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Retrobulbar Amphotericin B in Patients of Rhino-Orbital-Cerebral Mucormycosis (ROCM) - A Case Series

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Aims and Objectives

To identify outcome of Retrobulbar Amphotericin B in severely affected eye in patients of ROCM

Keywords: Amphotericin B, Rhino-orbital-cerebralmucormycosis, Retrobulbar

1. Introduction

Mucormycosis is an uncommon opportunistic infection, which represents the third most common angio-invasive fungal infection.[1]Mucormycosis-infection of the sinuses is a form of life-threatening invasive fungal sinusitis that typically affects immunocompromised individuals with an impaired neutrophilic response in uncontrolled diabetes mellitus, acquired immunodeficiency syndrome, iatrogenic immunosuppression and haematologicalmalignancies.[1] Overzealous use of steroids suppress immunity. Clinically, rhinocerebral-mucormycosis can present with atypical signs and symptoms similar to complicated sinusitis, such as nasal blockade, crusting, proptosis, facial pain and oedema, ptosis, chemosis, and even ophthalmoplegia with headache and fever and various neurological signs and symptoms if intracranial extension is present.A black eschar often seen in the nasal cavity or over the hard palate region, is characteristic.[2] Retrobulbar Amphotericin B can be given to patients who are awaited for surgical approach. If Retrobulbar Amphotericin B is given along with intravenous antifungal agent and endoscopic debridement, it may decrease intracranial extention of disease and prevent further local pregress of disease. Patients who are not fit for surgery or who are not willing for orbital exenteration for cosmetic reason are also the candidates for Retrobulbar Amphotericin B.There are very few studies for Retrobulbar Amphotericin B and are not enough to justify role of retrobulbar.

2. Materials and Methods

Prospective interventional case series was done at tertiary care hospital. Patientswith signs and symptoms like unilateral facial numbness or swelling , discoloration of skin, loose teeth, orbital pain, loss of vision, drooping of upper eyelid,proptosis, decreased ocular movements were taken with the following inclusion and exclusion criteria.

Inclusion criteria:

Pt having any one of followingcriteria for confirmation of disease were diagnosed as ROCM[3]

1) Positive 10%KOH mount for mucormycosis
2) Culture / HPE positive finding on tissue biopsy.
3) Positive radiological finding of orbital involvement by MM i.e. optic neuritis and/or paranasal sinuses involvement, etc.

Exclusion criteria:

1) Patients not giving consent
2) Patients not falling into the inclusion criteria
3) Patients with pure indication for orbital exenteration

SION Scoring system for evaluation of need of orbital exenteration in ROCM

This scoring is based on clinical signs and symptoms, direct and indirect ophthalmoscopy findings and radiological imaging. If score is more than or equal to 23, it's an indication for orbital exenteration.

1) Clinical signs and symptoms :

	0	2	3
Vision	Normal	Decreased V/A	Total blindness
Pupil	Normal	RAPD	Fixed
Ocular movement	Normal	EOM palsy/Diplopia	Fixed eyeball
Proptosis	Absent	+/-	Present
Intracranial spread	No	Headache, projectile vomiting, confusion	Altered consciousness

2) Ophthalmoscopy examination :

Fundus changes	Points
Normal	0
Cotton wool spots	1
Congested tortuous retinal blood vessels	2
Optic disc edema	2
CRVO	2
CRAO	2
Retinal detachment	2
Choroidal folds	2
Optic disc pallor	2
Total	**15**

3) Imaging

Imaging changes	Points
Orbital involvement	3
Intracranial spread/SOF/IOF	3
Optic neuritis	3
Sphenoid sinus involvement	2
Frontal sinus involvement	1
Ethmoid sinus involvement	1
Infratemporal fossa involvement	1
Maxillary sinus involvement	1

After taking consent in both English and local language, patients were taken for the case series who were falling into the inclusion criteria after explaining the procedure and its advantages and disadvantages. 50 mg of deoxycholate Amphotericin B is diluted in 14 ml of distilled water. 3.50 mg/ml Amphotericin B (1 ml) is taken in syringe with 26 gauge needle, it is injected in Retrobulbar space by piercing skin below medial canthus at lower lid.Further dose given approximately 72 hours later.

