CRIMSON PUBLISHERS
Wings to the Research

Experiments in
Rhinology & Otolaryngology

ISSN 2637-7780

Research Article

Invasive Fungal Sinusitis: Management of the Orbit, a Multi Institutional Study and Review of Literature

Abhishek Kumar Ramadhin[1]* and Diptarka Bhattachayya[2]

[1]*Deportment of Otolaryngology, Elizabeth Medical Center, USA*

[2]*Deportment of Otolaryngology, Sinai Hospital of Baltimore, USA*

***Corresponding author:** Abhishek Kumar Ramadhin, Clinical fellow, Rhinology, Inst. St. Elizabeth Medical Center, Otolaryngology, Boston, MA, USA

Submission: May 11, 2018; **Published:** June 08, 2018

Abstract

Introduction: Invasive fungal sinusitis is an uncommon disease but with high mortality and morbidity, and the treatment is multi-modal However, the management of the orbit is still unclear, with a fine line between orbital conservation and worsening disease outcomes.

Aim: This study is an anonymized, multi institutional retrospective study undertaken in two large tertiary referral centers, whereby patient records and charts from 2007 to 2017 were systematically reviewed, and patients meeting the inclusion criteria were selected.

Materials and methods: A total of 47 patients (n=47) were found to fulfill the inclusion criteria. Out of these, 14 were found to have extensive intraorbital disease, and 33 were found to have limited periosteal involvement. In all, a total of 23 patients underwent orbital exenteration.

Results: In our series of patients, we found that extensive orbital disease patients need orbital exenteration early, even though the survival benefit is unclear. However, in patients with limited orbital disease, a trial of conservative management yielded orbital conservation in 72.7% patients, and it does seem that the results for limited anterior disease is even better, achieving 85% conservation

Introduction

In the last century, fungal diseases of the par nasal sinuses have emerged as a major challenge for physicians, clinical microbiologists and scientists. The incidence of mitotic infection and the number and diversity of pathogenic fungi have increased dramatically in the recent years. Both immune competent and immune compromised individuals are at risk. The growing breadth, complexity and significance of mycological disease needs an in depth study of treatment of fungal rhino sinusitis that is increasing in incidence and often difficult to diagnose and manage. While there is a fair amount of literature about Invasive Fungal Sinusitis (IFS), still there exists controversy regarding the orbital management protocol in this disease, and this article attempts to take an in depth look at this particular aspect, and also review current existing literature.

Materials and Methods

This study is an anonym zed, multi institutional retrospective study undertaken in two large tertiary referral centers, whereby patient records and charts from 2007 to 2017 were systematically reviewed, and patients meeting the inclusion criteria were selected. The data was assessed regarding medical vs. surgical management of orbital fungal invasive disease and statistical analysis done. A literature review was conducted and a comparative analysis done. The IRB approval was obtained prior to this (ENT/ECARP/14/63).

Inclusion criteria

As this is a retrospective study, the criteria were:

a. Proven fungal tissue invasion noted on tissue samples irrespective of eventual fungal culture results.

b. Orbital involvement described on initial imaging study which in all cases was CT Para nasal Sinuses.

c. Duration of symptoms less than 1month at the time of first presentation to the study center

d. Follow up of 6 months.

Exclusion criteria

Patients who had symptoms greater than 3months at initial presentation to the study center or patients whose tissue biopsy showed granulomatous inflammation and fibrosis. Patients whose initial imaging showed intracranial disease was also excluded, as these patients have a uniformly dismal prognosis, and the purpose of this study is to look at management of Sino-orbital disease. The

patients who had extensive orbital disease, defined on imaging as intraconal disease spread, involvement of orbital apex or extensive Loss of contrast enhancement in orbital soft tissue suggestive of necrosis within, OR by direct visualization of necrosis extending extensively intra orbit ally during Endoscopic debridement underwent early debridement.

