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Case reports

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DEATH DUE TO RARE RHINOCEREBRAL MUCORMYCOSIS INFECTION: A CASE REPORT

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A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Rhinocerebral mucormycosis is the most common form of mucormycosis in patients with diabetes mellitus; it is linked to poor prognosis, presenting most commonly in an acute setting, mimicking symptoms of sinusitis or periorbital cellulitis. The general survival rate in chronic cases is 83%, compared to 10–35% in acute.

Aim of the study: To report a death due to rhinocerebral mucormycosis in a 45-year-old male patient.

Case report: In this case report a 45-year-old male presented with acute rhinocerebral mucormycosis and was admitted in a state of unconsciousness with complaints of sudden onset weakness of right upper and lower limb, motor aphasia, right facial swelling, orbital swelling, and diminished distant vision. Upon primary diagnosis of stroke, treatment started immediately. However, past medical history from patient's attendants revealed that the patient underwent a tooth extraction procedure 20 days prior, and had since developed redness of the right eye, diminished distant vision, and swelling of the right side of the face. Pus was drained, and reports revealed orbital cellulitis with an intracranial spread. By the time of admission to hospital, the patient had abnormal lab profiles (WBC, ESR, serum creatinine), acute kidney injury, with MRI revealing rhinocerebral mucormycosis. The patient developed septic shock and died during treatment.

Conclusions: Acute mucormycosis carries a high mortality rate. Pleiotropic manifestations and organ dysfunction add to the further risk of mortality. Timely diagnosis and management may increase the chances of the survival rate of the patient.

KEYWORDS: Mucormycosis, Diabetes mellitus, Orbital cellulitis, amphotericin B

Background

Mucormycosis is a rare fungal infection caused by fungi in the family Mucoraceae which mainly develops in immunocompromised hosts [1]. *Rhizopus* species are the most common causative organisms [2]. Patients with impaired immune function, such as those suffering from diabetes mellitus, hematologic malignancy, HIV, and immune suppression after organ transplantation are predisposed to this infection [3–5]. This infection develops after inhalation of fungal spores into the paranasal sinuses, providing access to the central nervous system; CNS disease is the most prevalent manifestation of mucormycosis [5]. Among all the types of mucormycosis, rhinocerebral mucormycosis is the most common form occurring in patients with diabetes mellitus [2] and is associated with poor prognosis [6]. This most commonly presents in an acute setting, mimicking symptoms of sinusitis or periorbital cellulitis [7]. However, 25% mortality was reported in patients without any underlying disease process, 40% for patients with metabolic abnormalities and 80% for immunocompromised patients [8]. Timely diagnosis and intervention are important for successful management. The treatment of choice is surgical debridement of necrotic tissue and systemic antifungal therapy, including amphotericin B [2].

Aim of the study

This report aimed to present a rare case of rhinocerebral mucormycosis, associated septic shock, renal failure, and death in a 45-year-old male patient.

Case report

A 45-year-old male patient was admitted to the general medicine department in a state of unconsciousness. Symptoms reported were sudden onset of weakness of right upper and lower limb, motor aphasia, right facial swelling, orbital swelling, and diminished distant vision. Medical history revealed hypertension for two years and type 2 diabetes mellitus for six months. The patient was an alcoholic and occasional smoker, and was not on antidiabetic therapy. 20 days prior to presentation, the patient underwent a tooth extraction procedure for dental caries. In the days following, he complained about right eye redness, diminished distant vision, and swelling of the right side of the face. A minor procedure was used to drain the pus. The provisional diagnosis was a stroke on day 1, with treatment initiated accordingly (Tab. 1). An MRI scan and laboratory tests were ordered to rule out the correct diagnosis on day 1.

Table 1. Treatment for Stroke.

