Orbital involvement in fungal sinusitis

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A dissertation submitted in partial fulfillment of MS Branch IV, ENT examination of the Tamil Nadu Dr. MGR Medical University, to be held in March 2010

Department of Otorhinolaryngology
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Certificate

This is to certify that the dissertation entitled 'Orbital involvement in fungal sinusitis' is the bonafide original work of Dr Ramanathan C submitted in fulfillment of the rules and regulations for the MS Branch IV, ENT examination of the Tamil Nadu Dr. MGR Medical University, to be held in March 2010.

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Acknowledgements

I express my deep sense of gratitude to my esteemed professor and guide Dr Rupa Vedantam for all her encouragement and guidance at every stage of the work on this dissertation.

I am extremely grateful to Dr Meera Thomas of the Dept of Pathology for going through all the histopathology slides.

I would like to thank Dr Reji Kurien and Dr Suryaprakash for helping me enter the data and Ms.Tunny Sebastian for patiently analysing the data.

I am indebted to all the patients who consented to be a part of this study and each and every ENT surgeon for the meticulous recording of the findings.

My sincere thanks to all my professors, seniors, colleagues and friends for all their encouragement and help.

A special thanks to my family, especially my wife and daughter, for supporting me throughout the work on this study.

And to God Almighty for all his blessings.

AIMS & OBJECTIVES

1. To study the prevalence of orbital involvement in fungal sinusitis.
2. To determine whether orbital involvement is more common in histologically invasive fungal sinusitis as compared to histologically non invasive fungal sinusitis.

PRESENT KNOWLEDGE AND REVIEW OF LITERATURE

Introduction

Fungi are eukaryotic organisms comprising moulds, yeasts, mushrooms and similar organisms. More than 1,00,000 species of fungi have been described. Of these, only about 0.1% are recognized as human pathogens, although the number capable of producing human disease continues to increase.[1] The incidence of mycotic infections and the number and diversity of pathogenic fungi have increased dramatically in recent years. Although many humans are colonized by fungi, an intact immune system prevents subsequent infection.[2] The pathogenicity of fungi is poorly understood. Fungi may cause disease by establishing an infection, elaborating toxin(s),or by inducing allergic response(s).[3]

Fungal rhinosinusitis is broadly defined as the spectrum of pathologic conditions associated with sinonasal inflammation that is related to the presence of fungi.[4] Common fungal genera implicated in fungal rhinosinusitis include Zygomycete species (which include Rhizopus (Figure 1), Mucor, Cunninghamella which cause invasive fungal rhinosinusitis), hyaline moulds like Aspergillus species (Figure 2) and dematiaceous moulds like Alternaria, Bipolaris, Curvularia species (which cause allergic fungal rhinosinusitis).[3]

Classification of fungal rhinosinusitis

Fungal rhinosinusitis is broadly categorized into invasive and non invasive types. Invasive fungal rhinosinusitis is defined by the presence of fungal hyphae in the mucosa, submucosa, bone or blood vessels of the paranasal sinuses.

Invasive fungal rhinosinusitis is subdivided into:

- Acute invasive fungal rhinosinusitis
- Chronic invasive fungal rhinosinusitis
- Chronic granulomatous invasive fungal rhinosinusitis

Non invasive fungal rhinosinusitis is defined by the absence of hyphae within the mucosal and other tissues of paranasal sinuses. Non invasive fungal rhinosinusitis is subdivided into:

- Allergic fungal rhinosinusitis
- Fungus ball

Summary of clinical features, diagnosis, radiology and treatment of various types of fungal sinusitis

Allergic fungal rhinosinusitis

It is the most common form of fungal rhinosinusitis in warm humid climates.Allergic fungal rhinosinusitis was first described as a distinct clinical entity by Millar in 1981 and Katzenstein et al in 1983. The overall prevalence of allergic fungal rhinosinusitis is estimated at 5-10% of all cases of chronic hypertrophic sinus disease who undergo surgery.[6] . In north India, it has been reported in upto 51% of patients with chronic rhinosinusitis.[7]

Allergic fungal rhinosinusitis represents both Gell and Coombs type 1 and type 3 responses. It represents type 1 response because of the elevated level of IgE to the specific fungus. It also represents a type 3 response because IgG antibodies to the specific fungus can be demonstrated in the serum. There is no cytotoxic event associated with these IgE antibodies as is seen with Gell and Coombs type 2 immunologic event; therefore this is believed to be a type 3, non IgE mediated, non cytotoxic,antibody-dependent immunologic event.[8]

No consensus exists among rhinologists concerning diagnostic criteria for allergic fungal rhinosinusitis. In 1994, Bent and Kuhn described what probably are

the most widely accepted criteria for diagnosis. On the basis of analysis of 15 cases, 5 common characteristics were observed. (Table 1)

In 1997, deShazo proposed a similar set of 5 criteria, including radiographic evidence of sinusitis, presence of allergic mucin (identified grossly or histopathologically), positive fungal stain or culture from the sinus at the time of surgery, absence of contributory factors (eg, diabetes mellitus, immunodeficiencies), and absence of fungal invasion.[10] (Figure 3) The usual presenting symptoms include nasal obstruction, rhinorrhoea,frontal headache, postnasal drip, facial pain,anosmia and periorbital pain.[11]

CT scan findings include complete unilateral or bilateral opacification of multiple paranasal sinuses, sinus expansion and erosion of a wall of the involved sinus and scattered intrasinus high attenuation areas amid mucosal thickening. These features are noted on unenhanced CT scans.[12] (Figures 4,5,6)

MRI scan findings in allergic fungal sinusitis are also typical. T1 weighted images may show high intensity or low intensity or intermediate signal intensity whereas T2 weighted images show characteristic low signal intensity or signal void due to the high concentration of various metals such as iron, magnesium and manganese concentrated by the fungi and also due to the high protein and low free water content of the allergic mucin.[13]A protein concentration above 28% can lead

to decreased signal intensity in both T1 and T2 weighted images because of increased cross-linking and slower macromolecular motion.[14] On gadolinium contrast, T1 and T2 weighted images show peripheral high signal intensity.[14]

Fungus Balls

Fungus balls are composed of matted fungal hyphae in the absence of allergic mucin. Earlier, these were referred to as aspergilloma and mycetoma. They are usually found in only one sinus, most frequently the maxillary followed by the sphenoid.[4] Ethmoid sinus involvement is rare and when it occurs, it is frequently contiguous with the maxillary sinus. Frontal sinus involvement is uncommon. Geographically, these lesions are commonly found in France.

The age range for patients with fungus balls is 18 to 86 years. (Mean age 59.5 years) There is a female preponderance of 2:1.[4] Clinical presentation is typically non specific and is identical to that of chronic sinusitis. In decreasing frequency, nasal congestion, obstruction, discharge, fever, cough, blurred vision, cacosmia and ocular symptoms can be present. The symptoms may be present for months or even years. Nasal endoscopy may reveal minimal evidence of sinusitis. 10% of patients have polyps.[15].

