Radiological Imaging in Diagnosis and Management of Fungal Rhinosinusitis

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Abstract: Fungal sinusitis has been increasing in number throughout the world off lately. The classification of fungal rhinosinusitis has evolved drastically. Broadly it is classified in two groups that is invasive fungal rhinosinusitis and non-invasive fungal rhinosinusitis. There are five subgroups to these. The invasive group comprises of acute invasive fungal sinusitis (AIFS), chronic invasive fungal sinusitis (CIFS), chronic granulomatous invasive fungal sinusitis (CGIFS) whereas the non-invasive group consists of fungal ball and allergic fungal rhinosinusitis (AFRS). These five subtypes have specific radiological and clinical features. The treatment strategies and prognoses for the subtypes are also different, and depends on their characteristics features. It is important to understand the different types of fungal sinusitis and knowledge of their particular radiologic features are important for the clinician to use appropriate diagnostic techniques for confirmation. Relevant diagnosis and initiation of adequate therapy are essential to avoid any adverse consequence.

Keywords: Mucor mycosis, chronic granulomatous rhinosinusitis, Allergic fungal rhinosinusitis, Black Turbinate sign, De Shazo classification.

Introduction

Fungal infections can be opportunistic or pathogenic. Opportunistic infections mostly occur in immunocompromised patients and pathogenic infections occur in immunocompetent patients. Fungi in general cannot penetrate skin and intact mucosa because they lack keratolytic enzymes. Paranasal mycosis can affect immunocompetent as well as immunocompromised hosts. Changes in body defense such as change in acid base balance, lowered body resistance atopy, ingestion of antibiotics and steroids lead to fungal infections. Fungal infections in India is increasing off late.
Methods:
Systematic review with data taken from PubMed database with Keywords viz. Radiology, Fungal Rhinosinusitis, AFRS, Mucormycosis, Rhino-orbitocerebral mucormycosis.

Mini Review:
The CT scan of the sinuses have succeed the conventional radiography in the diagnosis and confirmation of disease of the paranasal sinuses as it depicts appropriately the anatomical landmarks to the surgeon as it shows all sinus cavities and their complex drainage pathways, in particularly the osteomeatal complex. The coronal plane is the best section because it shows all the sinuses in one view and the approach of the surgeon correlates to this view.

The utilization of a high-resolution bony algorithm is recommended. An intermediate CT scan window of 2500 with a centre of 250 Hounsfield Units (HU) is sufficient for nearly all diagnosis. For approaching sphenoid sinus and posterior ethmoid sinus, direct axial cuts are very important for surgeons understanding. MRI plays a limited role in the evaluation of a non-complicated sinusitis. But MRI has supplanted the CT scanner in the appreciation of intracranial and orbital complications of sinusitis because it provides better visualisation and differentiation of soft tissues than the CT scan. MRI gives details of the soft tissue, orbital and intracranial involvements while the CT scan serves as the road map to the surgery in view of giving accurate bony anatomic details and variations. In all complicated cases of sinusitis it is advised to inject contrast. The inflamed and vascularised tissues take up more contrast in relation to normal tissues, while the necrotic tissue appears as hypodense.

Groppo et al in 2011 demonstrated that Magnetic resonance imaging was more sensitive than CT for the diagnosis of Acute fulminant invasive Fungal Rhinosinusitis (AFIFS) with sensitivity of 85% in MRI compared with 57% that of CT. The most sensitive parameter with MRI was Extra-sinus invasion (87% sensitivity). Magnetic resonance imaging and CT had similar specificities, and the most specific parameter was peri sinus invasion with 83% for MRI and 81% for CT. Peri sinus invasion with MRI was the most sensitive and specific single parameter.

In a study done by Chua et al in 2021, it was demonstrated that Both CT and MRI had high sensitivity and negative predictive value for unilateral maxillary sinus opacification (UMSO), although MRI was more specific (79%) than CT (14%) with a higher positive predictive value. MRI had significantly higher diagnostic certainty than CT. MRI is more specific than CT in diagnosing UMSO, with greater diagnostic certainty.