Drug	Dose	Frequency	Indication
Tab. Citicholine	500mg	BD	CNS protectant
Tab. Atorvastatin	40mg	OD	Preventing Secondary Stroke
Tab. Aspirin	150mg	OD	Preventing Secondary Stroke
Tab. Clopidogrel	75mg	OD	Preventing Secondary Stroke
Tab. Pantoprazole	40mg	OD	Preventing Acidity
Inj. Ceftriaxone (IV)	1g	BD	Prevention of nosocomial Infections

His complete blood count test revealed abnormal WBC, ESR, and serum creatinine. His glycemic control was poor (Table 2). Coupled with this, there was increased heart rate, respiratory rate, and body temperature, the levels of which met SIRS criteria. MRI scan reports revealed rhinocerebral ocular mucormycosis along with ischemic changes of blood vessels (Fig. 1, Fig. 2, and Fig. 3). The patient developed septic shock on day 2. Intubation was performed to facilitate ventilation. He was admitted to the intensive care unit immediately. Blood was drawn for culture sensitivity tests. Meanwhile, the patient was administered with stroke treatment protocol (Tab. 1), intravenous infusions, and empiric antibiotic treatment. Additionally, to treatment specified in Tab. 1, tab. Metronidazole 500mg, BD, for suspected anaerobic infections was also added. An insulin drip was administered for normalizing blood glucose levels.

Table 2. Abnormal laboratory blood test results.

Test	Value	Reference
White Blood Cells	30800 cells/cumm	4000–10000 cells/cumm
Erythrocyte Sedimentation Rate	19mm in 1 hour	10mm or less in 1 hour
Serum Creatinine	2.64mg/dl	0.7–1.3mg/dl
Random Blood Sugar	260mg/dl	80–140mg/dl

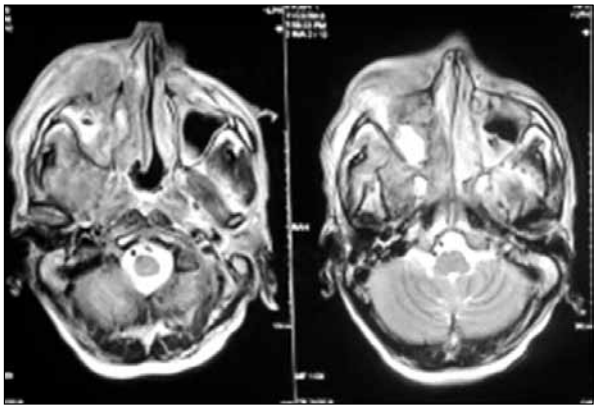

Figure 1. MRI scan report showing right maxillary sinus problem: The ill-defined disease is involving the right pre-septal space, extending posteriorly to the right maxillary ethmoid, sinus and orbital apex. The disease is infiltrative in nature with ill-defined borders.

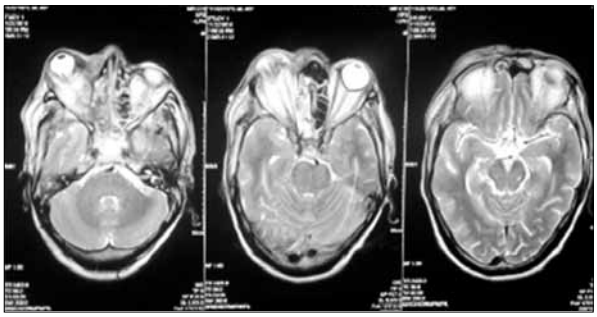

Figure 2. MRI scan report showing eye orbit involvement in the fungal infection: Entire volume of the disease is hypointense on both T2W & T1W images posterior, the disease extending up to the cavernous sinus with possible infiltration of the internal carotid artery.

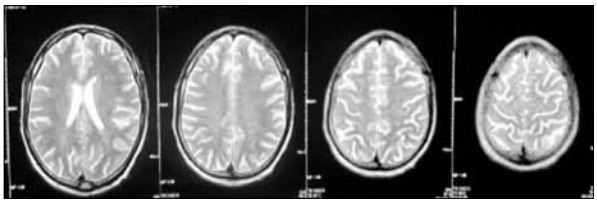

Figure 3. MRI scan report showing the ischemic changes of small vessels, non-hemorrhagic infarcts.

