

## Original Research Article

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# Understanding acute invasive fungal rhinosinusitis for better treatment outcomes

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### ABSTRACT

**Background:** Objectives of the study were to identify factors that affect patient survival, determine treatment outcomes in various clinical presentations, increase awareness amongst clinicians and provide more accurate treatment options to patients. Study design was a retrospective study. Study places were Tertiary care centre and a Medical College.

**Methods:** A series of patients diagnosed and treated for acute invasive fungal rhinosinusitis over a period of 7 years.

**Results:** Twelve patients were reviewed out of which eleven were diabetic. Most common fungus encountered was mucor. Six cases presented as sinonasal disease, four as rhino-orbital disease and two as rhino-orbito-cerebral disease. All the patients underwent surgical debridement with systemic antifungal treatment. It was seen that diseases confined to sino nasal areas had good prognosis. Early diagnosis and prompt intervention is major factor for better prognosis.

**Conclusions:** Immunocompromised patients in ICU with ocular symptoms should be meticulously screened for invasive fungal rhinosinusitis. Early diagnosis and prompt management with surgical debridement and systemic antifungal treatment is utmost important factor in good prognosis. Intensivists and also the physicians should be made cognizant as they play important role in patient management as well. Multidisciplinary approach is the need of hour.

**Keywords:** Hypocalcemia, Parathyroid, Recurrent laryngeal nerve, Thyroidectomy

### INTRODUCTION

Acute invasive fungal rhinosinusitis (AIFRS) is increasingly recognized to have a high mortality and morbidity. Sinonasal mycotic infections account for 10% of chronic rhinosinusitis.<sup>1</sup> Distinguishing invasive from non invasive disease is important for treatment and outcome of the disease. The causative pathogens are a diverse group of fungal species. Out of them Zygomycetes (Rhizopus, Mucor, Rhizomucor) and Aspergillus species are most commonly responsible for invasive fungal rhinosinusitis.<sup>2</sup>

The existing knowledge regarding invasive fungal rhinosinusitis can at times be quite confusing for treating

clinicians. Delay in diagnosing and initiation of treatment severely affect the disease prognosis. Thus it demands attention of clinicians for suspecting and diagnosing these cases. Here we present a review of clinical case series in a tertiary care hospital over last 7 years.

### METHODS

**Study design:** A observational retrospective study.

**Study place:** A tertiary care hospital.

**Duration:** January 2011 to December 2017

The data of all the diagnosed and treated cases of acute invasive fungal rhinosinusitis was assessed retrospectively.

A proper informed consent was taken from all the patients during admission and before each surgical intervention. In unconscious patients or minors; the consent was taken from surrogate decision maker.

The aim and objectives were to identify factors that affect patient survival, determine treatment outcomes in various clinical presentations and to increase awareness amongst clinicians and provide more accurate treatment options to patients.

Preoperative workup included a thorough bedside Ear, Nose and Throat (ENT) examination and a diagnostic nasal endoscopy whenever possible. Investigations included a nasal smear study for fungus, tissue biopsy, high resolution computed tomography of the nose and paranasal sinuses and magnetic resonant imaging (MRI) of the orbit/brain in few cases. Based on the clinical examination all patients underwent endoscopic

debridement of the disease and orbital exenteration wherever indicated. Confirmatory diagnosis was made on the basis of histopathology. Based on the morphology of fungus appropriate antifungal agents were started and a total cumulative dose of Amphotericin B; 2.25 gm was given. Patients were followed up closely; repeat debridements were done as required.

**RESULTS**

The study included twelve patients out of which eight were male and four were females. Age ranged from 05 to 65 years. The results are shown in Table 1. Most commonly reported predisposing factor seen in 11 patients was diabetes mellitus (DM). Other factors included malignancy seen in 2 patients. Most common presenting complaints were nasal discharge and headache. Orbital involvement was seen in 58% cases who presented with proptosis, ophthalmoplegia and 85% of those with orbital involvement had loss of vision. Nasal discharge and obstruction were seen in almost all patients.

