INTRODUCTION

Fungi are ubiquitous in nature, and human exposure to fungi is unavoidable. The extent of fungal infections of the nose and paranasal sinuses is, therefore, primarily determined by the immune status of the host rather than the presence or absence of fungal organisms and can range from saprophytic colonization to orbital and cerebral involvement with often fatal outcomes. Due to a growing number of chemotherapy, human immunodeficiency virus (HIV) infections, and diabetes mellitus, the number of susceptible immunocompromised hosts is increasing. Sinonasal fungal infections can be broadly divided into invasive and noninvasive forms. Invasive fungal sinusitis is defined by the presence of fungal hyphae within the mucosa, submucosa, bone, or blood vessels of the paranasal sinuses, differentiating it from noninvasive forms.\(^1,2\) Depending on the immunologic response of the host and the course of the disease, invasive fungal sinusitis can be categorized into acute, chronic, or chronic granulomatous entities. Mycetoma and Allergic Fungal Rhinosinusitis are considered non-invasive forms. Computer tomography is the gold-standard in sinonasal imaging and is complimented by Magnetic resonance imaging (MRI) as it is superior in the evaluation of intraorbital and intracranial extensions. The knowledge and identification of the characteristic imaging patterns in invasive – and non-invasive fungal rhinosinusitis is crucial and the radiologist plays an important role in refining the diagnosis to prevent a possible fatal outcome.

Key words: Complications, fungal infections, invasive, magnetic resonance imaging and computed tomography, non-invasive, sinonasal

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rhinosinusitis are considered noninvasive forms. Figure 1 summarizes the forms and characteristics of fungal rhinosinusitis and Figure 2 gives an overview of organisms involved in sinonasal and orbital fungal infections. Risk factors for the development of fungal rhinosinusitis and treatment options are summarized in Table 1.

Computer tomography (CT) is the gold standard in paranasal sinus imaging and is complemented by magnetic resonance imaging (MRI) as it is superior in the evaluation of intracranial and intraorbital extensions.

NONINVASIVE FUNGAL SINUSITIS: MYCETOMA (FUNGUS BALL)

A mycetoma is a noninvasive, dense conglomeration of fungal hyphae within a sinus cavity secondary to a deficient mucociliary clearance mechanism. It is primarily caused by *Aspergillus fumigatus*, resulting in chronic rhinosinusitis predominantly involving the maxillary sinus (84%) and it is often found in older immunocompetent females.

On noncontrast CT imaging, a mycetoma appears as a hyperattenuating mass with intraslesional metal-dense spots corresponding to fungal waste products and it is often accompanied by perilesional reactive osteitis. On T1- and T2-weighted imaging (WI), a fungal ball appears hypointense due to the absence of water and with an hyperintense-inflamed mucosal lining on T2-WI.

ALLERGIC FUNGAL SINUSITIS

Allergic fungal sinusitis is an IgE-mediated hypersensitivity reaction to fungal elements and the most common form of fungal sinusitis. Disease tends to be bilateral and asymmetric involving multiple sinuses with a frequent nasal component. Patients typically have an intact immune system and a history of atopy, including allergic rhinitis or asthma and can present with proptosis, telecanthus, or gross facial dysmorphia. Causative agents include dematiaceous (*Bipolaris, Curvularia, and Alternaria*) and hyaline molds (*Aspergillus and Fusarium*).

On CT imaging, the paranasal sinuses appear enlarged with near-complete opacification due to mucin accumulation, which appears hyperdense on noncontrast CT imaging.

MRIT1-WIs show mixed signal intensities of the allergic mucin and characteristic signal voids on T2-WI, which are attributed...
Causative agents most commonly identified are categorized into acute, chronic, or granulomatous subtypes. Depending on the progression of the disease and the immune status of the host, invasive fungal sinusitis can be characterized by the presence of fungal hyphal forms within the mucosa, submucosa, blood vessels, and bone, often resulting in orbital and intracranial involvement. Complications may include orbital and intracranial extensions from neoplastic entities.

### INVASIVE FUNGAL SINUSITIS

Depending on the progression of the disease and the immune status of the host, invasive fungal sinusitis can be categorized into acute, chronic, or granulomatous subtypes. Causative agents most commonly identified are _Aspergillus_ and fungi of the order Murocales (Zygomycetes). Their ability to angi-invade reflects in the presence of fungal hyphal forms within the mucosa, submucosa, blood vessels, and bone, often resulting in orbital and intracranial involvement. Complications may include orbital and intracranial extensions with cavernous sinus thrombosis, parenchymal cerebritis or abscess, meningitis, osteomyelitis, mycotic aneurysm, stroke, and hematogenous dissemination.