On the day 3, patient became hypovolemic due to septic shock. Noradrenaline, 3mcg/kg/min and Dopamine, 5mcg/kg/min were infused immediately, however, despite appropriate management, the patient died on the day 4 due to cardiac arrest.

Discussion

The initial symptoms of rhinocerebral mucormycosis are consistent with those of sinusitis and periorbital cellulitis; these include eye and/or facial pain, and facial numbness followed by blurry vision. Signs and symptoms that suggest mucormycosis in susceptible individuals include unilateral periorbital facial pain, facial cellulitis, orbital inflammation, eyelid edema, proptosis, acute ocular motility changes, nasal discharge, nasal stuffiness headache, and acute vision loss [9, 10]. Intracranial extension occurs in 80% of cases and

causes encephalopathy, cerebritis, and angioinvasion, leading to cavernous sinus thrombosis and cerebrovascular accidents [11]. In our case, the patient presented with an ischemic stroke which could have been due to the intracranial extension and comorbid conditions. There is no exact definition of chronicity in the case of mucormycosis, which can vary from weeks to months. Classically, it is defined by symptoms that last for more than 4 weeks. In the reported chronic cases, the average duration was seven months. [12]

Sepsis is a systemic inflammatory response to a confirmed or suspected infection. Clinically, the Systemic Inflammatory Response Syndrome (SIRS) is the occurrence of at least two of the following criteria: fever >38.0°C or hypothermia <36.0°C, tachycardia >90 beats/minute, tachypnea >20 breaths/minute, leukocytosis >12*109/l or leucopenia <4*109/l [13]. In this case, SIRS criteria were necessary to rule out confirmed infection and administrate the empirical antibiotics while waiting for the blood culture reports.

Amphotericin B deoxycholate (AmB) is the only licensed antifungal agent for the treatment of mucormycosis, but nephrotoxicity and poor CNS penetration limit its place in therapy. Lipid formulations of AmB (LFABs) exist, however, which are significantly less nephrotoxic, and can be safely administered at higher doses for longer periods, but are more expensive than AmB. [14] Starting dosages of 1 mg/kg/day for AmB and 5–7.5 mg/kg/day for LFAB are commonly used for adults and children. [15] Among the second-generation triazoles, only posaconazole and isavuconazole display appreciable activity against the Mucorales. De-escalation to posaconazole or isavuconazole remains a viable strategy once the pathogen and susceptibility to these agents are identified. Refractory or intolerance to amphotericin B can be managed effectively using triazoles as salvage therapy. [16]

The mainstay of therapy is extensive debridement of all infected and necrotic tissue, with drainage of all sinus and abscess fluid collections. Immediately obtain a consultation with a surgeon. Conservative attempts to spare tissue may result in the retention of the organism and subsequent treatment failure. A delay in surgery may decrease the likelihood of survival in all forms of invasive mucormycosis. Multiple debridements are sometimes required. Due to the vaso-occlusive effect of mucormycosis, the involved tissue rarely bleeds, so debridement until normal, well-perfused, bleeding tissue is encountered, is ideal. Intraorbital irrigation of amphotericin B may be considered as an adjunct treatment. Orbital exenteration along with the removal of the sinuses may be necessary. No standard exists to guide physicians on the best timing of exenteration. [17]

In our case, the patient was treated for ischemic stroke, followed by empirical treatment with broad-spectrum antibiotics. Indeed, empirical treatment with broad-spectrum antibiotics is advisable, as amphotericin B is contraindicated in severe renal impairment. However, despite efforts to improve renal function in order to initiate amphotericin B treatment, the patient died.