The most likely cause of fungus balls is the persistence of fungal spores within the nasal cavity or entrance of spores into the sinus and subsequent

germination and growth. The host is immunocompetent but if immunocompromise develops, then this non invasive manifestation may become invasive and life threatening.[16]

Paranasal sinus CT scan findings in this disease include opacification of the affected sinus with a rim of soft tissue attenuation along the bony walls of the involved sinus. Several well defined hyperdense foci may be detected.[4] (Figure 7)

MRI shows hypointense T1 and T2 weighted images. Fungal cultures are frequently negative. Grossly, they appear as either soft moist clumps of debris or firm gritty and crumbly balls. The colour may vary from white, yellow, greenish,tan brown and black. Common etiologic organisms include Aspergillus fumigatus, Pseudallescheria boydii, Alternaria or other species. The histological features are typical.(Table 2, Figure 8)

Acute invasive fungal Rhinosinusitis

Acute fulminant invasive rhinosinusitis is a disorder which occurs in patients with an impaired neutrophilic response secondary to disorders like poorly controlled type 1 diabetes mellitus, AIDS, hemochromatosis, aplastic anemia, iatrogenic immunosuppression, organic transplantation or hematologic malignancy (Table 3). Absolute neutrophil counts below 500 cells/mL are strongly correlated

with the development of invasive fungal disease.[17]A number of clinical conditions may be associated with acute invasive fungal sinusitis.

The disease has a rapid onset and progression.Typically, the symptoms will be of less than 4 weeks duration. In the absence of treatment, the disease is rapidly fatal in 50-80% of the patients secondary to invasion of the orbit and intracranial cavity.[17]

Medical advancements have prolonged the survival of immunocompromised patients which in turn has increased the population at risk for developing invasive fungal rhinosinusitis. The disease is thought to originate in the nasal cavity in most cases before extending into the paranasal sinuses or deeper body compartments such as the orbit or intracranial cavity.

The initial symptoms are often subtle and a high index of suspicion should be there while managing an at risk patient. The most common symptom in upto 90% of patients is fever of unknown origin that has not responded to 48 hours of appropriate broad spectrum intra venous antibiotics. Local symptoms like facial and periorbital pain, nasal congestion and rhinorrhoea, and headache are variably present in 20-60% of patients. Late signs and symptoms include loss of visual acuity, ophthalmoplegia, proptosis, change in mental status,focal neurologic signs and seizure.[17]

The most consistent finding on nasal endoscopy is an alteration in the appearance of normal pale pink nasal mucosa. White discoloration indicates tissue ischemia secondary to angiocentric invasion whereas black discoloration signifies tissue necrosis. Mucosal abnormalities are seen most commonly affecting the middle turbinate followed by the septum, palate and inferior turbinate. Decreased mucosal bleeding or sensation also may be noted because these may be signs of fungal invasion.[17]

CT scan of the paranasal sinuses shows minimal abnormalities in the early stages of the disease. Often, only mild mucosal thickening may be evident in the affected sinus(Figure 9).This may be associated with features of cavernous sinus thrombosis or dural enhancement suggesting intracranial invasion. Contrast studies may show periorbital or dural inflammation.

Whereas CT is better to assess bone changes,MR imaging is superior in evaluating intracranial and intraorbital extension of the disease.Inflammatory changes in the orbital fat and extraocular muscles and resulting proptosis herald intraorbital invasion by the fungal infection.Leptomeningeal enhancement may be seen with intracranial invasion and is subtle in the initial stages.With progressive infection, adjacent cerebritis, granulomas and cerebral abscess formation may be encountered.Intracranial granulomas appear hypointense on T1 and T2 weighted images with minimal enhancement on contrast enhanced images.[13] Silverman and

Mancuso[18] noted that soft tissue infiltration of periantral fat planes around the maxillary sinus provides early evidence of invasive fungal sinusitis.

With rare exceptions, the disease usually starts in the sino-nasal tissues(limited sino-nasal disease), progresses to the orbits(limited rhino-orbital disease) and finally affects the central nervous system (rhino-orbito-cerebral disease)[19].Infection gains entrance to the central nervous system through the orbital roof, orbital apex and cribriform plate.Internal carotid artery,middle cerebral artery, ciliary artery, retinal artery,cavernous sinus are all subject to the progression of the disease. Histopathological features are typical (Table 4,

Figures 10,11)

Chronic invasive fungal sinusitis

This disease is characterized by a chronic course with slow disease progression and invasion of the mucosa, submucosa, blood vessels or bone.[5] It usually occurs in healthy individuals, though many have a previous history of chronic rhinosinusitis type symptoms,upper respiratory allergies or nasal polyposis.[18]

Symptoms directly related to the invasive disease may take months or years to appear and may only develop once the orbit or skull base are involved. Erosion into orbit may produce proptosis. Invasion of maxillary floor may produce palatal

erosions. Erosion of cribriform plate may produce chronic headache, seizures, decreased mental status or focal neurologic deficits. Extension through the sphenoid sinus may produce cavernous sinus thrombosis or orbital apex syndrome.[18] Intranasally, there may be polypoid mucosa or a soft tissue mass that can be mucosa covered or ulcerated. Crusting or black discoloration of the mucosa may be seen in some patients.

Chronic invasive fungal sinusitis has specifically been associated with Aspergillus, Mucor, Alternaria, Curvularia, Bipolaris, Candida, Drechslera, Sporothrix and Pseudallescheria boydii.[18]

Radiologically, a hyperattenuating soft tissue collection is seen in non contrast CT within one or more of the paranasal sinuses. There may be destruction of sinus walls and extension beyond sinus confines. There is decreased signal intensity on T1 weighted MR images and markedly decreased signal intensity on T2 weighted images.[13] Histopathologically, characteristic features are seen (Table 5) and it has to be differentiated from acute invasive (Table 6).

<u>Chronic granulomatous invasive fungal sinusitis</u>

This is primarily found in Sudan and Southeast Asia, usually caused by Aspergillus flavus.[20,21] However, there have been a few reports from India and Pakistan.[22] Most patients are immunocompetent. It is characterized by non

caseating granulomas in the tissue and invasion of the mucosa, submucosa, blood vessels or bone. Proptosis is the most common presenting complaint.[18] Clinically patients present with a nasal, sinus and/or orbital mass. Grossly it may appear as firm rubbery hard fibrous grayish white masses with an irregular surface. Histological features are typical (Table 7, Figure 12)

Veress et al have described 3 variants: Proliferative (granulomatous pseudotubercles in a fibrous tissue stroma), Exudative-necrotizing (with prominent foci of necrosis), and a mixed form.[23]

Unless removed surgically, the resulting fibrous fungal mass may spread to orbit, dura and brain.[5]

Pathways of orbital spread in fungal sinusitis

The orbit is the adjacent anatomic site most likely to be affected by extension of the disease, with routes of access provided through erosion of the lamina papyracea, superior wall of the maxillary sinus and floor of the frontal sinus.[24]

Visual loss as a consequence of acute inflammatory paranasal disease is a rare but well recognized complication first noted in the literature in 1893. A classification system for orbital complications of paranasal sinuses was presented by Hubert in 1937 and further refined by Chandler in 1970.

Chandler [25] classified the orbital complications of sinusitis into 5 groups.

1.Preseptal Cellulitis where the eyelids are swollen but the extra ocular movements are intact and the vision is normal.

2.Orbital Cellulitis is characterized by a more diffuse orbital edema with or without impaired extra ocular movements. Vision is usually normal.

3.Sub periosteal abscess is characterized by proptosis and impaired extra ocular movements.

4.Orbital abscess is characterized by severe exophthalmos, chemosis, complete ophthalmoplegia. Visual impairment is common.

5.Cavernous sinus thrombosis.

