent with an imaging study consisting 43 subjects with rhinocerebral mucormycosis in which CT showed minimally enhancing hypodense soft tissue thickening as the predominant finding in involved areas, while MRI showed T2 isointense to mildly hypointense soft tissue thickening and heterogeneous post contrast enhancement as the main finding. Bony erosion was seen in only 40% (17 of 43) of their cases [18]. MRI also may be a preferred imaging method because of coincident use of nephrotoxic drugs and CT contrast, which would both worsen the renal function of patients [10]. Reactive inflammation may be difficult to distinguish from true invasion in orbital cavity and so surgical exploration may provide crucial diagnostic information. If clinical suspicion of the disease is high, a negative imaging study does not provide a rationale to delay aggressive surgical and medical treatments.

As previously stated Mucormycosis is an aggressive disease that can rapidly progresses to the from its site of origin to the orbit, paranasal sinuses, oral cavity, and brain. Intracranial involvement of mucormycosis, like in our case, has been observed in multiple case reports. Toumi et al. had one of five patients in their five case report that demonstrated intracranial involvement. That patient exhibited mucor extension to frontal lobes, dilatation of the ventricular system and cortical grooves, and thrombophlebitis of the right lateral sinus. MRI performed in that patient revealed filling of a facial sinus predominantly in ethmoidal air cells, a right internal intra-orbital collection, and confirmed intracerebral extension [19]. Interestingly that

patient would be one of the two survivors following surgical debridement, antifungal therapy with amphotericin B, and a subsequent dose of amphotericin B after patient suffered a relapse [19]. Another documented case report had a less positive outcome in which resulted in death despite aggressive surgical and medical treatment [20]. In both cases patients with intracranial involvement by mucormycosis underwent surgical and medication based therapy with amphotericin B.

Yoon et al. also demonstrated a successful case outcome in which a patient initially developed a right-sided nasal sinus infection that later progressed through the paranasal sinuses leading to invasion of the periorbital and frontotemporal region, due to the delayed diagnosis and treatment. This case as with the others previously mentioned involved a patient with poorly controlled diabetes mellitus. Utilizing valuable information from an ENT biopsy which revealed fungal hyphae patient was immediately started on amphotericin B. Because the patient refused to have aggressive debridement of her facial and periorbital lesions, she was medically treated with amphotericin B, up to 4,525mg for the initial 30 days, along with the strict control of her blood glucose levels [21]. This therapy proved to have a moderate improvement of her facial and periorbital lesions, however the patient finally agreed to undergo neurosurgical intervention when a follow up MRI showed osteomyelitis with extensive bone invasion and pericranial abscess in the frontotemporal region. Extensive bony debridement, removal of the involved dura and surrounding necrotic tissues and drainage of the pericranial abscess were performed. Post-surgical antifungal therapy consisted of Amphotericin B administered for a total of 5,225mg, used for 31 days. She had no adverse effects related to amphotericin B and follow up MRI revealed the disappearance of the pericranial abscess and a decrease in the enhanced periorbital lesions, but residual lesions were present. Patient was finally discharged on a with Posaconazole 400mg for 26 days and at 15 month follow up still remained disease free. For comparison, in our case, the patient was treated with a total dose of 24,200mg during a 62 day admission. Our patient was managed surgically early on in his treatment course so only 640mg of amphotericin B was administered between admission and right orbital exenteration (3 days). Following exenteration patient was given a total dose 24,200mg of amphotericin B over the remainder of his stay. The 30 day post-surgical (post exenteration) antifungal therapy of amphotericin B was 11,600mg which was more than double the given to the patient in the 31 day period by Yoon et al. However, since the medication is dosed by weight and our patients were of different genders and likely different weights these factors need to be considered in accounting for the difference.

