A Fatal Outcome of Rhino-Orbital-Cerebral Mucormycosis in Newly Diagnosed Diabetic Patient

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Abstract: Mucormycosis is a progressively invasive disease, with a fatal outcome, on late presentation. A 37-year-old male with recently diagnosed diabetes mellitus presented with orbital cellulitis and signs of sinusitis. He underwent transnasal endoscopic debridement of paranasal sinuses. The histopathology specimen revealed the growth of mucormycosis. He was treated with intravenous (IV) amphotericin B, Posaconazole, IV insulin, and extensive debridement surgery, but had an unfavorable outcome due to rapid mucor invasion to the brain.

Keywords: Mucormycosis, diabetes mellitus, paranasal sinuses, amphotericin B, Posaconazole

1. History

37 years old a Saudi male referred to our hospital- king Fahad Specialist Hospital Dammam as a case of Maxillary and Ethmoidal sinusitis with orbital cellulitis suspected of mucormycosis. The patient is known to have newly diagnosed diabetes mellitus diagnosed six weeks from his presentation (HbA1c was 9.4), hypertensive (newly diagnosed) and dyslipidemic.

The history goes back to five days prior to his admission to the local hospital where he initially started to have upper respiratory tract symptoms followed by greenish blackish secretions from his right eye; then he started to have swelling in the right cheek and eye as well as discoloration of the overlying skin and facial pain. Two days later, he started to have dysphagia mainly to solid food. He also gave a history of fever without chills for four days. There was no history of head trauma, limb weakness, vomiting or loss of consciousness; He gave history of good compliance to his diabetic treatments.

He was transferred from a local hospital where he stayed for two days and was admitted to an ENT floor on 17th Jan 2018.

- Medication History: Insulin  
- Surgical History: Unremarkable  
- Family History and Review of system: Unremarkable

Examination on the day of Admission:

Right eye edema, eyelid partial necrosis, right side of the face blackened with areas of skin sloughing (ImageA), necrotic hard and soft palate, necrotic left hypo pharyngeal -wall Nasal scope: Edematous, congested Laryngoscope: restricted left vocal cord and arytenoid movement with blackish discoloration over right arytenoids

Patient’s picture showing extensive Bilateral facial and periorbital oedema (eye’s covered) more in the left side (note the presence of an extensive black necrotized nasal wall, skin overlying maxillary sinuses and skin sloughing).

2. Hospital Course

He was transferred to ICU on 18th of January for decrease level of consciousness and high blood pressure for observation. The patient had emergent computed tomography scan of the brain and paranasal sinuses without contrast (Figure 1).

Image A

Patient’s picture showing extensive Bilateral facial and periorbital edema (eye’s covered) more in the left side (note the presence of an extensive black necrotized nasal wall, skin overlying maxillary sinuses and skin sloughing).
eyelid edema, proptosis, and blackish discoloration of his right cheek. He was conscious drowsy for that elective intubation was done, he was seen by Infectious disease team and was started empirically on Amphotericin –B (liposomal) 10mg/kg daily, Posaconazole 200mg po Q 6hours, in addition to ceftriaxone and clindamycin after septic work-up. His blood sugar was 23.8 mmol/l so also he was started on insulin infusion.

On Jan19th, he underwent urgent FESS (functional Endoscopic Sinus Surgery) in operating room (OR) and kept intubated because of decrease level of consciousness and vocal cord edema. The Intra-operative findings: necrotic mucosa of the right maxillary sinus posterior wall, necrotic mucosa and bony defects of the right sphenoid sinus walls and the clivus. The left ethmoid and maxillary sinuses were healthy.

Procedure: Right middle turbinate resection, right maxillary antrostomy, maxillary mucosa debridement, right anterior and posterior ethmoidectomy, right sphenoidotomy and sphenoid mucosa debridment, right posterior septal mucosa debridment, left anterior and posterior ethmoidectomy. All necrotic mucosa and bones were removed and sent to microbiological, mycological and histopathological examinations. The culture came positive for zygomyces (Absidia corymbifera)

He was seen and evaluated by Ophthalmology and eye exam showed early retinal haemorrhage, total retinal detachment, Retinal necrosis, right pupil fixed and dilated with right afferent papillary defect and no light perception.

The patient showed interval deterioration of the general condition with decreased level of consciousness. The patient had CT brain followed by MRI brain (Figure 2).

Figure 1: A: Paranasal CT scan without contrast soft tissue algorithm showed bilateral maxillary antral mucosal thickening. The right maxillary antrum shows air bubbles with extension through the anterior and posterior wall into the edematous inflamed subcutaneous tissue.

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Up on admission, he was a febrile, vitally stable, with a pulse of 110/min, blood pressure of 130/70 mm Hg. He had right
He was seen by neurology team and advised for aspirin. Patient condition didn’t improve and he was difficult to wean from the ventilator, so he underwent elective tracheostomy on 30-January. His condition deteriorated further on Feb-5th, his left eye became fixed and dilated, he started to be more hypotensive requiring increasing doses of vasopressors, his antimicrobials were escalated empirically to Imipenem, vancomycin and amikacin in addition to the antifungal. Because of his overall condition and the poor prognosis, goals of care were changed to DNR (Do not Resuscitate) on Feb -5th, and patient condition deteriorated further and he passed away on Feb-6th.