The prognosis and pathogenesis of the visual loss appears to differ depending on the underlying nasal pathology.[26] The ethmoid sinus is separated from the medial wall of orbit by the paper thin lamina papyraceae which is the weakest part of the medial wall. It is perforated by numerous foramina for nerves and blood vessels. Congenital or other dehiscences of the lamina papyraceae expose the orbital contents to direct extension of sinusitis.[26] In addition, superior and inferior ophthalmic veins are valveless, allowing direct communication between nose, ethmoid sinuses, face, orbit and cavernous sinus.[26]

Orbital periosteum/periorbita is the only soft tissue barrier between the paranasal sinuses and the orbital contents. It is composed of fibrous tissue that can be elevated easily off the underlying bone. Orbital septum is a reflection of the periorbita at the margins of the orbit. It passes centrally to fuse with the tarsal plates. Periorbita prevent infection from passing through the eyelids into the orbit.[26]

The periosteum of the orbit functions as a barrier between the paranasal sinuses and the orbital contents, but is potentially breached by multiple anatomic pathways. The ethmoidal artery foramina, dehiscences in the lamina papyracea and thin floor of the frontal sinus, as well as valveless ethmoidal veins provide routes for extension of infection to the orbit.[26] Orbital involvement primarily results from a thrombophlebitis and interference with venous drainage of orbital contents. The combination of phlebitis and direct entry of the pathogen into perivascular structures results in both infectious and inflammatory changes.[26] Extension of the disease into the orbit or the intracranial cavity results from a natural progression of disease once the erosion occurs.[24]

Proposed mechanisms for visual loss associated with sinonasal disease include 1) optic neuritis as a result of an adjacent inflammatory process, 2) venous congestion of the optic nerve due to incrceasing intraorbital pressure or

thrombophlebitis within the valveless orbital veins, or 3) increased intraorbital pressure resulting in occlusion of the central retinal artery.[26]

Orbital involvement is indicated by loss of vision, ocular motility restriction, proptosis, external and internal ophthalmoplegia, conjunctival pallor, chemosis and central retinal artery occlusion. Some studies have shown that orbital complications are seen more often in invasive fungal sinusitis than in the non invasive form.[26]

Radiological features in fungal sinusitis that suggest orbital involvement include erosion of the medial orbital margin, obliteration of periorbital fat and features of orbital cellulitis/abscess formation. Inflammatory changes in the orbital fat and extraocular muscles and resulting proptosis herald intraorbital invasion by the fungal infection.

Whereas CT scan is better for assessment of bone changes, MR imaging is superior in evaluating intracranial and intraorbital extension of the disease.[27] Bone erosion alone should not be interpreted as evidence of fungal invasion.[24]

Orbital manifestations in fungal rhinosinusitis

In mucormycosis, spread of infection into the orbit results in orbital cellulitis, loss of extraocular movement function and proptosis with failing vision. Ultimately

there is full blown orbital apex syndrome reflecting the destruction of cranial nerves 3,4 and 6, ophthalmic branch of trigeminal nerve and blood vessels traversing the optic foramen and superior orbital fissure.[28] Some patients present with ptosis and proptosis(Figures 13,14)

Clinical features include complete ophthalmoplegia, fixed dilated pupil, corneal and upper facial anaesthesia, chemosis and conjunctival haemorrhage and blindness resulting from retinal artery thrombosis caused by direct invasion of fungal elements. The fungi can also invade cavernous sinus and internal carotid artery causing thrombosis and cerebral infarction as a result of vascular compromise.[28]

Bhadada et al[29] published a series of 6 patients with Type 1 Diabetes Mellitus with mucormycosis. Proptosis and ptosis were the most common symptoms noted. 5 patients had ophthalmoplegia and vision loss. On imaging orbital involvement was seen in all patients except one. Maxillary sinus was the most commonly involved sinus followed by ethmoid, frontal and sphenoid.

CT scan or MRI scan can demonstrate the extent of the disease. CT is better to assess bone changes and MR imaging is superior in evaluating intraorbital and intracranial extension. Orbital involvement may be seen as an intra orbital mass,

intraorbital muscle involvement, cavernous sinus extension or optic nerve compression. Lamina papyracea may be breached.[2]

In allergic fungal rhinosinusitis,the disease may extend into the orbit and compress the optic nerve causing proptosis and progressive vision loss. It may also present as telecanthus and malar flattening.[30].The orbital symptoms are quite responsive to surgical debridement and steroids.[31]Radiologically, there may be expansion into the orbit, displacement of intraorbital contents and demineralization of bone.(Figure 15)

Fungus balls can produce a compressive optic neuropathy when they involve the posterior ethmoid or sphenoid sinuses.[31]Radiologically, there may be evidence of expansion into the orbit. Bony destruction may also be seen.[16]

Granulomatous invasive fungal rhinosinusitis is associated with other cranial nerve palsies but may present with an isolated optic neuropathy mimicking idiopathic retrobulbar neuritis with pain on extra ocular movements.[31] It may cause progressive exophthalmos and loss of vision can be the presenting complaint. Isolated sphenoid sinusitis can lead to involvement of optic nerve in the optic canal. [32] Radiologically, there may be erosion of the orbital walls with invasion of the orbital soft tissues.[13] (Figures 16,17,18,19,20)

MATERIALS AND METHODS

a) Study design:

This was a descriptive study in which data collection was performed both prospectively and retrospectively.

b) Subjects:

Patients with a diagnosis of fungal sinusitis as confirmed by fungal smear and/ culture managed in the Department of ENT, Christian Medical College,Vellore.

c) Exclusion criteria:

Patients who did not have a CT or MRI scan of the paranasal sinuses and those patients with sinusitis in whom fungus was not identified either by histology or fungal culture.

d) Informed Consent:

For all prospective patients, informed consent was taken in the patient's language. The consent form and the patient information sheet are attached as Appendix A.

e) Methods:

In the prospective part, all patients with a diagnosis of fungal sinusitis as confirmed by histopathology and fungal smear and/ culture presenting in the Out

patient section of the Department of ENT from April 2008 to October 2009 were included. A detailed ear, nose, throat examination including rigid nasal endoscopy was performed for all patients as per the proforma (attached as Appendix B). A complete eye examination was performed by the Ophthalmologist. For all patients,the diseased nasal mucosa was sent for histopathological examination and for fungal smear and culture. Post operatively, rigid nasal endoscopy was performed for all patients at 1 week. Thereafter, patients with non invasive fungal sinusitis or those with invasive fungal sinusitis on oral medication were followed up every 3 months till 1 year then at 6 monthly intervals for 2 years. Patients receiving Amphotericin B for invasive fungal sinusitis were followed up every month till conclusion of therapy, then at 3 monthly intervals for a year and at 6 monthly intervals for 2 years.

In the retrospective series, patients with a diagnosis of fungal sinusitis as confirmed by histopathology and fungal smear and/ culture managed in the Department of ENT from 1998 to 2008 having complete medical records were included.

Institutional Review Board approval was obtained prior to commencing the study. The presence of co-morbidities was noted. Information regarding laboratory tests, histopathological examination, fungal smear, culture and sensitivity results and treatment given were recorded till the treatment was

complete. Specific features on CT scanning +/- MRI scanning of the paranasal sinuses were noted.

f) Sample size:

The prevalence of orbital involvement in allergic fungal sinusitis has been determined in a previous study to be 56% [21] and in acute invasive sinusitis to be 67% [19]. Sample size was calculated as per the former study.