Mucormycosis is considered a medical emergency and successful treatment requires an aggressive multidisciplinary approach [22]. The mainstay of treatment is correction of the underlying medical condition, antifungal therapy with amphotericin B, and surgical debridement of the necrotic tissue. Early recognition of symptoms and initiation of surgical and medical therapy is essential to improve prognosis. Invasion seen on the histopathology specimen of biopsied tissue is the gold standard test to confirm the diagnosis. Surgical approach (open vs endoscopic vs combined) depends on the extent of the disease. Reduction in mortality rate of up to 20% has been seen in patients with diabetes mellitus when surgical and antifungal therapy have been combined [23]. Amphotericin B has been the choice of antifungal therapy for the treatment of mucormycosis with total dose ranging from 2 to 4g. Depending on the patient's cardiorenal status, dosage may be gradually increased. Careful monitoring of the side effects (ie chills, fever, phlebitis, renal damage, and anaphylaxis) is important during administration. Lipid complex amphotericin B is a formulation designed to be less nephrotoxic than conventional formulation [24]. Lipid based formulation increases circulation time and alters biodistribution of the drug. Drugs complexed with lipid vehicles are able to localize and reach greater concentrations in tissues with increased capillary permeability (infection and inflammation) compared to normal tissue, which are impermeable to lipid-complexed drugs. This passive targeting concept increases localization of drugs to diseased sites while minimizing exposure of the drugs to normal tissue. Within the diseased sites, drug release occurs through the action of the lipases from the surrounding inflammatory cells. Lethal dose (LD50) of lipid based amphotericin B is approximately 10-15 times higher than conventional formulation with significantly reduced renal toxicity. For the stated reasons, Lipid complex amphotericin B is well suited for therapy against rhinocerebral mucormycosis infections, which require large doses of drugs given for long periods of time [25]. Delay in antifungal therapy has shown to increase mortality rates [26]. It was reported that survival rate ranged from 76-81% in patients whose antifungal treatment was started within 6-days of symptoms onset, however survival rate ranged from 36-42% in patients whose antifungal treatment was delayed more than 12 days after the onset of symptoms [27].

In our case, intravenous liposomal amphotericin B was started just after appearance of suspicious clinical presentation and radiological findings supporting mucormycosis. Additionally, posaconazole has a wealth of evidence supporting its use in zygomycosis and may have indication in patients who cannot tolerate amphotericin B [28]. Surgical debridement of the necrotic tissue is essential and multiple debridements are often necessary for cure. Orbital involvement of the mucormycosis leaves practitioners with difficult surgical choice: whether or not to complete exenteration. Orbital exenteration may be lifesaving in the presence of active fungal invasion of the orbital content and even after intracranial spread. Progression of the angioinvasion and vaso-occlusive characteristic of the disease, delivery of the intravenous amphotericin B becomes limited. In such cases, irrigation and packing of the surgical site with amphotericin B- solution (5mg/100cc sterile water) has shown to improve delivery of the drug to to poorly perfused infected and/or necrotic tissue. In addition to rapid and aggressive surgical debridement, amphotericin B therapy, and controlling the underlying immunosuppressive state, hyperbaric oxygen therapy has been used as adjunct therapies. Hyperbaric oxygen therapy aids with the neovascularization of the poorly perfused and hypoxic tissue. Hyperbaric oxygen therapy should consist of exposure to 100% oxygen for 90 minutes to 2-hours at pressures from 2.0-2.5 atmospheres with 1 or 2 exposures daily for a total of 40 treatments. Hyperbaric oxygen therapy is limited to larger centers and so transporting patients to such centers would be warranted in patients who appear to be deteriorating despite maximal surgical and medical therapy. Despite all these measures, there is a high mortality rate of 50–85% associated with rhinocerebral mucormycosis even when aggressive surgery is done [22,29,30]. The aspect of intracranial involvement in the context of mucormycosis infection adds more complexity to an already difficult surgical and medical situation. Though the approaches to therapy and the degree to which they are carried out have some uniformity, the outcomes of treatment are variable as seen in the case reports discussed. In our case, our patient was fortunate enough to survive after aggressive surgical and medical therapy despite having intracranial involvement, which was left, untouched surgically. The outcome of survival surpassed expectations.

Conclusion

All oral and maxillofacial surgeons, otolaryngologists, ophthalmologists, emergency medicine physicians and other clinicians evaluating and treating patients with head and neck infections should be vigilant in always including the possibility of mucormycosis in the differential diagnosis of necrotizing midfacial infections, and must have the wherewithal to move forward with aggressive surgical debridement when indicated. Proper clinical acumen in the diagnosis and treatment of mucormycosis most definitely can improve survival. Mucormycosis is a rapidly progressing fungal infection often presenting in diabetic and immunocompromised patients. Diabetics, especially those with ketoacidosis, are predisposed to rhinocerebral mucormycosis, the most common form of the disease. The non-specific nature of rhinocerebral mucormycosis infections on initial presentation makes correct diagnosis extremely difficult until significant morbidity has been inflicted. The cornerstones of treatment include the correction of the underlying medical condition, antifungal therapy with amphotericin B, and aggressive surgical debridement of the necrotic tissue. Although CT imaging is a sensitive imaging means to determine extent of disease, MRI is a better modality to detect vascular occlusion prior to manifestation of clinical signs. If clinical suspicion of the disease is high, a negative imaging study should not preclude aggressive surgical and medical treatments. Amphotericin B has been the choice of antifungal therapy for the treatment of mucormycosis with total dose ranging from 2 to 4g and the development of lipid complex amphotericin B helps assure maximal medical treatment while inflicting minimal renal damage. As demonstrated by literature, cases of intracranial involvement by mucormycosis, can have unpredictable outcomes despite undergoing the necessary surgical and medication based therapy.

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