Hahnel et al in 1999 studied 30 patients who had inflammation of the paranasal sinuses. Both Coronal CT and coronal T1-weighted, MR imaging of the paranasal sinuses were performed in all patients. The scores were compared by using the Wilcoxon matched pairs signed rank test. Anatomy of brain and orbit were better visualised on MR imaging than at CT. Similar results were found in MRI and CT in depiction of any pathology or extension of disease, except the mucosal thickening of nasal cavity, maxillary sinus, frontal sinus and infundibulum. It was concluded that CT was better in depicting fine bony details and anatomical variations and therefore was more helpful in planning functional endoscopic sinus surgery. However, in some patients MR imaging can be used as a primary tool in screening for sinusitis.
### Discussion:

Fungal rhinosinusitis has been classified according to the clinical course, outcome and Tissue invasion. The treatment strategies for the subtypes are also different, as are their prognoses. An understanding of the different types of fungal sinusitis and knowledge of their particular radiologic features are important for the clinician to use appropriate diagnostic techniques for confirmation. Prompt diagnosis and initiation of appropriate therapy are essential to avoid a fatal outcome.²

**Classification of fungal rhinosinusitis**

**De Shazo classification⁵**

<table>
<thead>
<tr>
<th>Based on tissue invasion:</th>
<th>Non – invasive (Extra mucosal / Non penetrating)</th>
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<tr>
<td>Invasive (Mucosal/Penetrating)</td>
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<tr>
<td>• Acute fulminant/ Mucor mycosis – occurs in immunocompromised individuals</td>
<td>• Fungal ball</td>
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<tr>
<td>• Chronic invasive – occurs in people mostly with diabetes mellitus</td>
<td>• Allergic fungal sinusitis /eosinophilic fungal sinusitis</td>
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<tr>
<td>• Granulomatous invasive – occurs in immunocompetent individuals</td>
<td>• Saprophytic fungal infection</td>
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<th>Based on underlying disease</th>
<th>Secondary</th>
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<td>Primary</td>
<td>Acute fulminant course, occurs in immunocompromised individuals,</td>
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<td>Occurs in healthy individuals with no other disease.</td>
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**Acute fulminant invasive fungal sinusitis / Mucormycosis**

It is an acute fulminant fungal infection with a violent and catastrophic clinical course. It is mostly found in immunocompromised individuals i.e., patients with systemic diseases like renal failure, diabetes mellitus, AIDS. Patients with iron overload, patients on immunosuppressive drugs antineoplastic drugs. Patients with malignancy or due to prolonged and injudicious use of steroids and antibiotics.⁶

The neutrophils in diabetic people are not able to properly phagocytose and adhere to endothelial wall hence predisposing them to mucormycosis. Along with this, diabetic ketoacidosis and hyperglycemia provide an excellent environment for the fungus to grow. Iron overload is seen with
deferexamine treatment (patients receiving dialysis) and hemochromatosis. Iron enhances fungal growth and increases susceptibility. Etiological agents consist fungus of mucoraceae family i.e., mucor, Rhizopus, absidia also aspergillus species.7

Clinical presentation

There are many initial nonspecific signs like severe fever, bloody nasal discharge, swelling of sinuses. Crusting of inferior turbinates7 and cartilaginous septum are some of the specific early signs but they mimic sinusitis because they are mostly associated with rhinorrhea, pain, nasal obstruction. The lateral nasal walls and sinuses get involved within days. Facial swelling, gangrenous necrosis of nasal mucosa with purulent discharge with black necrotic crusts inside nose are seen on examining the patients. Black eschar is characteristic if mucormycosis which is black necrotic areas in sinuses/ nose/medial maxillary bone, turbinate or septum and may spread to hard palate.2

Further progression leads to involvement of front ethmoids that leads to swelling and ecchymosis around eye. Involvement of orbit progresses to ophthalmoplegia with palsy of 2,3,4,5 cranial nerves along with ptosis, proptosis, dilated pupils, loss of vision. Through direct extension or vascular route brain can be involved leading to headache, lethargy, coma, death. In investigations blood tests should be done including sugar levels, hba1c, serum creatinine, electrolytes, HIV, neutrophil counts, urgent fungal smear should be done along with biopsy and frozen section of middle turbinates.6

Imaging

Non-contrast CT demonstrates hypoattenuating mucosal thickening or an area of soft-tissue attenuation within the lumen of the involved paranasal sinus and nasal cavity. Spread of disease beyond the intact bone can be seen on CT scan. The earliest sign on CT scan is soft tissue infiltration of perinatal fat planes, however most patients presenting to us were in a advanced stage of disease. Which is probably due to ongoing Covid pandemic and low index of suspicion among clinicians which led to late detection of invasive fungal sinusitis. Rapid and aggressive bone destruction occurs which leads to intracranial and intra-orbital extension. Sometimes mucosal thickening and bony erosion are very mild. Extension occurs through vessels and also through intact bony walls.8

MRI helps in knowing extra sinus extension, orbital involvement (involvement of orbital fat and muscles), intracranial extension.