Formula for calculating sample size → $n = (z@/2)^2 PQ/d^2$

n (number of subjects)

z@/2 = 1.96 (a constant)

P = 56

Q = 100 – P = 44

d(Precision) = 10

$n = (z@/2)^2 PQ/d^2 = 1.96^2 \times 50 \times 50/10^2 = 95.$

h) Statistical Analysis:

Categorical variables are presented using frequencies and percentages. Association between categorical variables was assessed using Chi-square test and Fisher's exact test. *P-value < 0.05* is considered statistically significant. All statistical analyses were performed using SPSS 16.0.

RESULTS AND ANALYSIS

Of the100 patients included in the study, 34 patients had invasive fungal rhinosinusitis and 66 had non invasive fungal rhinosinusitis.

1.Invasive fungal rhinosinusitis

Table 1. Types of invasive fungal rhinosinusitis (n=34)

Type	Number of patients
Acute invasive	25
Chronic granulomatous invasive	8
Chronic invasive	1
Total	34

Invasive fungal rhinosinusitis includes patients with acute invasive, chronic invasive and chronic granulomatous invasive fungal rhinosinusitis. The demographic and orbital signs and symptoms and radiological findings of each were considered together and separately.

Table 2.Demographic Table (n=34)

Age range	**Male**	**Female**	**Total**
<15	3	0	3 (8.8%)
16-25	1	0	1 (2.9%)
26-40	7	1	8 (23.5%)
41-55	9	5	14 (41.2%)
>55	5	3	8 (23.5%)
Total	25 (73.5%)	9 (26.5%)	

64.7% of the patients were over 41 years. Age range was 7 to 78 years with the mean age 47.43 years. 25 (73.5%) of the patients were male.

Table 3. Ophthalmic symptoms (n=34)

	Periorbital Swelling	**Decreased vision**	**Diplopia**	**Periorbital Pain**	**Duration mean**	**Range**
Right	12 (35.3%)	10(29.4%)	7 (20.6%)	10(29.4%)	100 days	2 days – 3 years
Left	11(32.3%)	9(26.5%)	8 (23.5%)	11 (32.3%)		
Bilateral	1 (2.9%)	1 (2.9%)	0	0		
Total	23(67.6%)	20(58.8%)	15 (44.1%)	21(61.7%)		

23 (67.6 %) of the patients had ocular symptoms. Periorbital swelling and pain were the most common symptoms. Decreased vision was seen in 20 (58.8%) patients. The mean duration of symptoms was 100 days.

Table 4. Ophthalmological examination (n=34)

	Proptosis	**Impaired vision**	**EOM restriction**	**Optic Atrophy**	**Papilloedema**
Right	12(35.3%)	10(29.4%)	12(35.3%)	8(23.5%)	1 (2.9%)
Left	9 (26.5%)	8 (23.5%)	9 (26.5%)	6(17.6%)	1 (2.9%)
Total	21(61.8%)	18 (53%)	21(61.8%)	14(41.2%)	2 (5.8%)

Proptosis was the most common sign with 61.8% of patients having it. Optic atrophy was seen in 14 (41.2%) and impaired vision was seen in 18 (53.5%) patients. Papilloedema was seen in 2 (5.8 %) of patients.

Table 5.Radiology (n=34)

	Lamina papyracea erosion	**Roof of orbit erosion**	**Floor of orbit erosion**	**Intra ocular mass**	**Intra ocular muscle involvement**	**Optic nerve compression**
Right	9 (26.5%)	2 (5.8%)	4 (11.8%)	4 (11.8%)	4 (11.8%)	4 (11.8%)
Left	4 (11.8%)	1 (2.9%)	1 (2.9%)	3 (8.8%)	1 (2.9%)	0
Bilateral	0	0	0	0	0	0
Total	13 (38.3%)	3 (8.8%)	5 (14.7%)	7 (20.6%)	5 (14.7%)	4 (11.8%)

13(38.3%) patients had erosion of the lamina papyracea and 7(20.6%) had intraocular mass. 5 (14.7 %) had intra ocular muscle involvement. 4(11.8%) had optic nerve involvement.

1a) Acute invasive fungal rhinosinusitis

Table 1.Demographic Table (n=25)

Age range	Male	Female	Total
<15	3	0	3 (12%)
16-25	0	0	-
26-40	5	1	6 (24%)
41-55	5	4	9 (36%)
>55	4	3	7 (28%)

16 patients(64%) were above 41 years. Age range was 7 to 78 years with the mean age 45.28 years. 17 (72%) of the patients were male.

Table 2. Ophthalmic symptoms (n=25)

	Periorbital Swelling	Decreased vision	Diplopia	Periorbital Pain	Duration mean	Range
Right	7 (28%)	5 (20%)	4 (16%)	7(28%)	10.82	2-21 days
Left	9(36%)	7(28%)	6(24%)	9 (36%)		
Bilateral	1 (4%)	1 (4%)	0	0		
Total	17(68%)	13(52%)	10 (40%)	16(64%)		

17 (68%) of the patients had ocular symptoms. Periorbital swelling and pain were the most common symptoms. Left side was more affected than right side. The mean duration of symptoms was 10.82 days.

Table 3. Ophthalmological examination (n=25)

	Proptosis	**Impaired vision**	**EOM restriction**	**Optic Atrophy**	**Papilloedema**
Right	7 (28%)	5 (20%)	7 (28%)	3 (12%)	1 (4%)
Left	7 (28%)	6 (24%)	6 (24%)	4 (16%)	1 (4%)
Total	14 (56%)	11 (44%)	13 (52%)	7 (28%)	2 (8%)

Proptosis (56%)was the most common sign . Optic atrophy was seen in 7 (28%) and impaired vision was seen in 44% patients. Papilloedema was seen in 8 % of patients.

Table 4. Radiology (n=25)

	Lamina papyracea erosion	**Roof of orbit erosion**	**Floor of orbit erosion**	**Intra ocular mass**	**Intra ocular muscle involvement**	**Optic nerve compression**
Right	4 (16%)	0	2 (8%)	2 (8%)	1 (4%)	0
Left	4 (16%)	1 (4%)	1 (4%)	3 (12%)	0	0
Bilateral	0	0	0	0	0	0
Total	8 (32%)	1 (4%)	3 (12%)	5 (20%)	1 (4%)	0

8 (32%) patients had erosion of the lamina papyraceae and 5 had an intraocular mass (20%). No patient had optic nerve compression.

1b)Chronic granulomatous invasive fungal rhinosinusitis

Table 1. Demographic Table (n=8)

Age range	Male	Female	Total
<15	0	0	0
16-25	1	0	1 (12.5%)
26-40	2	0	2 (25%)
41-55	3	1	4 (50 %)
>55	1	0	1 (12.5%)
Total	7	1	8

62.5% patients were over 41years. Age range was 20 to 58 years with the mean age 41.5 years. Most of the patients were male.

Table 2. Ophthalmic symptoms (n=8)

	Periorbital Swelling	Decreased vision	Diplopia	Periorbital Pain	Duration mean	Range
Right	5 (62.5%)	5 (62.5%)	3(37.5%)	3 (37.5%)	168.6 days	5 days-3 years
Left	1 (12.5%)	1(12.5%)	1(12.5%)	1(12.5%)		
Total	6(75%)	6 (75%)	4 (50%)	4 (50%)		

75% patients had periorbital swelling. 75% had decreased vision. Right side was more affected than left side. The mean duration of symptoms was 168.6 days.

Table 3. Ophthalmological examination (n=8)

	Proptosis	Impaired vision	EOM restriction	Optic Atrophy
Right	5 (62.5%)	5 (62.5%)	5 (62.5%)	5 62.5%)
Left	1 (10%)	1 (10%)	1 (10%)	1 (10%)
Total	6 (72.5%)	6 (72.5%)	6 (72.5%)	6(72.5%)

Proptosis, impaired vision & extra ocular movement restriction were seen in 5 (62.5%) of patients. Optic atrophy was seen in a high proportion (72.5%) patients.

