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Case Report

Medicine Section

Rhino-Orbital-Cerebral Mucormycosis: Successful Medical Management in a Resource Poor Setting

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ABSTRACT

Mucormycosis is commonly associated in diabetes. Rhino orbital cerebral mucormycosis (RCOM) is the most common type of presentation. Here we present a case of rhino orbital cerebral type of mucormycosis in a naïve Type 1 diabetic whose symptoms became apparent immediately after the correction of hyperglycaemia and ketoacidosis. Though, extensive surgery is the accepted modality of treatment, this case was managed by 14 day intravenous Amphotericin B with some residual diminution of vision in the right eye. This case is reported to emphasize the importance of early diagnosis and timely management is critical for the survival. The present concept of extensive surgical procedures may be challenged by timely medical management with similar efficacy.

Keywords: Diabetes, Proptosis, Ketoacidosis, Sepsis

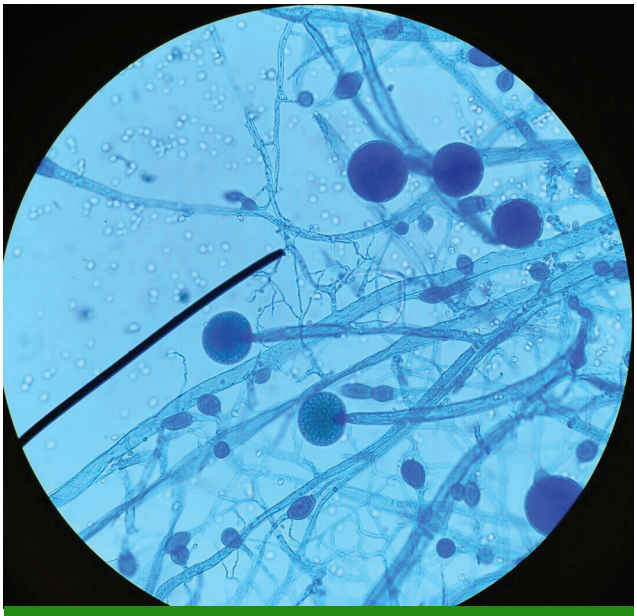
CASE REPORT

A 20-year-old gentleman was hospitalized to SCB Medical College, Cuttack in the Department of Medicine with complaints of pain in the abdomen, vomiting, breathlessness and altered sensorium for one day without any significant past medical or surgical history. On examination he was drowsy and Glasgow coma scale was 8/15. He was of thin body built and dehydrated. His temperature was 101°F, Heart rate was 112/min and regular, Respiratory rate was 42/min and acidotic, blood pressure was 94/60 mmHg. Systemic examination revealed no abnormality. Point of care investigations revealed total leukocyte count 16,000/cmm with 80% polymorphs, haemoglobin-10 g/dl, random plasma glucose 540mg/dl, HbA1c-9.8% and urine ketone body was positive. Arterial blood gas analysis showed pH=7.28, pCO2=12, HCO3 - 5.9 with base excess of (-17.3), SpO2 94%, anion gap =28.5. He was provisionally diagnosed to be Type 1 diabetes mellitus with ketoacidosis and sepsis. Patient was shifted to ICU and managed with intravenous insulin, piperacillin-tazobactam and adequate IV fluids. On day 2, C-peptide value was 0.48ng/ml (normal 0.81-3.85), urine pus cells 4-6/ high power field liver function and renal function tests were normal. On the 3rd day we noticed that the face was deviated to left side and was associated with ptosis and diplopia in the right eye [Table/Fig-1]. On the 4th day he developed proptosis, complete ophthalmoplegia, chemosis and loss of vision of right eye. Examination revealed cranial nerve II, III, IV, V1, V2, VI and VII palsies on the right side which was lower motor neuron type. On examination of the nose black necrotic mass was found in right nostril. MR imaging of brain, para-nasal sinuses and orbit showed enhanced mucosal thickening with saggy enhancement of right ethmoid, sphenoid and maxillary sinuses extending up to the nasopharynx suggestive of chronic inflammatory entity.

