Case report

A case of malignant mucormycosis in a diabetic

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Abstract:

Rhino-orbito-cerebral mucormycosis is rapidly growing as a common infection in immunocompromised patients and its rapid diagnosis with prompt initiation of treatment is the mainstay of approaching it. However receiving complete treatment with monitoring other factors like blood sugars, blood pressure and local care is as essential as antifungal therapy is. However in our patient, treatment was received for only 6 days following diagnosis during which signs of improvement marked positive outcome, which was finally discontinued due to patient’s financial constraints and he expired 2 months later. Given the rapidly progressive nature of rhinocerebral mucormycosis and marked increases in mortality, any diabetic patient with headache and visual changes needs prompt evaluation with imaging studies and nasal endoscopy to rule out mucormycosis. Cost of liposomal Amphotericin B and confirming diagnosis early have been factors that are hindering the battle against this disease.

Introduction:

A 67 year old male with diabetes and hypertension on medications since 5 years was admitted to medical ICU with complaints of right hemifacial and hemicranial pain with watering in right eye that aggravated on ocular movements since 5 days. This was followed by drooping of right eyelid following which he visited the hospital. He gave no history of fever, trauma or surgery. On examination, his pulse was 88/min and regular and blood pressure was 210/100.

His neurological examination showed right sided II, III, IV, VI with VIIth UMN type facial cranial nerve involvement. There were no motor and sensory deficits or signs of meningeal irritation. His ocular examination showed copious sticky discharge from right eye with proptosis and signs of severe inflammation like chemosis and redness. Examination of the nasal cavity showed blood clots in right nasal cavity with maxillary tenderness. He was immediately started with antibiotics like ceftazidime and metronidazole intravenously along with anti hypertensive treatment like amlodipine followed by nitroglycerine infusion drip. His diabetic status was monitored and controlled with human regular Insulin. Local pain relief for eye was provided. His investigations revealed a haemoglobin of 9.4 and raised total leucocyte counts of 14,000. His renal parameters were deranged with a urea of 77 and creatinine of 2.8. Fundoscopy of both eyes showed non proliferative diabetic retinopathy while an abdominal ultrasound showed grade 1 renal parenchymal disease. With further investigations like neuroimaging studies showed white matter ischemia, proptosis of right eye with preseptal orbital edema, and thickening of right orbital muscles on a plain CT brain while a CT paranasal sinus showed peripheral mucosal thickening in bilateral maxillary sinuses, right ethmoidal, right frontal and sphenoid sinus.

On 2nd day of admission, MRI brain with venogram showed ischemic foci in high parietal, corona
radiata, and centrum semiovale with pansinusitis and proptosis of right eye, periorbital swelling with bulky inferior rectus muscle. Four samples were taken from nasal swabs which revealed Rhizopus on KOH mount. Subsequently on 4th day, nasal swab culture from both nasal cavities isolated Aspergillus niger. FESS with debridement was done on 6th day post admission with due risk and biopsy taken from right nostril showed grayish black friable specimen of necrotic tissue with fungal hyphae.

Summarizing the clinical profile and investigations, he was diagnosed with Rhino-orbito-cerebral mucormycosis and was given Inj. Amphotericin B (Liposomal) 5mg/kg in 500ml normal saline slowly over 8 hours daily with antibiotics, Insulin and anti hypertensives, eyedrops Ciplox & Timolol.

His condition improved over a week, however due to financial reasons he stopped treatment and expired 2 months later.

Discussion:

Rhinocerebral mucormycosis is rare fungal infection affecting immunocompromised patients.[1] Mucormycoses is a group of invasive infection caused by Mucoraceae family.[2] First described by Pauliff A in 1885, this infection has six manifestations: rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated, and localized. [3] The most frequently isolated species is Rhizopus oryzae as was in our case. The remaining five families of Mucorales have rarely been reported with an exception of Cunninghamallacae family. [4]

Predisposing factors for development of this infection are mostly immunocompromised states like diabetes mellitus, aplastic anemia, myelodysplastic syndrome, immunosuppressive drugs following graft or transplant.[5] Our patient was a diabetic since 4 years and was taking oral hypoglycemic drugs although he never regularly followed up for sugar levels.