**Table 1: Clinical profile of patients with AIFRS.**

Sr no.	Variable	Number	
1	Total cases	12	
2	Age	Range 05-65 years	
3	Gender	Male	8
		Female	4
		M:F	2:1
4	Underlying disease	DM	11
		ALL	1
		NHL	1
		Corticosteroid use	1
5	Symptoms	Nasal discharge	11
		Nasal obstruction	11
		Headache	8
		Ophthalmoplegia	7
		Loss of vision	6
		Palate involment	1
6	DNE	Eschar and Necrotic tissue	9
		Purulent nasal discharge	11
		Crustations	8
7	Radiology	Opacification of PNS	10
		Intracranial extension	3
		Orbital involvement	7
		Palate erosion	3
8	Extent of disease	Sino nasal	6
		Rhino orbital	4
		Rhino-orbito-cerebral	2
9	Surgical treatment	Endoscopic debridement	12
		Orbital exenteration	4
		Decompression craniectomy	1
	Medical treatment	Amphotericin B	9
		Voriconazole	3

Continued

Sr no.	Variable	Number of patients	Mortality
10	Initiation of treatment	Within 4 days	7
		5-7 days	4
		>15 days	1
11	Outcome	Stable response	5
		Succumbed	6

Blackish necrotic discolouration (eschar) seen in 9 (75%) patients, ulcerations and crusts were seen in the nose frequently involving the area near middle turbinate and septum. Presence of eschar is a characteristic finding which is seen in cases of acute invasive fungal rhinosinusitis due to mucor. Diagnosis was confirmed on histopathological examination.

Computed tomography showed opacification of the paranasal sinuses in 10 (83%) patients with adjacent bony erosion in 9 (75%) patients. Palatal erosion was seen in 3 (25%) patients. Intracranial extension in 3 patients and orbital involvement in 7 patients was confirmed on MRI study.

A nasal swab smear examination taken bedside was helpful to see presence or absence of fungi and morphology of the fungus at the earliest. Fungal smear studies revealed septate fungal hyphae in 6 (50%) patients and aseptate fungi in 3 (25%) patients. In three patients fungal smear was negative for fungus. Confirmatory findings were after histopathological examination only. Histopathological examination revealed septate hyphae with acute angle branching s/o Aspergillus in 2 cases and aseptate hyphae with right angle branching s/o Mucor in 10 cases. All the patients had tissue invasion of the hyphae with few patients showing angioinvasion and bony invasion.

Patients underwent endoscopic nasal debridement based on presumptive diagnosis of acute invasive fungal rhinosinusitis and started on injection Amphotericin B. Surgical debridement of palatal lesions was done for 2 cases; orbital exenteration done for 4 cases. Multi disciplinary approach was initiated by ENT surgeon, Ophthalmologist, Neurosurgeon, Physicians, Infectious disease consultant, Pathologist and Microbiologist. After confirmatory diagnosis (histopathological report); patients affected with mucormycosis were continued with Amphotericin B and those with Aspergillus were given Voriconazole. One patient in spite of multiple debridements and Inj. Amphotericin B showed no signs of improvement. Culture sensitivity of the sample revealed Fusarium species sensitive to Voriconazole. The patient was then started on Voriconazole.

Out of the 12 patients more than half of them presented to the hospital when the disease process had breached the nose and paranasal sinuses and progressed to the orbit/brain. Four patients had rhino-orbital and 2 had rhino-orbito-cerebral mucormycosis. Out of the 12 patients in five patients treatment initiation was done

after 4 weeks of presentation. Close follow up of the patients 6 patients succumbed; 5 survived and 1 was lost to follow up. Five patients showed a complete response to the treatment.