3. Discussion

The most common clinical presentation of mucormycosis is rhino-orbital-cerebral and pulmonary infection [1]. Mucormycosis can also cause gastrointestinal, cutaneous, renal, and disseminated disease as well as can spread to contiguous structures, such as the heart and the mediastinum.

Rhino-Orbital-Cerebral Mucormycosis (ROCM) is a rare but fatal infection of nasal cavity and sinuses, with mortality in excess of 50 percent. Poor prognosis has been linked to 1) delayed diagnosis and treatment; 2) hemiparesis or hemiplegia; 3) bilateral sinus involvement; 4) leukemia; 5) renal disease; and 6) treatment with deferoxamine. Diabetes and particularly diabetic ketoacidosis is one of the commonest predisposing factors for the disease [2]; rarely presents without any apparent risk factor. Typically presents acutely in patients with diabetic ketoacidosis or immunosuppression, although chronic form has been described. In the literature, it is generally regarded that immunocompromised hosts are most commonly affected and
that the disease is less invasive and has a better prognosis in immunocompetent patients [3].

Although this infection does occur at all ages, there is a tendency for patients with this infection to be >45 years old. The pathogenesis of the disease probably starts with inhalation of the fungus into the paranasal sinuses. On germination, the fungus may spread inferiorly to invade the palate manifesting as black eschar, posteriorly to invade the sphenoid sinus and spread into the cavernous sinus causing cranial nerve palsies, laterally to involve the orbits causing proptosis, ophthalmoplegia, or loss of the vision, or superiorly to invade the brain causing stroke secondary to occlusion of the carotid artery [4].

Rhino-orbital-cerebral mucormycosis is most commonly caused by Rhizopus oryzae. A high index of suspicion is very critical for early detection and treatment and is necessary to optimize the outcome of this fatal disease. As mucorales are environmental isolates, definitive diagnosis requires a positive culture from sterile site. Unfortunately, cultures are positive in fewer than half of cases of mucormycosis.

Treatment begins with elimination of the predisposing factors such as hyperglycemia, immunosuppression, metabolic acidosis, neutropenia, along with surgical debridement and antifungal therapy [6]. IV amphotericin B is the drug of choice with its lipid formulation (L-AMB) being more effective with less side effects, the recommended dose is 5mg/kg and higher doses up to 10 mg/kg is recommended for CNS infections [7]. The duration of the treatment should be individualized, and roughly should be continued until the clinical and radiological findings are completely resolved and all risk factors have been eliminated. Posaconazole which is available as an oral therapy can be used instead for those who can’t tolerate L-AMB or as a maintenance therapy [8].

To our knowledge, there have been no randomized trial comparing different antifungal medications against mucormycosis and combination therapy with echinocandin or posaconazole is not supported by evidence and is not recommended by major guidelines [7]. However, in the cases where the first line therapy is ineffective, the combination therapy is worthy of consideration [9]. Other adjunctive therapies such as deferasirox – an iron chelating agent and hyperbaric oxygen have been used, but their benefit has yet to be established [10], [11], [12].

The need for complete orbital exenteration as a treatment of ROCM has never been adequately studied. Surgeons advocate a “conservative-aggressive” approach [13], in which all necrotic material is removed, but the limits of surgical debridement are defined by use of frozen sections intraoperatively, and when possible, uninvolved orbital structures are spared. The data lend credence to the belief that total exenteration may not be necessary in every case and does not necessarily improve survival. It is the recommendation that endoscopic surgeons make real-time decisions regarding the extent of surgery required on the basis of intraoperative findings and frozen sections from debrided materials [13]. Our case is peculiar since our patient is newly diagnosed to have diabetes mellitus. Although ROCM has been reported in immunocompetent patients it is essential to alert clinicians of the emergence of this rare disease among healthy individuals or patients with newly diagnosed diabetes mellitus.

4. Conclusion

Mucormycosis in diabetic patients requires high clinical suspicion and prompt diagnosis, in order to prevent a fatal outcome. It is clinically challenging to treat rhino-orbital mucormycosis with intravenous amphotericin B alone. Thus, the surgical debridement becomes mandatory as mucorales are rapidly invasive and progressive. We are reporting this case of ROCM in a young patient with newly discovered DM, who presented very late in the course of his illness. Unfortunately, the hyper acuity of the disease course and cerebral involvement as well as the extent of the disease didn’t allow for an optimal and timely surgical intervention. It needs to be emphasized that, treatment might depend mostly on high clinical suspicion, as the patient might be lost until cultures are awaited.

5. Additional Information Disclosures

Human subjects: Consent was obtained by all participants in this study. Conflicts of interest: all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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