Table 4. Radiology (n=8)

	Lamina papyracea erosion	**Roof of orbit erosion**	**Floor of orbit erosion**	**Intra ocular mass**	**Intra ocular muscle involvement**	**Optic nerve compression**
Right	4 (50%)	2 (25%)	2 (25%)	2 (25%)	3 (37.5%)	4 (50%)
Left	0	0	0	0	0	0
Bilateral	0	0	0	0	0	0
Total	4 (50%)	2 (25%)	2 (25%)	2 (25%)	3 (37.5%)	4 (50%)

Four(50%) patients had erosion of the lamina papyracea and 2 had an intraocular mass (25%) Three patients had intraocular muscle involvement (37.5%) and 4 (50%) had optic nerve compression.

1c) Chronic invasive fungal rhinosinusitis (n=1)

The patient was a 55 year old male.

Table 1. Ophthalmic symptoms (n=1)

	Periorbital Swelling	**Decreased vision**	**Diplopia**	**Periorbital Pain**	**Duration**
Left	Present	Present	Present	Present	4 months

He presented with left sided periorbital swelling and pain, diplopia and decreased vision of 4 months duration.

Table 2. Ophthalmological examination (n=1)

	Proptosis	**Impaired vision**	**EOM restriction**	**Optic Atrophy**
Left	Present	Present	Present	Present

On examination he had proptosis, ophthalmoplegia and optic atrophy.

Table 3. Radiology (n=1)

	Lamina papyracea erosion	**Roof of orbit erosion**	**Floor of orbit erosion**	**Intra ocular mass**	**Intra ocular muscle involvement**	**Optic nerve compression**
Right	1	0	0	0	0	0
Left	0	0	0	0	1	0

He had erosion of right lamina papyracea and left intra ocular muscle involvement

Patients with acute invasive fungal rhinosinusitis were compared with those with chronic invasive and chronic granulomatous invasive fungal rhinosinusitis and tests of significance were performed to see whether there was any significant difference in terms of orbital involvement. Orbital involvement was considered as clinical and radiological involvement.

Comparison between acute invasive fungal rhinosinusitis and chronic invasive & chronic granulomatous invasive fungal rhinosinusitis

Table 1. Ophthalmic symptoms

	Periorbital Swelling	**Decreased vision**	**Diplopia**	**Periorbital Pain**
Acute (n=25)	17 (68%)	13 (52%)	10 (40%)	16 (64%)
Chronic (n=9)	8 (88.9%)	7 (77.8%)	5 (55.6%)	5 (55.6%)
P value	.386	.250	.462	.704

There was no significant difference in orbital symptoms between patients with chronic invasive and chronic granulomatous fungal rhinosinusitis and acute invasive fungal rhinosinusitis.

Table 2. Ophthalmological examination

	Proptosis	**Impaired vision**	**EOM restriction**	**Optic Atrophy/ Papilloedema**
Acute (n=25)	14 (56%)	11 (44%)	13 (52%)	9 (36%)
Chronic (n=9)	7 (77.8%)	7 (77.8%)	7 (77.8%)	7 (77.8%)
P value	.427	.125	.250	.052

Although there was no significant difference in orbital signs like proptosis, impaired vision and ophthalmoplegia between patients with acute invasive and patients with chronic invasive and chronic granulomatous invasive fungal

rhinosinusitis, optic atrophy/papilloedema was significantly more in chronic invasive and chronic granulomatous invasive fungal rhinosinusitis.

Table 3.Radiology

	Lamina papyracea erosion	**Roof of orbit erosion**	**Floor of orbit erosion**	**Intra ocular mass**	**Intra ocular muscle involvement**	**Optic nerve compression**
Acute (n=25)	8 (32%)	1 (4%)	3 (12%)	5 (20%)	1 (4%)	0
Chronic (n=9)	5 (55.6%)	2 (22.2%)	2 (22.2%)	2 (22.2%)	4 (44.4%)	4 (44.4%)
P value	.254	.164	.591	1.000	.012	.003

Radiologically, intraocular muscle involvement and optic nerve compression were significantly more in chronic invasive and chronic granulomatous invasive fungal rhinosinusitis as compared to acute invasive fungal rhinosinusitis.

2.Non invasive fungal rhinosinusitis

Table 1. Types of non invasive fungal rhinosinusitis

Type	Number of patients
Allergic fungal	54
Fungus ball	12
Total	66

Non invasive fungal rhinosinusitis includes patients with allergic fungal rhinosinusitis and those with fungus ball. The demographic and orbital signs and

symptoms and radiological findings of each were considered separately and together.

Table 2.Demographic Table (n=66)

Age range	**Male**	**Female**	**Total**
<15	0	0	0
16-25	3	5	8 (12.1%)
26-40	5	15	20(30.3%)
41-55	8	15	23 (34.8%)
>55	4	11	15 (22.7%)
Total	20 (30.3%)	46 (69.7%)	66

38 (57.5%) of the patients were above 41 years. Age range was 16 to 72 years with the mean age 48 years. 46 (69.7%) of the patients were female.

Table 3. Ophthalmic symptoms (n=66)

	Periorbital Swelling	**Decreased vision**	**Diplopia**	**Periorbital Pain**	**Duration mean**	**Range**
Right	3 (4.5%)	0	0	1(1.5%)	8 months	8 days – 2 years
Left	3(4.5%)	2(3%)	0	3 (4.5%)		
Bilateral	2(3%)	1 (1.5%)	1 (1.5%)	1(1.5%)		
Total	8(12.1%)	3 (4.5%)	1 (1.5%)	5(7.6%)		

8 (12.1%) of the patients had ocular symptoms. Periorbital swelling and pain were the most common symptoms. 3 (4.5%) patients had decreased vision. The mean duration of symptoms was 8 months.

Table 4. Ophthalmological examination (n=66)

	Proptosis	Impaired vision	EOM restriction	Optic Atrophy	Papilloedema
Right	3 (4.5%)	0	0	0	0
Left	2 (3%)	4 (6.1%)	3 (4.5%)	2 (3%)	0
Bilateral	1 (1.5%)	0	0	0	0
Total	6 (9%)	4 (6.1%)	3 (4.5%)	2 (3%)	0

Proptosis(9%) was the most common sign.Optic atrophy was seen in 2 (3%) and impaired vision was seen in 4 (6.1%) patients. None had papilloedema.

Table 5. Radiology (n=66)

	Lamina papyracea erosion	Roof of orbit erosion	Floor of orbit erosion	Intra ocular mass	Intra ocular muscle involvement	Optic nerve compression
Right	8 (12.1%)	1 (1.5%)	0	5 (7.6%)	2 (3%)	1 (1.5%)
Left	8(12.1%)	4 (6.1%)	1(1.5%)	5 (7.6%)	0	2(3%)
Bilateral	1 (1.5%)	0	0	1 (1.5%)	0	0
Total	17 (25.7%)	5 (7.6%)	1 (1.5%)	11 (16.7%)	2 (3%)	3 (3%)

17(25.7%) of the patients had erosion of the lamina papyracea and 11 (16.7%) had intraocular mass. 3(3%) had optic nerve compression.

