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Original Research Article

The Colt for Phoenix: Mucormycosis in COVID-19 times

Sharanabasamma M[1], **Varshitha B M**[1,*]

[1]*Dept. of Ophthalmology, Rajiv Gandhi University of Health Sciences, Bengaluru, Karnataka, India*

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ABSTRACT

Purpose: To compare whether treatment incorporating retrobulbar liposomal amphotericin B for rhino-orbital mucormycosis in ongoing covid 19 time can reduce the risk of exenteration compared to treatment with intravenous liposomal amphotericin B without compromising the survival rate.

Materials and Methods: In this retrospective, comparative institutional study 23 patients of biopsy-proven mucormycosis and radiographic evidence of orbital involvement were enrolled and 13 were divided into group A and 10 in group B. Group A consists of patients who were treated with retrobulbar liposomal amphotericin B and group B consists of patients who were treated with intravenous liposomal amphotericin B.

Results: In group A, out of 13 patients, only one patient underwent exenteration and the patient survived post exenteration. Among the other 12 patients, 10 patients survived. In group B, out of ten, four patients were subjected to exenteration, out of which two survived. Among the other six patients without exenteration, five of them survived.

Conclusion: In comparison, patients who were treated with retrobulbar amphotericin B had a lower risk of disfiguring exenteration without an apparent increase in the risk of mortality.

1. Introduction

The tale goes in ancient Greek mythology that the phoenix (a long-lived bird) is born again by rising from the ashes of its predecessor.

Such is the tale of this pathogen, which in recent times has risen like the phoenix from the ashes. [1]

Like most monsters, a Phoenix could be killed, by being shot with the 'Colt'.

Rhino-orbital mucormycosis is a infection of the orbital tissues by the fungus Mucor of the class Phycomycetes (order Mucorales). [2]

Mucormycosis is a severe and often fatal acute fungal disease. The angio-invasive behavior of the fungus leads to thrombosis, tissue necrosis, and invasion of adjacent tissues, thereby minimizing the local availability of systemic antifungals and making aggressive surgical approaches necessary. [3,4]

When affecting the sinus, rhinoorbito-cerebral mucormycosis (ROCM) can extend to the orbital tissues, increasing the risk of central nervous system (CNS) involvement and death. In such cases, exenteration is commonly indicated. [4–6]

With unclear guidelines regarding the optimal timing for exenteration, given this procedure's disfiguring outcome, alternative methods of treatment should be considered.

Unique and potentially globe sparing approach is retrobulbar antifungal injection

* *Corresponding author*.
E-mail address: bmvarshitha86@gmail.com (Varshitha B M).

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2. Materials and Methods

Retrospective, institutional study, carried out in the department of ophthalmology from March 2021 to June 2021.

23 patients of biopsy proven mucormycosis and radiographic evidence of orbital involvement were enrolled in this study.

2.1. Were in group A and 10 in group B

Group A consists of patients who were treated with retrobulbar liposomal amphotericin B and group B consists of patients who were treated with intravenous liposomal amphotericin B.

The patients of group A were treated with retrobulbar liposomal amphotericin B (1ml of 3 mg/kg/day LAMB with an antecedent retrobulbar injection of anesthetic comprised of 2 ml of 2% lidocaine) and the patients were given five retrobulbar injections during their course in the hospital.

And group B patients were treated with intravenous liposomal amphotericin B (5mg /kg/day liposomal Amphotericin B in 500 mL D5 with 10 Units Human insulin regular), intravenous micafungin 6mg/kg/day every 24 hours, and oral posaconazole 300 mg every 24 hour for a week.

3. Results

In this study which included 23 patients of rhino orbital mucormycosis, in which group A patients who were treated with retrobulbar amphotericin B and group B patients who were treated with intravenous amphotericin B.

Out of 13 patients in group A, only one patient underwent exenteration and the patient survived post exenteration. Among the other 12 patients, 10 patients survived.

In group B, out of ten, four patients were subjected to exenteration, out of which two survived. Among the other six patients without exenteration, five of them survived.

4. Discussion

Mucormycosis is a potentially life-threatening condition which requires prompt recognition and treatment.

Challenges in treating ROCM due to its underlying pathogenesis in which endothelial cell damage leads to vascular thrombosis decreasing the efficacy of systemic antifungals[5].