In patients who were found to have limited orbital disease, defined on imaging as orbital Contrast enhancement and on direct endoscopic visualization as disease extending up to periosteum, but not extensive enough as above, were given a trial of conservative management with cottonoid soaked Amphotericin B at 0.5mg/ml 3times per day Figure 1-6. This was done under direct visualization with bedside endoscopy for anterior disease adjacent to the lamina and especially for posterior disease adjacent to the sphenoid. This was supplemented by systemic antifungal treatment, i.e. Intravenous Amphotericin B (1.5mg/kg/day in patients receiving regular Amphotericin B and 5mg/kg/day in patients receiving liposomal Amphotericin B) with additional oral voriconazole added to patients diagnosed with aspergillus species as the causative agent, and nasal debridements every week [1]. If the patient was found to be worsening as per clinical symptoms (worsening of vision, new onset opthalmoplegia, diplopia or direct visualization of disease progress during endoscopy, orbital exenteration was done at that stage. Liposomal Amp B was reserved for patients who had toxicities from D Ampho B, and Voriconazole was added for patients who had Aspergillus as the causative agent.

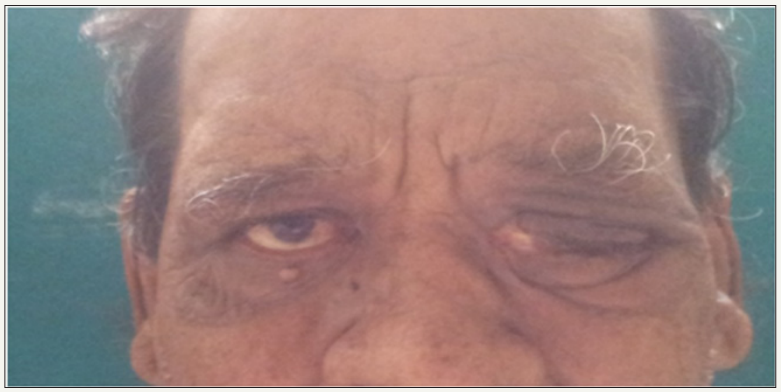

Figure 1: A 65 y/o Man who presented with chemosis, eyelid edema, decreased vision.

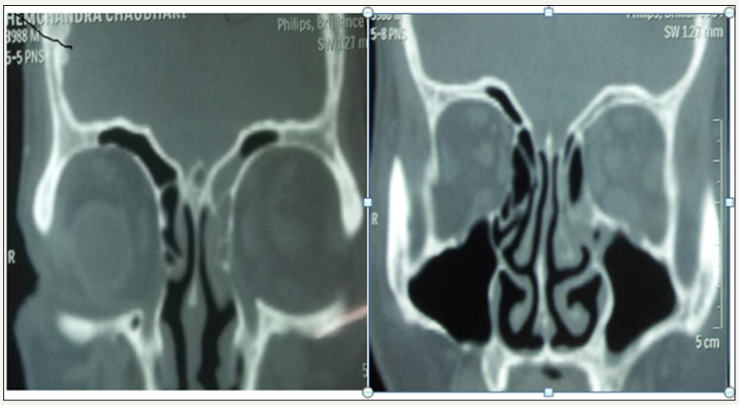

Figure 2: CT scan findings showing significant orbital inflammation (Note the globe is visible on the right, but not on the left-indicating proptosis), on the left showing limited lamina papyracea disease.

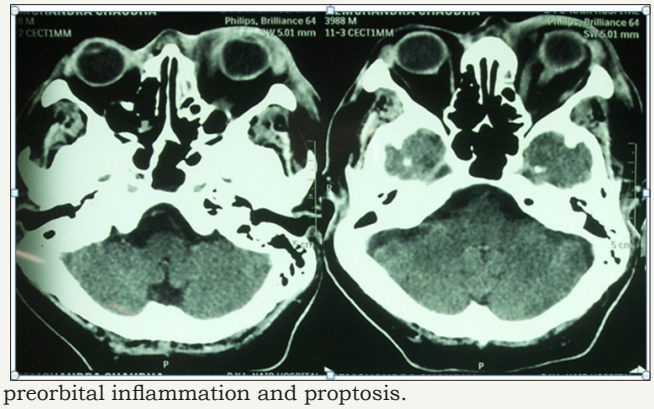

Figure 3: MRI findings showing preorbital inflammation and proptosis.