2a) <u>Allergic fungal rhinosinusitis</u>

Table 1.Demographic Table (n=54)

Age range	Male	Female	Total
<15	0	0	0
16-25	3	5	8 (14.8%)
26-40	5	14	19(35.2%)
41-55	7	13	20 (37%)
>55	1	6	7 (13%)
Total	16	38	54

37% of the patients were between the ages of 41 and 55 years. Age range was 16 to 67 years with the mean age 39.13 years. 38 (70.3%) of the patients were female.

Table 2. Ophthalmic symptoms (n=54)

	Periorbital Swelling	**Decreased vision**	**Diplopia**	**Periorbital Pain**	**Duration mean**	**Range**
Right	3 (5.5%)	0	0	1(1.8%)	8 months	8 days – 2 years
Left	3(5.5%)	1(1.8%)	0	2 (3.6%)		
Bilateral	2(3.7%)	1 (1.8%)	1 (1.8%)	1(1.8%)		
Total	8(14.8%)	2 (3.7%)	1 (1.8%)	4(7.4%)		

8 (14.8%) of the patients had ocular symptoms. Periorbital swelling and pain were the most common symptoms. The mean duration of symptoms was 8 months.

Table 3. Ophthalmological examination (n=54)

	Proptosis	**Impaired vision**	**EOM restriction**	**Optic Atrophy**	**Papilloedema**
Right	3 (5.5%)	0	0	0	0
Left	2 (3.6%)	3 (5.5%)	2 (3.6%)	1 (1.8%)	0
Bilateral	1 (1.8%)	0	0	0	0
Total	6 (11.1%)	3 (5.5%)	2 (3.7%)	1 (1.8%)	0

Proptosis was the most common sign (11.1%). Optic atrophy was seen in 1 and impaired vision was seen in 3 (5.5%) patients.

Table 4. Radiology (n=54)

	Lamina papyracea erosion	**Roof of orbit erosion**	**Floor of orbit erosion**	**Intra ocular mass**	**Intra ocular muscle involvement**	**Optic nerve compression**
Right	7 (13%)	1 (1.8%)	0	5 (9.25%)	2 (3.6%)	1 (1.8%)
Left	8(14.8%)	4 (5.5%)	1(1.8%)	5 (9.25%)	0	2(3.6%)
Bilateral	0	0	0	0	0	0
Total	15 (27.8%)	5 (7.3%)	1 (1.8%)	10 (18.5%)	2 (3.6%)	3 (5.4%)

15 (27.8%) patients had erosion of the lamina papyracea and 10 (18.5%) had intraocular mass. 3(5.4%) had optic nerve compression.

2b) Fungus Ball

Table 1. Demographic Table (n=12)

Age range	Male	Female	Total
<15	0	0	0
16-25	0	0	0
26-40	0	1	1 (8.3%)
41-55	1	2	3 (25%)
>55	3	5	8 (66.7%)
Total	4(33.3%)	8(66.7%)	

66.7% of the patients were above the age of 55 years. Age range was 39 to 72 years with the mean age 57 years. 8 (66.7%) of the patients were male.

Table 2. Ophthalmic symptoms (n=12)

	Periorbital Swelling	Decreased vision	Diplopia	Periorbital Pain
Right	0	0	0	0
Left	0	1 (8.3%)	0	1 (8.3%)
Bilateral	0	0	0	0
Total	0	1 (8.3%)	0	1 (8.3%)

Ocular symptoms were uncommon in fungus ball. Only 1 (8.3%) patient had decreased vision and pain of 1 week duration.

Table 3. Ophthalmological examination (n=12)

	Proptosis	**Impaired vision**	**EOM restriction**	**Optic Atrophy**	**Papilloedema**
Right	0	0	0	0	0
Left	0	1 (8.3%)	1 (8.3%)	1 (8.3%)	0
Total	0	1 (8.3%)	1 (8.3%)	1 (8.3%)	0

1 patient had impaired vision, restriction of extraocular movements and optic atrophy.

Table 4. Radiology (n=12)

	Lamina papyracea erosion	**Roof of orbit erosion**	**Floor of orbit erosion**	**Intra ocular mass**	**Intra ocular muscle involvement**	**Optic nerve compression**
Right	1(8.3%)	0	0	0	0	0
Left	0	0	0	0	0	0
Bilateral	1(8.3%)	0	0	1(8.3%)	0	0
Total	2 (16.6%)	0	0	1(8.3%)	0	0

2 (16.6%) patients had erosion of the lamina papyracea and 1 had intraocular mass (8.3%) on CT scan.

Patients with invasive fungal rhinosinusitis were compared with those with non invasive fungal rhinosinusitis and tests of significance were performed to see whether there was any significant difference in terms

of orbital involvement. Orbital involvement was considered as clinical and radiological involvement.

<u>Comparison between invasive fungal rhinosinusitis and non invasive fungal rhinosinusitis</u>

Table 1. Ophthalmic symptoms

	Periorbital Swelling	**Decreased vision**	**Diplopia**	**Periorbital Pain**
Invasive (n=34)	25(73.5%)	20(58.8%)	15(44.1%)	21(61.8%)
Non invasive (n=66)	8(12.1%)	3(4.5%)	1(1.5%)	5 (7.6%)
P value	.000	.000	.000	.000

Periorbital swelling and pain, decreased vision and diplopia were significantly more in patients with invasive fungal rhinosinusitis as compared to patients with non invasive fungal rhinosinusitis.

Table 2. Ophthalmological examination

	Proptosis	**Impaired vision**	**EOM restriction**	**Optic Atrophy/ Papilloedema**
Invasive (n=34)	21(61.8%)	18(52.9%)	20(58.8%)	16 (47.1%)
Non invasive (n=66)	6(9.1%)	4 (6.1%)	3(4.5%)	2 (3%)
P value	.000	.000	.000	.000

Proptosis, impaired vision, ophthalmoplegia and optic atrophy were significantly more in invasive as compared to non invasive fungal rhinosinusitis.

Table 3.Radiology

	Lamina papyracea erosion	**Roof of orbit erosion**	**Floor of orbit erosion**	**Intra ocular mass**	**Intra ocular muscle involvement**	**Optic nerve compression**
Invasive (n=34)	13(38.2%)	3(8.8%)	5(14.7%)	7(20.6%)	5(14.7%)	4(11.8%)
Non invasive (n=66)	21(31.8%)	3(4.5%)	2(3%)	13(19.7%)	3(4.5%)	1(1.5%)
P value	.521	.406	.043	.916	.117	.044

Radiologically, erosion floor of orbit and optic nerve compression were significantly more in invasive compared to non invasive fungal rhinosinusitis. There was no significant difference in erosion of lamina papyraceae, erosion of the roof of orbit, intra ocular mass and intra ocular muscle involvement between patients with invasive and patients with non invasive fungal rhinosinusitis.

DISCUSSION

Orbital involvement is clinically apparent in most cases of fungal sinusitis and proper evaluation of ocular function should be part of the evaluation of the affected patient. The various aspects of evaluation for orbital involvement include clinical assessment for proptosis, periorbital pain and swelling, diplopia, loss of visual acuity, fields, restriction of ocular movements, fundus examination and radiological assessment. While in most instances clinical involvement mirrors the degree of radiological involvement of the orbit, in certain rapidly progressive cases of fungal sinusitis such as acute invasive fungal sinusitis, orbital symptoms may be disproportionate to the degree of orbital invasion seen radiologically. In the present study we have specifically looked for orbital involvement in both invasive and non-invasive fungal sinusitis and found a number of differences between the two categories.