Conclusions

Acute rhinocerebral mucormycosis is a rare presentation that requires a high index of suspicion due to atypical presentations. It is important to rule out mucormycosis in diabetic patients, as early diagnosis and treatment can reduce morbidity and mortality. Delay in management often leads to a fatal outcome.

Ethical approval

The study was approved by institutional ethics committee (VIPT/IEC/CR/16). The patient care giver was clearly explained the purpose of case report and obtained patient consent form from the care giver.

References

1. McSpadden R, Martin J, Mehrotra S, Thorpe E. Mucormycosis causing ludwig angina: a unique presentation. J Oral Maxillofac Surg 2017; 75(4): 759–762.
2. Yeo C, Kim J, Kwon S, Lee E, Lee M, Kim S, et al. Rhinocerebral mucormycosis after functional endoscopic sinus surgery. Medicine 2018; 97(51): e13290.
3. Kwon-Chung K. Taxonomy of fungi causing mucormycosis and entomophthoramycosis (zygomycosis) and nomenclature of the disease: molecular mycologic perspectives. Clin Infect Dis 2012; 54(suppl_1): S8–S15.
4. Roden M, Zaoutis T, Buchanan W, Knudsen T, Sarkisova T, Schaufele R, et al. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis 2005; 41(5): 634–653.
5. Ibrahim A, Spellberg B, Edwards J. Iron acquisition: a novel perspective on mucormycosis pathogenesis and treatment. Curr Opin Infect Dis 2008; 21(6): 620–625.
6. Mulki R, Masab M, Eiger G, Perloff S. Lethargy and vision loss: successful management of rhinocerebral mucormycosis. BMJ Case Reports 2016; bcr2016215855.
7. Sahota R, Gambhir R, Anand, Dixit A. Rhinocerebral mucormycosis: report of a rare case. Ethiop J Health Sci 2017; 27(1): 85.
8. Spellberg B, Edwards J, Ibrahim A. Novel perspectives on mucormycosis: pathophysiology, presentation, and management. Clin Microbiol Rev 2005; 18(3): 556–569.
9. Reddy S, Rakesh N, Chauhan P, Sharma S. Rhinocerebral mucormycosis among diabetic patients: an emerging trend. Mycopathologia 2015; 180(5–6): 389–396.
10. Hosseini S, Borghei P. Rhinocerebral mucormycosis: pathways of spread. Eur Arch Otorhinolaryngol 2005; 262(11): 932–938.
11. Kolekar J. Rhinocerebral mucormycosis: a retrospective study. Indian J Otolaryngol Head Neck Surg 2015; 67(1): 93–96.
12. Dimaka K, Mallis A, Naxakis S, Marangos M, Papadas T, Stathas T, et al. Chronic rhinocerebral mucormycosis: a rare

case report and review of the literature. Mycoses 2014; 57(11): 699–702.
13. Dellinger R, Levy M, Carlet J, Bion J, Parker M, Jaeschke R, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med 2008; 36(1): 296–327.
14. Reed C, Bryant R, Ibrahim A, Edwards, Jr. J, Filler S, Goldberg R, et al. Combination polyene-caspofungin treatment of rhino-orbital-cerebral mucormycosis. Clin Infect Dis 2008; 47(3): 364–371.
15. Spellberg B, Walsh T, Kontoyiannis D, Edwards Jr J, Ibrahim A. Recent advances in the management of mucormycosis: from Bench to Bedside. Clin Infect Dis 2009; 48(12): 1743–1751.
16. Riley T, Muzny C, Swiatlo E, Legendre D. Breaking the mold: a review of mucormycosis and current pharmacological treatment options. Ann Pharmacother 2016; 50(9): 747–757.
17. Baugh WP. Rhinocerebral mucormycosis treatment & management: approach considerations, amphotericin B, other antifungal therapies [online] 2018 [cit. 13.12.2019]. Available from URL: https://emedicine.medscape.com/article/227586-treatment#d11.

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