In intracranial extension we see leptomeningeal involvement (abscess, granuloma), cerebral infarction, thrombosis of internal carotid artery, cavernous sinus thrombosis, mycotic aneurysm. Black turbinate sign on MRI is very specific of mucormycosis – which is present on non-contrast enhancing foci of devitalised tissue in nasal cavity.9

Unlike chronic invasive fungal sinusitis, acute infection generally does not demonstrate hyperdense material within the sinus on non-contrast CT. CT is particularly effective at assessing bony changes.9
FIG 1. CT images of paranasal sinus sagittal view show soft tissue opacification in bilateral ethmoid sinuses and right maxillary sinus along with erosion of medial wall of right sided orbit, erosion of cribriform plate of right side, necrotic turbinate’s also noted, a case of acute invasive fungal rhinosinusitis.

Fig 2A. CT images showing right maxillary sift tissue attenuation along with erosion of inferior wall of left orbit.

Fig 2.B. The image on right side shows skull base erosion with intracranial invasion.

Fig 3. Black turbinate sign on MRI, showing necrosis of left middle turbinate, characteristic of acute invasive fungal rhinosinusitis.
**Fig 4.** Intracranial invasion in a case of acute fungal rhinosinusitis with infarction and necrosis of frontal lobe.

Treatment strategy consists of intravenous liposomal amphotericin B which should be started immediately after high degree of clinical suspicion, and should not wait for histopathology report. Radical surgical debridement of disease till histopathologically normal tissue is obtained. Involvement of orbit may even require orbital exenteration. Post operatively hyperbaric oxygen therapy should also be given.\(^\text{10}\)

**GRANULOMATOUS INVASIVE FUNGAL RHINOSINUSITIS**

This is also termed as indolent fungal sinusitis or primary paranasal granuloma, and is found in immunocompetent individuals. The disease has a chronic course, lasts more than 12 weeks. This is primarily found in Africa (Sudan) and Southeast Asia, with some cases reported in the United States.\(^\text{11}\) It is usually caused by Aspergillus flavus. Individuals are generally immunocompetent. The disease shows typical noncaseating granulomas in affected tissues characterised by slow course with eventual extension beyond walls of sinuses followed by intra orbital and intracranial extension.\(^\text{12}\)

**Fig 5.** Axial non-contrast CT scans shows absence of the normal fat planes along the posterior wall of the right maxillary sinus with increased attenuation in the right maxillary sinus. Peri antral soft tissue invasion can be seen anteriorly and posteriorly.

Treatment options consists of surgical debridement of disease followed by antifungal therapy. This disease responds good to long term itraconazole.
Chronic invasive fungal rhinosinusitis

Chronic Invasive Fungal Sinusitis occurs due to inhalation of fungal spores which are deposited in the nasal airways and paranasal sinuses. Slow progression occurs over several months to years in which fungal organisms invade the nasal mucosa, submucosa, blood vessels, and bony walls of the paranasal sinuses, eroding the orbital plate and dural plates leading to intracranial and orbital complications. This results in significant morbidity and may lead do mortality.\(^\text{13}\)

Etiological agents consist of aspergillus fumigatus, Rhizopus, mucor. Most of the individuals are immunocompetent but diabetes and immunocompromised state leads to increased predisposition.

Symptoms may include rhinorrhoea, epistaxis, nasal polyposis. Invasive symptoms like soft-tissue swelling with destruction of the bony sinus walls takes long duration to show. Palatal erosion is seen after maxillary floor destruction. Intra orbital invasion leads orbital apex syndrome with proptosis; third, fourth, and sixth cranial neuropathy; and decreased vision.\(^\text{14}\) with intracranial invasion seizures, decreased mental status, neurological disorders is seen. Steroid therapy leads to rapid increase in symptoms. To differentiate it from acute invasive fungal rhinosinusitis the following points are helpful

- Chronic course
- Absence of black eschar
- Pattern of spread is specific in both types

Treatment

Treatment includes surgical debridement of the affected tissues and systemic antifungal medication i.e. liposomal amphotericin B. Aggressive therapy with good control of diabetes is needed.

![Fig 6. Coronal non-contrast CT scan showing soft tissue lesion eroding left maxillary sinus.](image)
Coronal non-contrast CT scan showing soft tissue lesion in right nasal cavity, ethmoid, frontal and ethmoid sinuses with destruction of lamina papyracea.

Coronal non-contrast CT scan showing soft tissue mass in right sphenoid sinus.

**Fungal Ball**

Fungal ball is low grade chronic noninvasive fungal sinusitis seen in immunocompetent hosts, non-atopic causing saprophytic fungal colonization of abnormal sinuses. It consists of a Mycelial mass confined to lumen of sinus, hence noninvasive. Most commonly involved sinus is maxillary followed by sphenoid.\(^\text{15}\)

Clinical features consist of unilateral nasal obstruction, rhinorrhea, facial pressure, headaches, dental problems, green brown nasal discharge. Sometimes there are no clinical features and it gets detected radiologically by chance. These are better appreciated in soft tissue window than bone window. On CT scan opacification of involved sinuses with heterogeneous density and thickening of osseous wall of sinus will be seen.\(^{14,15}\)
Fig 9. Coronal CT scan showing complete opacification within atelectatic right maxillary sinus, with thickened walls the right inferior turbinate shows nodular calcification depicting fungal ball.