Rhinocerebral mucormycosis generally progresses in three stages. The first stage occurs after fungal spores have been inhaled and infect the paranasal sinuses resulting in formation of necrotic lesions in nasal mucosa, turbinates or hard palate. The second stage is characterized by direct extension of disease into maxillary sinus or invasion of surrounding vasculature. Third stage involves spread of fungus into cribriform or orbital apex. In our patient, the presentation of orbital pain with cranial nerve involvement confirmed the third stage.[6]

Rhinocerebral disease may manifest as unilateral orbital headache, facial pain, numbness, fever, hyposmia, black discharge, or may initially mimic sinusitis.[7]

Progressive vision loss may occur due to involvement of optic nerve or arteriolar invasion resulting in infarction or cavernous sinus thrombosis.[8]

Orbital swelling and cellulitis can be progressive and may cause proptosis, ptosis, chemosis and ophthalmoplegias with cranial nerve five and seven involvement. [1] Our patient presented with total ophthalmoplegia with loss of vision with 7th nerve affected on same side.

An early diagnosis of rhino-orbito-cerebral mucormycosis is considered as a step of grave importance for appropriate management of the patient. Histopathological isolation of the fungus typical of mucor species is diagnostic as no reliable serological or PCR based tests are available. Imaging studies aid in the diagnosis although they are not completely diagnostic. Multimodality imaging is helpful in prompting an early diagnosis.[9] MRI of sinuses, orbit and brain with venogram to rule out complications like sinus thrombosis show anatomic involvement as well as help in surgical planning.[10]
Imaging studies in our patient done on day 2 and 4 showed CT brain with white matter ischemia, proptosis of right eye with preseptal orbital edema, and thickening of right orbital muscles while a CT Paranasal sinus showed peripheral mucosal thickening in bilateral maxillary sinuses, right ethmoidal, right frontal and sphenoid sinus and the MRI showed pansinusitis and proptosis of right eye, periorbital swelling with bulky inferior rectus muscle.

As of now, treatment options for rhino-orbito-cerebral mucormycosis are still being optimized. Current therapy includes treating predisposing factors, antifungal therapy, and surgical debridement. Our patient was initiated with liposomal Amphotericin B and ceftazidime. Liposomal amphotericin is proved to be superior to amphotericin.\[1\]

A study in rabbits demonstrated that liposomal Amphotericin B penetrated brain parenchyma at levels more than five-fold above those of amphotericin B. Surgical debridement in combination with anti fungal therapy have high cure rates.\[12\] FESS (functional endoscopic sinus surgery) was done on 6\textsuperscript{th} day in our patient. Euglycemia should be restored in diabetic patients rapidly and immunosuppressed conditions be reversed if any.\[13\] In our patient, prompt commencement of insulin helped in achieving normal glucose levels over a period of 4 days.

**Conclusion**

Rhino-orbito-cerebral mucormycosis is rapidly growing as a common infection in immune-compromised patients and its rapid diagnosis with prompt initiation of treatment is the mainstay of approaching it. However receiving complete treatment with monitoring other factors like blood sugars, blood pressure and local care is as essential as antifungal therapy is. However in our patient, treatment was received for only 6 days following diagnosis during which signs of improvement marked positive outcome, which was finally discontinued due to patient’s financial constraints and he expired 2 months later. Given the rapidly progressive nature of rhinocerebral mucormycosis and marked increases in mortality, any diabetic patient with headache and visual changes needs prompt evaluation with imaging studies and nasal endoscopy to rule out mucormycosis.\[12\] Cost of liposomal Amphotericin B and confirming diagnosis early have been factors that are hindering the battle against this disease.  

CT Brain with PNS: Mild proptosis of right eye with preseptal orbital edema, and thickening of right orbital muscles is seen

Proptosis of right eye with ptosis and total ophthalmoplegia.
Diagnostic Nasal Endoscopy: Blackish friable mass above inferior turbinate.

References

1. Asman S, Meherdad M. Rhinocerebral mucormycosis: a rare fungal infection linked to diabetes mellitus. JAAPA, Dec 2011: 24(12)