Table 1: Distribution of patients according to sex:

Female	4
Male	5
Total	9

Table 2 : Distribution of patients according to spread of disease:

Type of spread	No.(%)
Focal	2(22.3%)
Diffuse	7(77.7%)

Table 3: Distribution of patients according to presence of systemic illnesses

Presence of Systemic illnesses	No.(%)
Yes	7(77.78%)
No	2(22.22%)

Table 4: Distribution of patients according to no. of TRAMB given

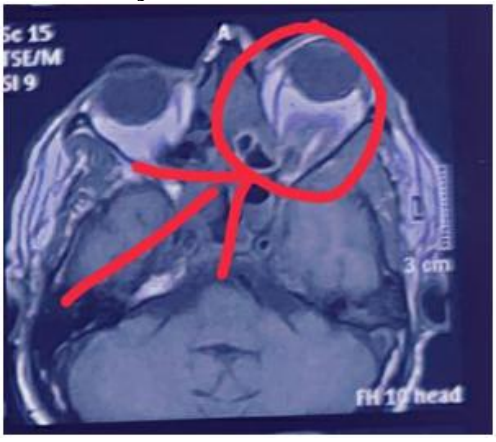
No. of TRAMB given	Type of Spread of ROCM	
	Focal (%)	Diffuse (%)
2	2(22.22%)	3(33.33%)
3	0	4(44.44%)

All of above patients underwent functional endoscopic debridement surgery.

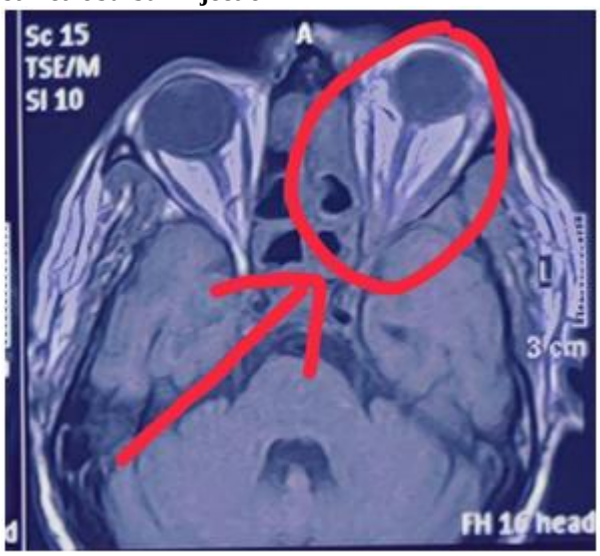
 # Focalintraorbital spread:

Image 1: Resolved focal lesion with improved MRI findings

Pre Retrobulbar injection



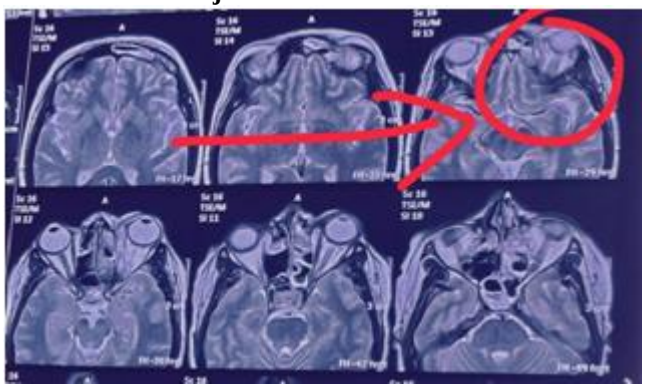
Post Retrobulbar injection



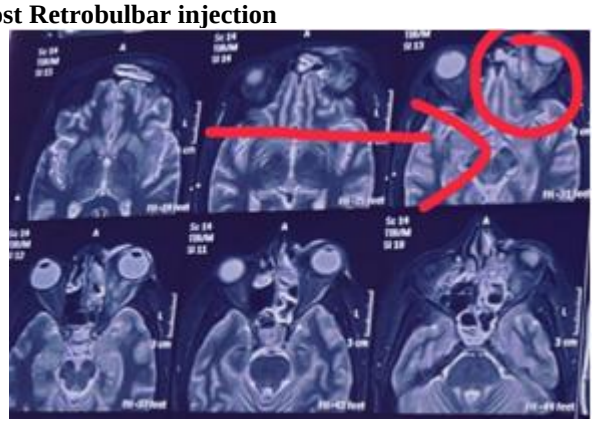
 # Diffuse intraorbital spread:

Image 2: Decrease local inflammation as well as delimitation of intracranial spread

Pre Retrobulbar injection



Post Retrobulbar injection



3. Discussion

Mucormycosis is a potentially life-threatening [1],which requires prompt recognition and treatment. In progressive orbital disease, exenteration may be recommended; however, there are no clear guidelines regarding optimal timing for exenteration. Although potentially life-saving, exenteration carries significant complications including certain blindness, cosmetic disfigurement and psychosocial

trauma.Our patients were treated initially with intravenous liposomal amphotericin B and to prevent further local orbital as well as intracranial extention of disease they were given Retrobulbar Amphotericin B.Faced with progressive disease on maximal systemic medication and after sinus debridement, retrobulbar anti-fungal treatment was selected as a non-surgical option to potentially halt orbital progression. Very few studies have been recorded for Retrobulbar Amphotericin B in patients of Rhino-ocular-cerebral mucormycosis.[5,6,7]Retrobulbar antifungal injection is a viable option to consider in halting orbital progression and providing an opportunity to avoid exenteration and maintain cosmetics of eye.Patient who didn't give consent for exenteration and who were awaited for fitness for GA showed good psychological response .

In this case series total 9 patients were taken. 2 patients (22.3%)were with focal(orbital) involvement of ROCM and 7 patients (77.7%)were with intracranial spread of ROCM.5 patients (55.55%)were male and 4patients (44.45%)were female. All 4 female patients were having diffuse ROCM.Out of 5 male patients 2 patients were having focal ROCM and 3 patients were having diffuse ROCM. 2 male patients who were having focal ROCMshowed good response clinically as well as radiologically. Other all 7 patients with diffuse ROCM didn't show satisfactory clinical response but they vary in their radiological findings as some patients showed improvement radiologically.Except 2 patients all were associated with systemic illnesses like DM, HTN, CKD, IHD. All patients in this case series were operated for functional endoscopic debridement as well as given daily systematic antifungal according to standard guidelines.[8] 2patients in this case series went for exentration later on as per surgical need.

In 2017 Kristin Hirabayashi et al did a study of Retrobulbar Amphotericin B in an immunocompromised patient and some other studies have also been done but they are not giving exact information about role of transcutaneous antifungal agent in ROCM.[5]

In 1996, J D Luna et al did a study of intraconal Amphotericin B for treatment of ROCM to achieve higher doses of the drug at the site of infection and better cosmic and psychological results.[9]

In 2022, Ramesh Murthy et al did a study of Retrobulbar injection Amphotericin B using intravenous cannula for post COVID-19 ROCM. Patients were more compliant and less distressed with this method compared with being given on injection with a needle daily.[10]

4. Conclusion

Retrobulbar injection Amphotericin Balong with nasal endoscopic debridement surgery and intravenous antifungal agent in patients of Rhino-ocular-cerebral mucormycosisreducesorbital extention of disease if given in early stages and prevent exentration in orbital extention. Patients of focal ROCM showed good response whereas patients with diffuse ROCM showed variable results.Patients felt good cosmetically as orbital structures were preserved. Through transcutaneous route increased concentration of drug is delivered in Retrobulbar space. Patients who were not willing for surgical approach or who were not giving consent for orbital exenterationfelt good clinical as well as psychological response.

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