**Allergic fungal rhinosinusitis**

It is an allergic reaction to fungal debris in which nasal polyposis and allergic mucin are seen. There is presence of fungal debris, nasal polyposis, allergic mucin. Etiological agents consist of *aspergillus flavus* and *fumigatus, bipolaris*. Clinical features consist of nasal blockage, discharge, headache, breathing difficulty, acute exacerbation in spring /pollen season. For diagnosis we use the Bent and Kuhn criteria 16

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<tr>
<th>MAJOR CRITERIA</th>
<th>MINOR CRITERIA</th>
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<td>• Type I hypersensitivity</td>
<td>• Asthma</td>
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<tr>
<td>• Nasal polyposis</td>
<td>• Unilateral disease</td>
</tr>
<tr>
<td>• Characteristic CT findings</td>
<td>• Bone erosion</td>
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<tr>
<td>• Eosinophilic mucin without invasion</td>
<td>• Fungal cultures</td>
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<tr>
<td>• positive fungal stain</td>
<td>• Charcot-Leyden crystals</td>
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<td>• Serum eosinophilia</td>
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Characteristic radiological features consist of

- CT scan showing Focal or diffused areas of increased attenuation caused by calcium and magnesium deposits in the fungal necrotic debris and allergic mucin.

- Bony destruction or Thinning as a result of pressure due expansile fungal growth or inflammatory mediators.

- Double density sign/ Rail track sign – heterogenous signal intensities filled with allergic mucin suggestive of double density sign.17

Characteristic MRI features

- T1 weighted images – Hypo-intensity in center with peripheral enhancement

- T2 weighted images – central areas of signal void or hypodensity with enhancement in periphery.17
Unenhanced CT scan showing soft tissue attenuation of maxillary, ethmoid sinus and left nasal cavity, with areas of hyperintensities at places. (Due to calcium and magnesium deposits in necrotic debris)

T2 weighted MRI showing signal void with peripheral enhancement, a case of allergic fungal rhinosinusitis.

Treatment consists of oral and intranasal corticosteroids preoperatively to reduce fungal load and polypoidal reaction. Surgical clearance of allergic mucin, to provide good ventilation and drainage of sinuses. Post operatively oral and intranasal corticosteroids should be continued along with alkaline nasal douches to prevent recurrence.18

**Conclusion**

Fungal sinusitis is an important clinical disease with wide range of clinical manifestations, radiological features, disease progression and treatment modalities are done accordingly. It should be considered in all patients having chronic rhinosinusitis and immunocompromised state. Manifestation of sinus diseases due to fungus depends a lot on the host immunological status. It has two broad categories invasive and non-invasive which is further classified into five subtypes.

Acute invasive fungal sinusitis affects immunocompromised patients and patients with poorly controlled diabetes. Aggressive treatment is necessary to counteract intra-orbital and intra-cranial...
invasion and further mortality. Early signs and symptoms are subtle, so the radiologists and clinicians need to be very alert while diagnosing. Chronic granulomatous invasive fungal sinusitis and chronic invasive fungal sinusitis are characterized by slow and prolonged clinical course. Imaging manifestations may mimic aggressive neoplastic lesions. Clinical features are similar to chronic rhinosinusitis along with invasion into orbit and intracranial structures that leads to a fatal course.

Allergic fungal sinusitis tends to be a disease of young, atopic, immunocompetent individuals. There is usually unilateral, pan sinus disease which is slow and progressive associated with history of asthma and nasal polyposis. Opacification of multiple sinuses with areas of central hyper attenuation from mucin, remodeling of paranasal sinuses and nasal polyposis is seen. Surgical removal of fungal debris, associated polyp and allergic mucin, establishment of drainage of sinuses along with antiallergic medications are the mainstay of therapy.

Fungus ball (mycetoma) tends to occur in a single sinus exerting mass effect, most often the maxillary sinus, followed by sphenoid sinus. Non atopic individuals are affected mostly. CT scan intra sinus inspissation with hyper attenuated areas suggestive of calcification along with hyperostosis and sinus remodelling. Surgical removal is generally curative and recurrence is unusual. Understanding the different types of fungal sinusitis and knowing their particular radiologic features allows the radiologist to play a crucial role in alerting the clinician to use appropriate diagnostic techniques for confirmation. Prompt and accurate diagnosis and initiation of appropriate therapy are essential to avoid a unfavourable or fatal outcome.

References