How to cite this article: Abhishek K R , Diptarka B. Invasive Fungal Sinusitis: Management of the Orbit, a Multi Institutional Study and Review of Literature. Exp Rhinol Otolaryngol. 1(5). ERO.000522.2018. DOI: 10.31031/ERO.2018.01.000522

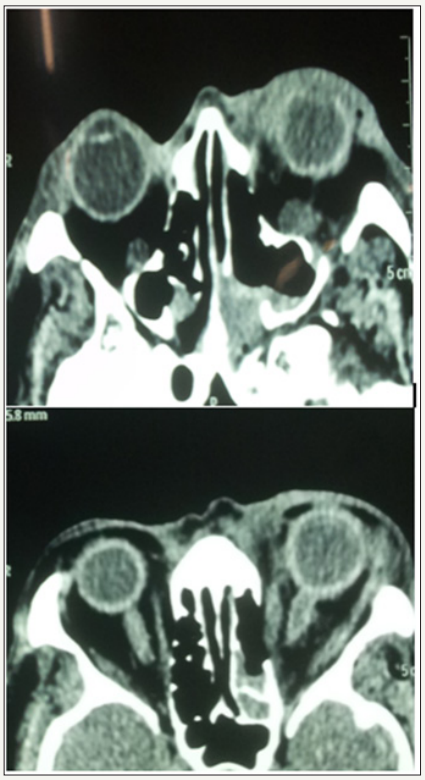

Figure 4: Patient of IFS, after debridement, showing residual disease posteriorly, which is difficult to treat (top) and enhancement of the medial rectus (Bottom).

Figure 5: Chemosis, conjunctival edema, visual loss in a 46 y/o Man.

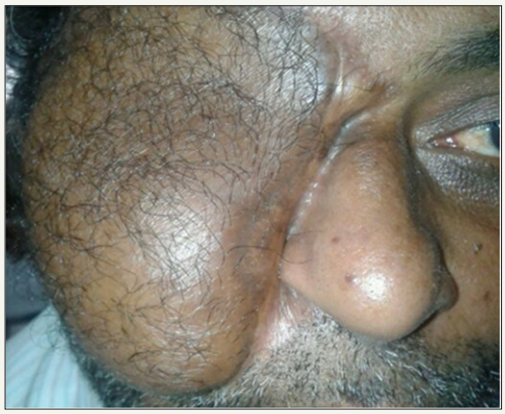

Figure 6: One of our orbital exenteration patients who later underwent a free flap reconstruction.

How to cite this article: Abhishek K R , Diptarka B. Invasive Fungal Sinusitis: Management of the Orbit, a Multi Institutional Study and Review of Literature. Exp Rhinol Otolaryngol. 1(5). ERO.000522.2018. DOI: 10.31031/ERO.2018.01.000522

Results

A total of 47patients (n=47) were found to fulfill the inclusion criteria as set above. All the patients had an underlying immunosuppressive cause, as outlined in Table 1 the demographic distribution was of 30 males and 17females. The age range was 42-77; with distribution as outlined in Table 2. The causative pathogen was Aspergillus in 21patients and Rhizopus in 25. At the end of the study, 20 out of these patients survived, and 17out of the ones afflicted by Aspergillus survived, both having a near 80% survival rate. Thus, we did not see any Species related differences in mortality in our study. However, it should be noted that out of the 4 patients who went on to have intracranial involvement following orbital exenteration and die, all had Diabetes and Rhizopus, which probably indicates that Diabetics with Rhizopus require more aggressive management, as in them, the disease can spread faster Table 2.

Table 1:

Co-Morbidity	No. of Patients
Diabetes	28
Chemotherapy/RT	10
Renal transplant	6
AIDS	3

Table 2:

40-50yrs	50-60yrs	60-70yrs	70-80yrs
4	11	17	15

The following table demonstrates the total exenteration statistics

In these 47patients, 14 were found to have extensive intraorbital disease, and 33 were found to have limited periosteal involvement. In all, a total of 23 patients underwent orbital exenteration. Table 3 & 4 detail the survival and the time of exenteration, from the day of first nasal endoscopy. The commonest clinical symptoms associated with orbital involvement were reduced visual acuity (63%), varying degree of opthalmoplegia (34%), and chemosis & proptosis (46%). However, in 12patients, that is 25.5% of patients, there were no orbital symptoms complained of. All of them had limited orbital disease noted on imaging, 9 of whom had limited anterior ethmoid and maxillary disease Table 3 & 4. In relation to co-morbidities, Diabetics made up the largest group of patients who underwent exenteration, as expected from the demographics. Thus in this study, in limited orbital disease there was an almost 72% conservation rate.