### Table 1: Summary of the risk factors and treatment options of fungal rhinosinusitis (modified after Soler, Sc., Schlosser)

| Condition                  | Risk factors                                                                 | Surgical treatment                        | Antifungal treatment | Anti-inflammatory treatment | Immune treatment |
|----------------------------|------------------------------------------------------------------------------|-------------------------------------------|----------------------|-----------------------------|------------------|
| Mycetoma                   | Overfilling of the maxillary cavities with zinc oxide, inadequate muco-ciliary clearance | Opening of affected sinus and evacuation of fungal elements | None                 | None                        | None             |
| Allergic fungal rhinosinusitis | History of atopy, allergic rhinitis, asthma                                         | Opening of sinus ostia, polyp and mucin removal | None                 | Yes (may include oral steroids, topical steroids, anti-histamines, leukotriene antagonists) | Yes (sublingual or subcutaneous immunotherapy) |
| Acute invasive fungal rhinosinusitis | Diabetes mellitus, chemotherapy, bone marrow transplant recipients             | Aggressive debridement                    | Systemic            | None                        | Yes (reverse immunosuppression) |
| Chronic invasive fungal rhinosinusitis | Diabetes mellitus, corticosteroid use, human immunodeficiency virus | Aggressive debridement                    | Systemic            | None                        | Yes (reverse immunosuppression) |
| Granulomatous invasive fungal rhinosinusitis | Predominantly found in India, Pakistan, Sudan | Aggressive debridement                    | Systemic            | None                        | None             |

Figure 3: A 65-year-old female, who presented with a history of chronic rhinosinusitis, headaches, and facial discomfort, is diagnosed with a mycetoma. Contrast computer tomography scan of the face in axial view in (a) soft tissue and (b) bone algorithm show complete opacification of the right maxillary sinus with intralesional calcification (arrows) and reactive ostectomy, indicative of chronic sinusitis. (c) Corresponding T2-weighted magnetic resonance imaging of the face in axial view shows a low attenuating mass in the right maxillary sinus with surrounding mucosal thickening, consistent with a mycetoma (asterisk). To its high concentration of metal ions, proteins, and low free-water content.[1,2,6] The overlying inflamed mucosal lining appears relatively hypointense on T1-WI and hyperintense on T2-WI, with increased signal intensity upon administration of intravenous gadolinium [Figure 4].[2] As the quantity of fungal mucin increases, the involved paranasal sinuses begin to resemble a mucocele and bony remodeling, and decalcification may occur with subsequent nasal, intraorbital, or intracranial involvement mimicking malignancy.

Acute invasive fungal rhinosinusitis is found in an immunocompromised setting with a course of disease of 4 weeks or less.[6] Chronic invasive fungal rhinosinusitis shows a prolonged clinical development of over more than 12 weeks and it is found in immunocompetent or slightly immunocompromised patients.[5,6] Granulomatous-invasive fungal sinusitis is characterized by the presence of noncaseating granulomas in immunocompetent hosts and a course of disease of over 12 weeks.[19] _Aspergillus flavus_ is mostly identified as the causative agent and infections are primarily found in Sudan, India, and Pakistan, with less prevalence in the United States.[7]
ACUTE INVASIVE FUNGAL RHINOSINUSITIS

Acute invasive fungal rhinosinusitis is the most urgent and lethal form of fungal sinusitis with a mortality of 50–80%.[2] Immunocompromised patients with poorly controlled diabetes mellitus and those receiving chemotherapy or chronic oral corticosteroids and patients with HIV are most commonly affected.[3,4,5] Aspergillus is the fungal species predominantly identified in patients with neutropenia and fungi of the Zygomycetes class are mostly encountered in diabetic patients.[2,6] Infection commonly begins as mucosal inflammation around the middle turbinate and rapidly spreads to the maxillary, ethmoid, or sphenoid sinus, usually affecting multiple unilateral sinuses.[6] Infectious spread to the adjacent soft tissue, and periantral fat planes, orbits, and central nervous system occur through direct extension or through vascular invasion owing to the angio-invasive nature of the fungi. Hyphal growth into the vessel lumen causes endothelial dysfunction and thrombosis.[8]