Our finding that orbital involvement in non-invasive fungal sinusitis is infrequent similar to that of other studies. In a large series of 82 patients with AFRS, Marple et al[26], found an overall incidence of ocular findings to be 18.3%. Telecanthus was the most common symptom (7.3%) followed by diplopia. Three(3.7%) patients had visual loss. Similarly, Cody et al found that 17% of a series of 42 patients with AFRS had orbitalinvolvement. However they did not specify what the symptoms and signs were. In the present study, we found that the

overall orbital involvement was 14.8%. Eight patients(14.8%) had periorbital swelling, 1 had diplopia and 4 (7.4%) presented with periorbital pain.

Proptosis and periorbital swelling are common features of AFRS and have been reported in as many as 50% of patients in some series (Manning et al). In our study, the most common orbital sign on examination was proptosis (11.1%). Proptosis resolves with surgical debridement of the sinuses and postoperative oral steroid therapy(Chang et al).

Visual loss is an unusual feature of non invasive fungal sinusitis. The prevalence of visual loss in some series varies from 3-10%. (Marple et al; Manning et al). Visual loss in AFRS is most often due to pressure by the expanding sinuses on the optic nerve. It is therefore reversible and often resolves with appropriate decompression along with oral steroid therapy. In our study, we encountered 2 (3.7%) patients presenting with decreased vision. One had bilateral nasal obstruction and watery nasal discharge of 6 month's duration and decreased vision on the left side of 8 day's duration. She was taken up for endoscopic sinus surgery and post operatively, was started on systemic steroids. On the second post operative day, her vision improved from negative perception of light to counting fingers at 20 metres. Two weeks after surgery her vision further improved. Our second patient with visual loss presented with bilateral proptosis and she underwent bilateral endoscopic sinus surgery and orbital decompression followed

by systemic steroids. Dunlop et al[33] reported 1 case of allergic fungal rhinosinusitis presenting with visual loss who was treated with debridement of sinuses and antibiotics initially without improvement. She was subsequently started on systemic corticosteroids and rapidly improved.

Visual loss due to fungus ball is even less common. In our study of patients with fungus ball, 1 patient (8.3%) presented with orbital apex syndrome with loss of vision and restriction of extraocular muscle movements. The patient was a 72 year old man with well controlled diabetes mellitus (HBA1C – 7.6). He underwent endoscopic sinus surgery and orbital decompression and was found to have a polypoidal mass in the posterior ethmoids and sphenoid sinus. He was started on the Inj. Amphotericin B which was subsequently changed to Voriconazole (because of resistance to Amphotericin B). There was rapid progression of symptoms and he died 4 days post operatively of pneumonia. The only other case report of fungus ball causing visual loss was that of Thiagalingam et al[34] who reported a case of fungus ball in the sphenoid sinus by Pseudallescheria boydii presenting with orbital apex syndrome. The patient was a 92 year old man who presented with painless loss of vision of 3 day's duration. He was started on Inj. Penicillin and oral Voriconazole. He underwent left endoscopic sphenoidotomy and was found to have a mycetoma in sphenoid sinus. Here again, the patient died 1 month after surgery due to unrelated causes.

Restriction of extraocular muscle movement is also an uncommon feature of orbital involvement in AFRS. Only 2 patients in our series were affected, similar to the few numbers seen in other series [26]. The reason for this is that restriction of muscle movement is purely mechanical unlike in patients with invasive sinusitis where actual invasion of the muscle may occur. A rare presentation of AFRS is subperisoteal abscess formation as reported by Meyer and Nagi[20]. The patient described underwent sinus drainage followed by left anterior orbitotomy and drainage of the abscess that contained yellowish fluid. Culture of this fluid showed Aspergillosis.

Radiological evidence of orbital erosion in noninvasive fungal sinusitis is seen more commonly than clinical involvement. In most patients this is manifested as erosion of the lamina papyracea and intraocular mass. As the ethmoid sinus is the most commonly involved sinus in AFRS, erosion of the lamina papyraceae may occur with expansion of the contents of the sinuses into the orbit. In the present series we noted lamina papyraceae erosion in upto 27.8% of patients and an intraocular mass in 18.5%. Nussenbaum et al[24] in a retrospective study of 142 patients with allergic fungal sinusitis, found that 21(15%) of patients had orbital involvement on CT scan. Ghegan et al[21] in a study of 27 patients found that 15 (56%) had skull base or orbital erosion. They did not specify exactly how many patients had purely orbital erosion. Manning et al[14] in a study of 10 patients

reported that 4 (40%) patients had orbital involvement. None of these studies specify which part of the orbit was involved. Erosion of the floor of orbit (1.8%), intraocular muscle involvement(3.6%) and optic nerve compression(5.4%) were less commonly seen radiological features in our cases.We could not find any reports mentioning bony erosion in patients with fungus ball. In our study, of the 12 patients with fungus ball, 2(16.7%) had erosion of the lamina papyracea and 1 had intra ocular mass.

Overall, patients with non invasive fungal sinusitis in the present study have a lesser degree of orbital involvement than those with invasive fungal sinusitis. Of the 8 (12.1%) of patients with orbital symptoms, periorbital swelling followed by periorbital pain, decreased vision and diplopia were the symptoms complained of. Proptosis was the most common sign. Radiological involvement of the orbit was also less at 25.7 %(17 patients). These findings are similar to other reports (Manning et al, Nussenbaum et al).

Unlike noninvasive fungal sinusitis, orbital involvement in invasive fungal rhinosinusitis is well documented. Nithyanandam et al[19] in a study of 34 patients with mucormycosis found that 23 (68%) had orbital involvement clinically. Loss of vision was the most common symptom(67.6%) followed by diplopia(29.4%). On examination, 23(67.6%) patients had ptosis and ophthalmoplegia and 14(41.2%) had proptosis. 9 patients(26.5%) underwent orbital exenteration and

11(32.4%) patients died. In our study, of the 34 patients with invasive fungal rhinosinusitis, the most common symptom was periorbital swelling (67.6%) followed by periorbital pain (61.7%), decreased vision (58.8%) and diplopia (44.1%). The commonest orbital signs on examination were proptosis and ophthalmoplegia(61.8%) followed by impaired vision (53%). 14 patients (41.2%) had optic atrophy on ophthalmoscopy and 2 (5.8%) had papilloedema. 12 (35.3%) patients underwent orbital exenteration and 8 (23.5%) patients died.

Bhansali et al[35] in a study of 35 patients of mucormycosis with diabetes mellitus found that 89% had ophthalmoplegia, 83% had proptosis and 80% had loss of vision. The most common symptom was periorbital swelling(66%) followed by periorbital pain (43%) In our study, the most common predisposing condition was uncontrolled diabetes mellitus (68%).

Ferry et al[36] in a report of 16 cases found that 6 (37.5%) had proptosis and 4 (25%) had visual loss at initial presentation. In the series of 114 patients by Yohai et al[37] 18 (16%) had proptosis, 34 (30%) had visual loss and 33 (29%) had ophthalmoplegia. Overall 80 patients (70%) had orbital involvement. In our series we found that 67.6% patients had orbital involvement clinically. Proptosis and visual loss were seen in a higher number of patients in our study.

Gillespie et al[17] reported a series of 25 cases of acute fulminant fungal rhinosinusitis, of whom 16 (64%) had periorbital pain and swelling and 7 (28%) had decreased visual acuity or ophthalmoplegia as the presenting complaint.