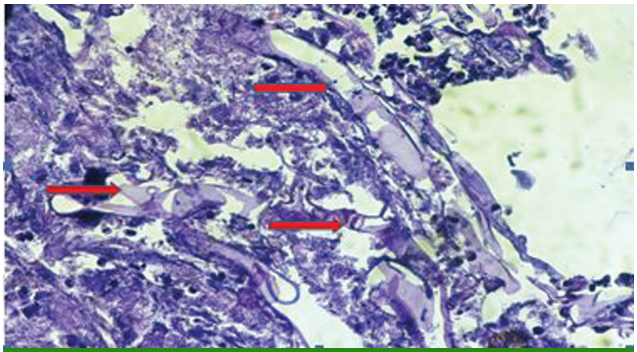
Endoscopic curettage biopsy was done and sent for histopathological and microbiological study. Potassium hydroxide (KOH) mounts revealed broad non-septate branched hyphae which on culture revealed rhizopus species. The microbiological culture report of biopsy specimen was received on 7th day. Lacto phenol cotton blue (LPCB) mount of cottony white growth from Sabouraud Dextrose Agar (SDA) showed broad aseptate hyaline hyphae with sporangiophores and sporangia filled with sporangiophores [Table/Fig-2]. The sporangiophores appeared erect, branched, forming large terminal spherical multispored sporangia, without apophysis and with well-developed subtending columella. As there were

[Table/Fig-1]: Right-sided ptosis, proptosis and facial palsy (lower motor neuron type).

no rhizoids so phenotypically the genus was confirmed to be mucor. The patient denied extensive surgical intervention. He was started with conventional injectable Amphotericin B in a dose of 1.5 mg/kg/day diluted in 500 ml of 5% dextrose and transfused over a period of 3-4 hours. On 10th day the histopathology features were consistent with angio-invasive mucormycosis [Table/Fig-3] and the final diagnosis was made as Rhino-orbital-cerebral mucormycosis (ROCM). Amphotericin B was continued for 14 days. The patient was discharged on day 24 with minimal residual visual impairment in right eye. The patient was followed-up till 10 months and was still having residual ptosis and diminution of vision in right eye.



[Table/Fig-2]: Non-septate branched hyphae of mucor (100X).



[Table/Fig-3]: LCB mount showing broad hyaline, aseptate hyphae with sporangiophores.

DISCUSSION

Mucormycosis is an opportunistic and frequently fulminant fungal infection caused by members of the family Mucoraceae, order Mucorales and class Zygomycetes. Among these, *Rhizopus*, *Mucor*, *Absidia* and *Cunningmella* species are ubiquitous fungi. The major predisposing factors for acquisition of mucormycosis are uncontrolled diabetes mellitus (DM) with ketoacidosis, haematological malignancies, haematopoietic stem cell transplantation, solid organ transplantation and immunosuppression [1]. Route of transmission is usually inhalation of spores. Mucormycosis mostly manifests as rhino cerebral, pulmonary, cutaneous, gastrointestinal and disseminated form. Rhino-orbito-cerebral mucormycosis (ROCM) is the most serious and fatal form of the disease with a mortality rate of 70-100% if not treated adequately [2]. There is no published literature of efficacy of medical management as compared to extensive surgical procedures. We managed successfully a case of ROCM with 14 days course of intravenous Amphotericin B.

Mucormycosis is an increasingly emerging life threatening infection particularly in uncontrolled diabetic patients. Rhino-cerebral mucormycosis is the most common and fatal form of the disease and presents in 35-50% of all the cases of mucormycosis [3]. Poorly controlled DM particularly if associated with ketoacidosis is an important predisposing factor for development of ROCM. DM is associated in 36%-88% of cases of mucormycosis [4]. This increased association has been ascribed to diabetic acidosis which is responsible for decreased neutrophil chemotaxis and phagocytosis. It also inhibits the iron binding of transferrin resulting in increased proportion of unbound iron which promotes the growth of mucor which is ferrophillic [5]. Rhizopus species is responsible for most of the rhinocerebral cases [6]. Our patient was a young patient of naïve Type 1 DM with ketoacidosis which is an important risk-factor for development of mucormycosis. He developed ptosis, proptosis, opthalmoplegia and visual loss along with multiple cranial nerve palsies on right side. It is well known that ROCM is common in uncontrolled DM but what is unusual in our case is that diabetes presented as ROCM and sepsis. No other similar case has been reported earlier in published literature.