Orbital involvement is often characterized by periorbital edema, ptosis, ophthalmoplegia, visual loss, or proptosis. Altered mental status is concerned for spread to the central nervous system, which is at an increased risk if the posterior ethmoid or sphenoid cells are affected, and its involvement is associated with twice the mortality.[8,9]

Nonspecific findings on CT scan include mass effect, bony dehiscence, thickening of the extraocular muscles, and inflammatory changes of the orbit and orbital apex. Mucosal secretions may be hyper- or hypo-attenuating, although hyperattenuation is mostly attributed to chronic invasive fungal rhinosinusitis. MRI further evaluates the soft tissue extension beyond the sinuses to the periantral fat (intraorbital or masticator space), the cavernous sinus, the cavernous sinus, and the brain and therefore, better demonstrates the findings of fulminant fungal invasion [Figures 5–7]. Biopsy remains crucial in the diagnosis of acute invasive fungal rhinosinusitis to isolate the fungus involved and initiate the appropriate treatment.

CHRONIC INVASIVE FUNGAL RHINOSINUSITIS

Patients are usually immunocompetent or slightly immunocompromised due to corticosteroid therapy, diabetes mellitus, or AIDS.[5,2,6] The most common pathogens identified are those causing acute invasive fungal sinusitis as well as dematiaceous molds (Bipolaris, Curvularia, Alternaria, and Pseudoalleschta), affecting mostly the ethmoid and sphenoid sinuses.[1,5,6] Patients usually endure sinus pain, nasal discharge, low-grade fever, and epistaxis, and infection can be recurrent and persistent.

Imaging features are similar to acute invasive fungal rhinosinusitis, noninvasive forms, or a combination of both. On noncontrast CT imaging, a hyperattenuating mass with bony wall destruction extending into the adjacent structures such as the orbits, maxillary floor, and hard palate visualizes the chronic invasive course of the infection and may mimic malignancy.[2] MRI is more accurate for the evaluation of extension into the orbital apex, cavernous sinus, or brain [Figure 8].

CONCLUSION

Invasive and noninvasive sinonasal fungal infections are closely associated with the host’s immune system and

Figure 5: A 44-year-old male, who presented with gradually increasing left jaw swelling and pain over the course of 2 weeks, is diagnosed with acute invasive aspergillosis. The patient had a history of hepatitis C and alcoholic liver cirrhosis. (a) Contrast-enhanced computed tomography scan of the face in the bone algorithm, axial view shows mucosal thickening of the maxillary sinuses with the erosion of the left maxillary bone (anterior and posterior walls) and obliteration of the periantral fat planes in the premaxillary and masticator spaces (arrows). (b) Magnetic resonance imaging T2-weighted and (c) gadolinium-enhanced T1-weighted fat saturated imaging of the face in axial view shows inflammatory changes and contrast enhancement in the described periantral planes and masticator muscles due to fungal invasion (arrows).

Figure 6: A 55-year-old male, who presented with headaches, rhinorrhea, vision loss, and acute myelogenous leukemia, is diagnosed with acute invasive aspergillosis. (a) Computed tomography scan with contrast and (b) T2-weighted magnetic resonance imaging of the face in axial view demonstrate inflammation of the left ethmoidal and sphenoid sinuses with thickening of the left medial rectus muscle due to intraorbital extension (arrows). T1-weighted fat saturated postgadolinium magnetic resonance imaging of the face in axial (c) and coronal (d) view shows absence of enhancement of the left posterior ethmoid and sphenoid sinus mucosa indicative of gangrenous necrosis (asterisk), intraorbital extension resulting in proptosis (line), intracranial extension through the partially thrombosed left cavernous sinus with abnormal leptomeningeal (black arrow) and pachymeningeal enhancement (white arrows), and abscess formation in the left temporal fossa (arrowhead).
ability to generate a proper immune response. Depending on the immune status of the host, infections may present as harmless colonization or include noninvasive or invasive forms. Knowledge and identification of the characteristic imaging patterns found in invasive and noninvasive fungal rhinosinusitis allow the radiologists to help refine the diagnosis and guide clinicians in the further evaluation and initialization of a proper and timely treatment to help prevent a possibly fatal outcome.

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Conflicts of interest
There are no conflicts of interest.

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