CT scans of patients with invasive fungal rhinosinusitis are non specific and do not correlate well with surgical and pathologic findings.[17] In the study by Nithyanandam et al[19] of 34 patients with mucormycosis, 18 patients had orbital changes on CT scan which included intraocular muscle involvement, and minimal obliteration of fat shadow at the orbital apex. They do not mention the exact site/frequency of radiological erosion. Of the 35 patients in the series reported by Bhansali et al [35] 28(80%) had CT findings of orbital erosion. The authors do not mention the exact site of erosion. In Bhadada et al[29] report of 6 cases of patients with mucormycosis, 5 (83.3%) patients had orbital erosion. They also do not mention which portion of the orbit was involved.

In the present study we found that 13 (38.3%) patients had CT scan evidence of lamina papyracea erosion, 7 (20.6%) patients had intraocular mass,3 (8.8%) had erosion of roof of orbit, 5 (14.7%) had erosion of floor of orbit and involvement of intraocular muscle. Further, orbital symptoms and signs like proptosis, impaired vision, diplopia, pain and optic atrophy/papilloedema were significantly more in patients with invasive as compared to patients with non invasive fungal rhinosinusitis. Radiologically, erosion of floor of orbit and optic nerve

compression were significantly more in invasive compared to non invasive fungal rhinosinusitis.

A literature search did not reveal any studies comparing the orbital involvement in acute invasive and chronic granulomatous and chronic invasive fungal rhinosinusitis. In our study, we found that there was not much difference in orbital symptoms between patients with chronic invasive and chronic granulomatous fungal rhinosinusitis and acute invasive fungal rhinosinusitis. However, optic atrophy and papilloedema were significantly more frequently seen in chronic invasive and chronic granulomatous invasive fungal rhinosinusitis as compared to acute invasive fungal rhinosinusitis. Radiologically, intraocular muscle involvement and optic nerve compression were significantly more in chronic invasive and chronic granulomatous invasive fungal rhinosinusitis as compared to acute invasive fungal rhinosinusitis.

CONCLUSION

In conclusion, orbital involvement is much more common in occurrence in invasive fungal sinusitis compared to non invasive fungal sinusitis. Clinical and endoscopic examination is an essential part of assessing orbital involvement. Radiological findings in invasive fungal sinusitis evidently bear no correlation with clinical findings. Indeed, despite the high prevalence of ocular involvement in patients with invasive fungal sinusitis, the radiological findings are often unremarkable. A high index of suspicion and early biopsy and fungal culture testing in suspected patients helps early identification and planning of subsequent management.

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Appendix A

Informed Consent form

Title: Orbital involvement in Fungal Sinusitis

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age:_____

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

Appendix B

PROFORMA

Serial Number :
Name :
Age/Sex : Hospital number :
Occupation : Contact number :
Address:
Admitting unit :
DOA: DOS: DOD:
Clinical Diagnosis
Acute (Fulminant) invasive fungal sinusitis, Chronic invasive fungal sinusitis, Granulomatous invasive fungal sinusitis, Allergic fungal sinusitis, Fungal Ball, Entomophthoromycosis
Clinical History

- **Sinonasal symptoms**

  - *Nasal Obstruction - Present/Absent*

Side	Duration

  - *Nasal Discharge - Present/Absent*

Type	Side	Duration

  - Sneezing - Present/Absent
  - Post Nasal discharge - Present/Absent

- **Eye symptoms** *Right* *Left*

Swelling of eye		
Decreased Vision		
Diplopia		
Pain eye		

- Headache, Fever, LOC, Seizures, Asthma/Atopy, Aspirin hypersensitivity

Co-morbidities

- DM - Controlled/Uncontrolled, Haematological diseases,Transplant,Renal diseases,Others

Current drug use

- Immunosuppressant, Systemic/Topical steroid

Prior Sinus Surgery – Y/N

Date	Details

Examination

- *Rigid Nasal Endoscopy* – Right Left

Inferior Turbinate		
Floor of Nose		
Inferior Meatus		
Nasopharynx		
Middle Turbinate		
Middle Meatus		
Sphenoethmoidal Recess		
Roof of nose		
Septum		
Nasal Cavity		

- *Eye –* *Right* *Left*

Visual Acuity		
Colour Vision		
Automated Perimetry		
Extra ocular motility		
Ophthalmoscopy		

Investigations

1.Radiology

Region	**Right**			**Left**		
Sinuses	Lund Mackay	Hyper dense areas	Bone Erosion	Lund Mackay	Hyper dense areas	Bone Erosion
Maxillary Sinus						
Anterior Ethmoid Sinus						
Posterior Ethmoid						

Sinus						
Frontal Sinus						
Sphenoid Sinus						
OMC						

Region	**Right**	**Left**
Nasal Cavity		
Nasopharynx		
Septum		

Region	**Right**	**Left**
Erosion of Roof of Ethmoid		
Erosion of Cribriform Plate		
Erosion of Lamina Papyraceae		
Erosion of Roof of Orbit		
Erosion of Floor of Orbit		
Optic Nerve compression		
Intraocular mass/abscess		
Intraocular muscle involvement		
Intracranial extension – extradural		
Intracranial extension – intradural		

2.Mycology –

Date	Fungal Smear (KOH)	Fungal Culture

3.HIV, Au.
4.Random Blood Sugar
Fasting/Post prandial
HbA1C
5.Skin Allergy test
6.Fungal Specific Ab
7.IgE
8.Histopathology –

- **Acute Invasive**

Fungal invasion of Mucosa/Submucosa/Blood vessels/Bone	Yes	No
Inflammatory exudates – Acute/Chronic		

cells		
Tissue necrosis		
Thrombosis		
Fibrinoid necrosis		
Fibrosis		
Vasculitis		

- **Chronic Invasive**

Necrosis	Yes	No
Fibrosis		
Vasculitis		
Fungal hyphae in Mucosa/Submucosa/Blood vessels/Bone Septate/Aseptate		
Chronic inflammatory infiltrate		

- **Chronic Granulomatous Invasive**

Granuloma	Yes	No
Fibrinoid Necrosis		
Vasculitis		
Fungal hyphae in Mucosa/Submucosa/Blood vessels/Bone Septate/Aseptate		
Chronic inflammatory cells		

- **Entomophthoromycosis**

Granuloma		
Fungal hyphae –Septate/Aseptate		
Splendor Hoeppli phenomenon		
Inflammation Acute/Chronic		
Tissue necrosis		

- **Allergic Fungal Sinusitis**

Specimen (Mucosa & Allergic mucin) sent as	Single	Separate
ALLERGIC MUCIN		
Layered eosinophilic mucus		
Necrotic eosinophils		
Charcot leyden crystals		
Fungal hyphae – Septate/Aseptate		
MUCOSA		
Edema		
Chronic inflammatory cells		
Eosinophils		
Invasion/Necrosis/Granuloma		

- **Fungal Ball**

Dense accumulation of fungal filaments		
Chronic inflammation		
Invasion		
Allergic mucin		

Treatment

- Medical treatment

Drug	Dosage	Start date	End date	Duration

- Surgical treatment

Date	Operation/Procedure & Sinuses involved M E S F	Operative findings Polyps AM Bone erosion Others
		M E S F M E S F M E S F M E S F

- Post operative visits (1 week)

Date	RNE findings	Others

Follow up

- Clinical symptoms

Date	Symptoms NB ND Allergic Other	RNE Grading

- Fungal Culture

Date	Report

- Outcome - Recurrence/ Exacerbation, Stable, Cure

  Death date –
  Cause of death : Fungal sinusitis related/ Non Fungal sinusitis related