In progressive orbital disease, exenteration may be recommended; however, there are no clear guidelines regarding optimal timing for exenteration.[6,7]

Although potentially life-saving, exenteration carries significant complications including certain blindness, cosmetic disfigurement and psychosocial trauma.[8]

Management of mucormycosis consists of immediate initiation of systemic anti-fungals.

In the recent years, with the purpose of reducing mortality and the need for potentially disfiguring procedures such as exenteration, several alternative, and/or adjuvant treatments have been proposed, including modern antifungal medications (e.g., posaconazole), local antifungals, hyperbaric therapy, and cautious debridement.

In 1969, Fleckner and Goldstein[9] reported 2 cases of rhino-orbital mucormycosis treated with both systemic and local irrigation of amphotericin B. Since then, descriptions of local antifungal irrigation both intra- and postoperatively have sporadically appeared in the medical literature.[10–12]

In the literature of invasive fungal infections caused by the Mucoraceae family of fungi treated with orbital irrigation of amphotericin B.

Treatment regimens reported in the literature consist of daily to 4 times daily irrigations of amphotericin B, with concentrations ranging from 0.25 to 1.25mg/ml, and volumes of 1 to 15ml. Durations of treatment range from 5 days to 4 weeks. Only 1/10 required orbital exenteration, and most retained excellent visual acuity; none of the patients died from the primary infection.[13]

Luna et al presented a case of rhino-orbital mucormycosis successfully treated with orbital irrigation of amphotericin B through an Abbocath No. 18 catheter (Hospira, Inc., Lake Forest, IL, U.S.A.) directly in the muscle cone.[13]

Saiff et al. reported a case of ROCM associated with left temporal cerebritis on nuclear MRI that was successfully treated with retrobulbar applications of amphotericin B, which resulted in avoidance of exenteration.[14]

And few other studies have been reported successful treatment after retrobulbar amphotericin B (TABLE)

Liposomal amphotericin B is often the antifungal agent of choice due to superior survival rates and the ability to achieve higher blood levels without the immediate nephrotoxic side effects commonly seen with the deoxycholate formulation.[15]

Intraorbital irrigation of amphotericin B, which is not yet routinely used in the management of this devastating and frequently fatal disease, is a modality that was found to be useful.

The use of this technique is recommended in all cases of rhino-orbital mucormycosis infections, except for cases in which exenteration is clearly indicated or when palliative therapy has been decided upon.

In this study,

Group A out of 13 patients, only one patient underwent exenteration and the patient survived post exenteration. Among the other 12 patients, 10 patients survived.

In group B, out of ten, four patients were subjected to exenteration, out of which two survived. Among the other six patients without exenteration, five of them survived.

Thus this study suggests that, with retrobulbar amophotericin B the incidence of disfiguring exenteration

GROUP A

CASES	AGE	SYSTEMIC ILLNESS	EXENTERATION	DEATH	VISUAL ACUITY ON ADMISSION	FINAL VISUAL ACUITY
1	55	DIABETIC	NO	NO	6/60	6/24
2	32	NIL	NO	NO	6/12	6/12
3	48	HYPERTENSIVE	NO	NO	6/24	6/24
4	28	NIL	NO	NO	6/9	6/6
5	39	NIL	NO	NO	6/18	6/6
6	42	NIL	NO	NO	6/36	6/12
7	62	DIABETIC AND HYPERTENSIVE	NO	YES	6/60	-
8	70	DIABETIC WITH CKD	YES	NO	1/60	-
9	57	NIL	NO	NO	3/60	6/60
10	44	DIABETIC	NO	NO	6/36	6/36
11	78	NIL	NO	YES	2/60	-
12	42	DIABETIC AND HYPERTENSIVE	NO	NO	6/24	6/12
13	37	NIL	NO	NO	6/12	6/6

Fig. 1:

GROUP B

CASES	AGE	SYSTEMIC ILLNESS	EXENTE-RATION	DEATH	VISUAL ACUITY ON ADMISSION	FINAL VISUAL ACUITY
1	63	NIL	YES	NO	1/60	-
2	42	DIABETIC	NO	NO	6/24	6/18
3	32	NIL	NO	NO	6/12	6/12
4	66	DIABETIC	YES	YES	2/60	-
5	59	DIABETIC AND HYPERTENSIVE	YES	NO	2/60	-
6	41	NIL	NO	NO	6/36	6/12
7	39	NIL	NO	YES	6/12	-
8	27	NIL	NO	NO	6/9	6/6
9	38	HYPERTENSIVE	YES	YES	3/60	-
10	46	NIL	NO	NO	6/18	6/9

Fig. 2:

Results from patients who received postoperative local irrigation with amphotericin B

Author	Underlying systemic illness	Regimen of local amphotericin B irrigation	Adjunct therapy	Final visual acuity	Exenteration	Outcome
Kohn and Hepler[3] (n = 2)	Case 1: DKA	1 mg/ml once daily (volume and treatment duration not specified), surgical packing of orbit and sinuses	Debridement, ethmoidectomy, IV AmB	Not specified, no vision loss reported	No	Alive at 3 years
	Case 2: DKA	1 mg/ml once daily (volume and treatment duration not specified), surgical packing of orbit and sinuses	Debridement, ethmoidectomy, IV AmB	Not specified, no vision loss reported	No	Alive at 4 years
Luna et al.[13]	DKA	Twice daily irrigation × 9 days (1 mg/ml, volume not specified)	IV AmB	NLP	No	Alive at 18 months
Seiff et al.[15] (n = 3)	Case 1: ALL	Intraoperative irrigation followed by 3–4 ml (0.25–1 mg/ml) 3 to 4 times daily × 5–14 days	Stop chemotherapy, IV AmB	20/20	No	Alive at 20 months
	Case 2: Diabetes mellitus, renal transplant	Intraoperative irrigation followed by 3–4 ml (0.25–1 mg/ml) 3 to 4 times daily × 5–14 days	Stop immunosuppressive therapy, conservative debridement	Not specified	Yes	Alive at 4 years
	Case 3: AIDS	Intraoperative irrigation followed by 3–4 ml (0.25–1 mg/ml) 3 to 4 times daily × 5–14 days	IV AmB, conservative debridement	20/100	No	Died at 1 month postoperative from unrelated causes
Pelton et al.[14]	Diabetes mellitus	15 ml (1 mg/ml) twice daily × 16 days, surgical packing with amphotericin-soaked gauze	Debridement with frozen sections, IV LAmB, hyperbaric oxygen	20/25	No	Alive at 18 months
Kim et al.[16]	DKA	10 ml (1 mg/ml) twice daily × 9 days	Debridement, IV LAmB	20/50	No	Alive, unknown follow-up period
Gelston et al.[18]	DM	5 days duration, volume, concentration and frequency not specified	Debridement, IV LAmB, Interferon, hyperbaric oxygen, posaconazole	20/60	No	Alive at 12 months
Kahana and Lucarelli[17] (n = 2)	Case 1: AIDS	2 ml (1.25 mg/ml) once daily × 4 weeks	Debridement, IV LAmB, poscaonazole, AmB nasal spray	Not specified	No	Survived infection, later died from hepatorenal failure
	Case 2: Pre-B ALL	1 ml (1 mg/ml) 2 to 3 times daily × 2 weeks	Debridement, IV LAmB, poscaonazole, AmB nasal spray	Not specified	No	Survived infection, later died from intracranial hemorrhage

AIDS, acquired immunodeficiency syndrome; ALL, acute lymphoblastic leukemia; AmB, amphotericin B; DKA, diabetic ketoacidosis; DM, diabetes mellitus; IV,

Fig. 3:

was lower compared to intrvenous amphotericin B.

Needs furthermore studies to conclude this.

5. Conclusion

Rhino orbital mucormycosis is best managed by immediate initiation of intravenous anti-fungals, reversing the patient's immunocompromised state. In the setting of progressive orbital disease, retrobulbar amphotericin B treatment should be considered as an option prior to exenteration.

In this study patients who were treated with retrobulbar amophotericin B had a lower risk of disfiguring exenteration without an apparent increase in the risk of mortality.

6. Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

7. Source of Funding

None.

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Author biography

Sharanabasamma M, Associate Professor

Varshitha B M, Junior Resident https://orcid.org/0000-0001-9617-1039

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