## DISCUSSION

Acute invasive fungal rhinosinusitis is a mycotic infiltration of mucosa and/ or bone and blood vessels. It occurs in immunocompromised patients (uncontrolled DM, chemotherapy, transfusion recipient, acquired immunodeficiency syndrome, haematological disease, patients on oral steroids). Defective immune system allows the invasion of fungal species into the surrounding tissues. In acute invasive rhinosinusitis the presentation of symptoms is usually <4 weeks.<sup>3</sup>

Most of the patients present to the emergency department with loss of unconsciousness with uncontrolled diabetes mellitus and are admitted to intensive care unit. The initial symptoms are often so delicate that it may be difficult to analyze. To start with the patient can present with fever and rhinorrhoea only. Presence of facial swelling, proptosis, ophthalmoplegia or any focal neurological deficit should raise suspicion of acute invasive fungal rhinosinusitis. Based on known or potential immunosuppression a high degree of suspicion should be raised for early diagnosis and initiation of treatment. A meticulous nasal examination preferably endoscopic is the crux of diagnosis. Blackish necrotic discolouration (eschar), granulations, ulcerations or crusts in the nose frequently involving the area near middle turbinate and septum are seen. Eschar is a trademark feature of mucormycosis but its absence does not rule out mucormycosis. Hence all such patients should undergo a complete ENT examination.

A presumptive diagnosis of AIFRS can be made on clinical grounds. Radiological investigations should be done to see the extent of the disease and in presence of any complications. But definitive diagnosis of invasive fungal rhinosinusitis is made only on histopathology.

Initiation of systemic antifungal treatment within 5 days after diagnosis was associated with improved survival, compared with initiation  $\geq 6$  days after diagnosis i.e. 83% survival vs 49%.<sup>4</sup> Total duration of therapy can be individualised for each patient depending on resolution of clinical signs and symptoms, resolution of underlying immunosuppression and negative histopathological report. Choice of antifungal formulation is based on the type of fungi, patient affordability and co morbidities, drug availability and can be made accordingly. Surgical

debridement is necessary to optimize cure rates. It helps reduce the fungal load, increases tissue penetration of the drug. The extent of surgical debridement should till all the dead necrotic tissues are debrided and healthy tissue seen with free blood flow thereby indicating vital and perfused tissue.

A systematic review was conducted by Turner et al in 2013 which concluded that overall mortality of patients with acute invasive fungal rhinosinusitis remains 50%.<sup>5</sup> Blitzer and Ochi et al found overall 78% survival with radical debridement versus 57.5% survival with only medical therapy. Patients with disease limited to sinonasal areas have better prognosis as compared to extensive disease.<sup>6,7</sup> Those with intracranial extension have poor prognosis.

Apart from factors like extension of disease and treatment with radical debridement; we firmly believe that duration of initiation treatment is also important prognostic factor. In our scenario patients with disease extending beyond the nose and paranasal sinuses into the orbit; early prompt treatment with radical debridement showed a good survival rate. Hence all patients presenting with uncontrolled diabetes and facial swelling in intensive care unit (ICU) should be screened for acute invasive fungal rhinosinusitis for better outcome.

Here we strongly recommend that clinical awareness amongst physicians; prompt diagnosis and early initiation of treatment are factors of paramount importance in the management of acute invasive fungal rhinosinusitis especially in an intensive care unit.

## CONCLUSION

A careful consideration of fungal infection should be given to all immunocompromised patients especially with ocular symptoms in an intensive care unit. All the patients in ICU, emergency medicine should be meticulously screened for invasive fungal rhinosinusitis. Multidisciplinary team involvement is the need of hour. Rapid diagnosis of invasive fungal rhinosinusitis by biopsy and culture sensitivity for fungus is a must to do and critical to rapid implementation of appropriate therapy. Early and radical debridement can be life saving.

Rapid reversal of immunocompromised status is equally important. Clinical awareness, prompt diagnosis and early initiation of treatment are factors of paramount importance in the management of acute invasive fungal rhinosinusitis

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