Table 3:

Orbital Exenteration	Survival
23	14 (52%)

Table 4:

Total No. of Pts	No of Pts Exenterated		No. of Pts Survived
Diabetes (28)	13		7
Chemo/RT (10)	6		4
Renal transplant(6)	2		2
AIDS (4)		2	1

Discussion

As discussed before, orbital management of invasive fungal sin nasal disease is still institution dependent. The accepted gold standard is orbital exenteration, although multiple large scale studies [2], the largest one being of 807 patients did not find any benefit to exenterations with around 45% of patients dying even after exenteration Figure 7. In our study also 39% patients died even after exenteration, however, we feel factors like initial extent of involvement, time to exenteration, and concomitant intracranial disease are other factors which affect this outcome, hence in carefully selected patients a trial of Local Irrigation is reasonable as it may avoid exenteration, and if the delay does not appear to worsen prognosis. Continuous irrigation has been described before [3,4] with mixed literature regarding benefits [5,6]. Side effects reported are pain and chemosis which may be difficult to distinguish from disease progression clinically [6].

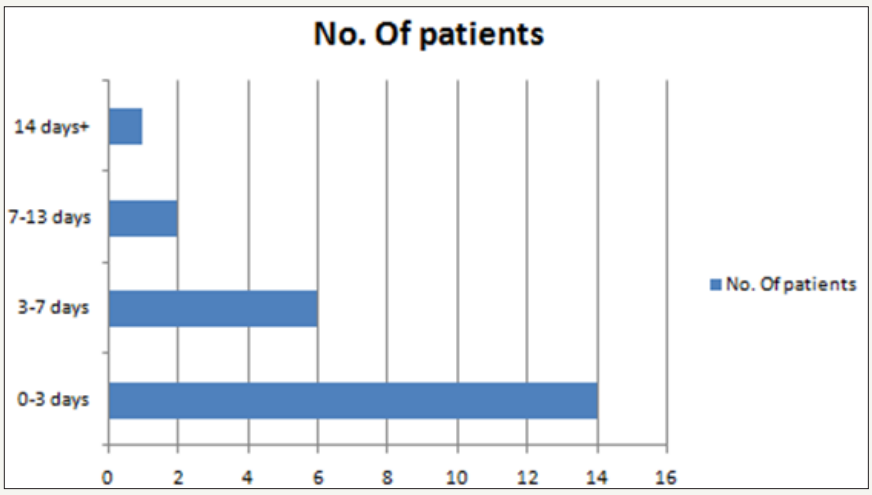

Figure 7:

How to cite this article: Abhishek K R , Diptarka B. Invasive Fungal Sinusitis: Management of the Orbit, a Multi Institutional Study and Review of Literature. Exp Rhinol Otolaryngol. 1(5). ERO.000522.2018. DOI: 10.31031/ERO.2018.01.000522

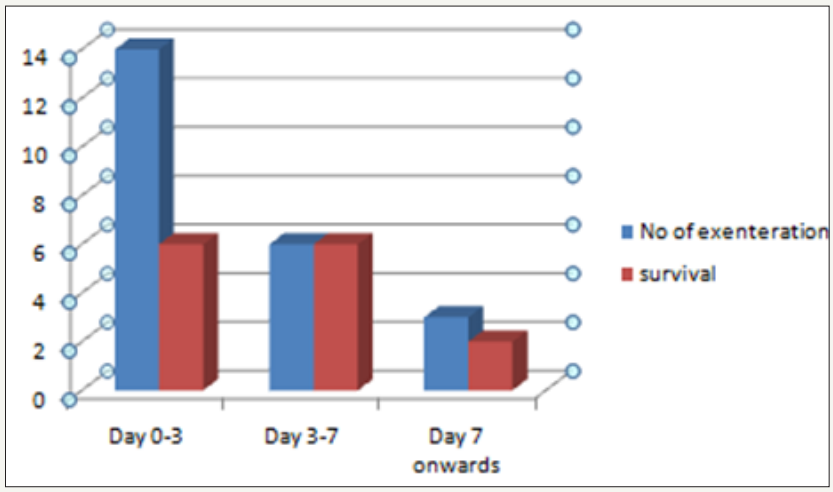

Figure 8:

In our series of patients, we found that extensive orbital disease patients need orbital exenteration early, even though the survival benefit is unclear. In our study inspite of early exenteration 28.5% patients went on to develop intracranial disease and all of them succumbed. In total, in patients who underwent early exoneration, there was a 42.8% survival rate Figure 8. However, in patients with limited orbital disease, a trial of Local cottonoid placement under direct visualization and Amp B irrigation in addition to systemic antifungal therapy and regular debridement's yielded orbital conservation in 72.7% patients. Out of these, 46% actually had improvement in their vision & ocular symptoms whereas the other 54% did prevent further worsening of vision. Out of the remaining 9 patients who went on to get exenteration, 6 of them were found to have posterior disease, in the initial scan. This could be due to a. Better visualization and cottonoid placement anteriorly resulting in better drug delivery or b. as the posterior orbit is less accessible and has lesser blood supply.

In this series of patients, 3 of the patients underwent the exenteration after 7days, on day 8, 9 and 14. The patient who underwent the procedure, though he improved initially, recurred with the disease in the other eye, and had to get the other eye exenterated too. The patient who had it on Day 9went on to develop intracranial involvement and died. The following table summarizes the above. We feel that early exenterations are mostly performed for aggressive disease, and as such many of these patients may have microscopic intracranial disease, probably explaining the poorer survival in these patients. Although Turner's study did not find a poorer prognosis associated with this, multiple other studies do contradict this, and so, we believe, it is justified to go ahead with urgent exenterations in these patients. However, in limited orbital disease, there definitely appears to be a role of a conservative trial, which in our series yielded a 72.7% conservation rate, although it does seem that the results for limited anterior disease is even better, achieving 85% conservation which is in agreement with other trials. Also, we did achieve a 50% conservation rate even with posterior disease, for which other authors have advised early exenteration. This is probably due to direct endoscopic visualization and placement of cottonoids, ensuring better delivery of antifungal.

Thus, in our series of patients, 48.9% patients had to undergo exenteration, and post exenteration survival was around 70%. This is better than Turner's review of overall 50% mortality [1], but is within the range of more recent studies [7-10] of 6-68% .Although some studies have demonstrated a difference, albeit not statistically significant, in survival between aspergillus and Rhizopus, [11,12] in our series we found no difference in survival. In our series, the best survival results are seen between days 3-7, though this is probably due to aggressive disease being exenterated within the first 3 days [13]. However, delay beyond 7 days may lead to poorer outcomes, as in our case series 2 out of 3 patients in this group had disease recurrence despite exenteration.

Conclusion

Invasive fungal sinusitis is a potentially lethal disease that can involve the orbit in up to 50% of cases [11]. Orbital exenteration has variously been recommended for post septal disease, inflammation of the orbit, or in blind eye [14,15] but survival benefits of exenteration have been difficult to prove [1]. However, we feel that there are 2 sub-groups of these patients, and while early exenteration is needed in those with aggressive necrotic disease in the intra orbital compartment, local irrigations under direct visualization could potentially avoid the need for exenteration in many patients with limited disease, and hence could be a worthwhile alternative [16-18]. However, the patients need to be under close observation, and the ideal time of switching to exenteration, if no improvement is noted seems to be lesser than 7 days; although there will need to be larger studies before drawing any definitive conclusions. Future randomized multi-institutional trials will be needed to draw up definite protocols for the management of the different stages of orbital involvement in Invasive fungal sinusitis.

References

1. Turner JH, Soudry E, Nayak JV, Hwang Turner JH, Soudry E, et al. (2013) Survival outcomes in acute invasive fungal sinusitis: a systematic review and quantitative synthesis of published evidence. Laryngoscope 123(5): 1112-1118.