Genera from the order Mucorales (*Rhizopus, Rhizomucor, Mucor, Absidia, Apophysomyces, Cunninghamella,* and *Saksenaea*) are the aetiologic agents for rapidly progressive, angioinvasive infections with rhinocerebral, orbital, pulmonary, disseminated, cutaneous, or (rarely) gastrointestinal involvement (mucormycosis). The other order of class Zygomycetes is Entomophthorales (*Basidiobolus ranarum* and *Conidiobolus coronatus*). Entomophthoromycosis are chronic indolent subcutaneous infections in immunocompetent persons residing in tropical climates [7]. As both mucorales and entomophthorales are rapid growers with similar clinical presentation and cultural characteristics it is important to confirm the genus by phenotypic or genotypic methods as in our case the isolate was phenotypically confirmed to belong to genus *Mucor*. Histopathology of a biopsy material from deep tissue if available is specific and reliably establishes the diagnosis.

Ideal management requires appropriate antifungal therapy, treatment of the underlying cause and surgical debridement whenever possible [8]. Jung et al., and Sachdeva in their

case series reported 100% mortality in ROCM with diabetic ketoacidosis [9,10]. Many of the case series opted extensive surgical procedures as a desperate measure. We had no options other than medical management as the patient did not consent for surgery. Our patient responded well to intravenous 14-day treatment with conventional Amphotericin B. Though visual loss persisted in the right eye, his left eye remained unaffected. What we can't explain is that why the symptoms of ROCM deteriorated after the correction of plasma sugar and recovery from ketoacidosis. There has been absolutely no literature in this regard.

CONCLUSION

RCOM may be a presenting opportunistic fungal infection even in a naïve DM. Though the mortality and morbidity are extremely high early diagnosis and prompt aggressive treatment can reduce the mortality. Timely medical management can be of equal or better efficacy than that of contemporary extensive devitalizing surgical procedures.

REFERENCES

[1] Gamaletsou MN, Sipsas NV, Roilides E, Walsh TJ. Rhino-orbital-cerebral mucormycosis. *Curr Infect Dis Resp*. 2012; 14: 423-34.

[2] Prabhu RM, Patel R. Mucormycosis and entomophthoramycosis: a review of the clinical manifestations, diagnosis and treatment. *Clin Microbiol Infect*. 2004;10(Suppl 1):31-47.

[3] Jayachandran S, Krithika C. Mucormyco¬sis presenting as palatal perforation. *Indian J Dent Res*. 2006;17(3):139–42.

[4] Petricos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestation of Mucormycosis. *Clin Infect Dis*. 2012; 54(S1): S23-24.

[5] Scheckenbach K, Cornely O, Hoffmann TK, Engers R, Bier H, Chaker A et al. Emerging therapeutic options in fulminant invasive rhinocerebral mucormycosis. *Auris Nasus Larynx.* 2010;37(3):322–28.

[6] Gonzalez CE, Rinaldi MG, Sugar AM. Zygomycosis. *Infectious Disease Clinics of North America*. 2002;16:895-914.

[7] Prabhu RM, Patel R. Mucormycosis and entomophthoramycosis: a review of the clinical manifestations, diagnosis and treatment. *Clin Microbiol Infect*. 2004;10(Suppl 1):31-47.

[8] Gamaletsou MN, Sipsas NV, Roilides E, Walsh TJ. Rhino-orbital-cerebral mucormycosis. *Curr Infect Dis Rep*. 2012;14(4):423-34. doi: 10.1007/s11908-012-0272-76.

[9] Jung SH, Kim SW, Park CS, Song CE, Cho JH, Lee JH, et al. Rhinocerebral mucormycosis: consideration of prognos¬tic factors and treatment modality. *Auris Nasus Larynx.* 2009;36(3):274–79.

[10] Sachdeva K. Rhino-ocular-cerebral mucormycosis with multiple cranial nerve palsies in diabetic patients: Review of six cases. *Indian J Otolaryngology Head Neck Surg*. 2013;65(4)375-79.

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