How to cite this article: Abhishek K R , Diptarka B. Invasive Fungal Sinusitis: Management of the Orbit, a Multi Institutional Study and Review of Literature. Exp Rhinol Otolaryngol. 1(5). ERO.000522.2018. DOI: 10.31031/ERO.2018.01.000522

2. Hargrove RN, Wesley RE, Klippenstein KA, Fleming JC, Haik BG (2006) Indications for orbital exenteration in mucormycosis. Ophthalmic Plast Reconstr Surg 22(4): 286-291.

3. Nithyanandam S, Jacob MS, Battu RR, Thomas RK, Correa MA (2003) Rhino-orbito-cerebral mucormycosis. A retrospective analysis of clinical features and treatment outcomes. Indian J Ophthalmol 51(3): 231-236.

4. Farooq AV, Patel RM, Lin AY, Setabutr P, Sartori J, et al. (2015) Fungal orbital cellulitis: presenting features, management and outcomes at a referral center. Orbit 34(3): 152-159.

5. Joos ZP, Patel BC (2017) Intraorbital irrigation of amphotericin b in the treatment of rhino-orbital mucormycosis. Ophthalmic Plast Reconstr Surg 33(1): e13-e16.

6. Seiff SR, Choo PH, Carter SR (1999) Role of local amphotericin B therapy for sino-orbital fungal infection Ophthalmic Plast Reconstr Surg 15(1): 28-31.

7. Mody KH, Ali MJ, Vemuganti GK, Nalamada S, Naik MN, et al. (2014) Orbital aspergillosis in immunocompetent patients. Br J Ophthalmol 98(10): 1379-1384.

8. Payne SJ, Mitzner R, Kunchala S, Roland L, McGinn JD (2016) Acute invasive fungalrhinosinusitis: A 15-Year Experience with 41 Patients. Otolaryngol Head Neck Surg 154(4): 759-764.

9. Sun HY, Forrest G, Gupta KL, Aguado JM, Lortholary O, et al. (2010) Rhino-orbital-cerebral zygomycosis in solid organ transplant recipients. Transplantation 90(1): 85-92.

10. Chen CY, Sheng WH, Cheng A, Chen YC, Tsay W, et al. (2011) Invasive fungal sinusitis in patients with hematological malignancy: 15 years experience in a single university hospital in Taiwan. BMC Infect Dis 11: 250

11. Trief D, Gray ST, Jakobiec FA, Durand ML, Fay A, et al. (2016) Invasive fungal disease of the sinus and orbit: a comparison between mucormycosis and Aspergillus. Br J Ophthalmol 100(2): 184-188.

12. Monroe MM, McLean M, Sautter N, Wax MK, Andersen PE, et al. (2013) Invasive fungal rhinosinusitis: a 15-year experience with 29 patients. Laryngoscope 123(7): 1583-1587.

13. Bhansali A, Bhadada S, Sharma A, Suresh V, Gupta A, et al. (2004) Presentation and outcome of rhino-orbital-cerebral mucormycosis in patients with diabetes. Postgrad Med J 80(949): 670-674.

14. Dhiwakar M, Thakar A, Bahadur S (2003) Invasive sino-orbital aspergillosis: surgical decisions and dilemmas. J Laryngol Otol 117(4): 280-285.

15. Mukherjee B, Raichura ND, Alam MS (2016) Fungal infections of the orbit. Indian J Ophthalmol 64(5): 337-345.

16. Gillespie MB, Omalley BW (2000) An algorithmic approach to the diagnosis and management of invasive fungal rhinosinusitis in the immunocompromised patient. Otolaryngol Clin North Am 33(2): 323-334.

17. Wang M, Lv D, Huang S (2014) [The diagnosis and treatment progress of invasive fungal sinusitis]. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi (11): 832-834.

18. Walsh TJ, Anaissie EJ, Denning DW, Herbrecht R, Kontoyiannis DP, et al. (2008) Treatment of aspergillosis: clinical practice guidelines of the Infectious Disease Society of America. Clin Infect Dis 46(3): 327-360.