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SPECTRUM OF INVASIVE FUNGAL SINUSITIS: A RADIOLOGICAL CORRELATION

Radiodiagnosis

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ABSTRACT

Invasive fungal and fungal-like infections contribute to substantial morbidity and mortality in immunocompromised individuals. The incidence of these infections is increasing—largely because of rising numbers of immunocompromised patients, including those with neutropenia, human immunodeficiency virus, chronic immunosuppression, indwelling prostheses, burns, and diabetes mellitus, and those taking broad-spectrum antibiotics. Invasive fungal pathogens include primary mycotic organisms such as *Histoplasma capsulatum*, *Coccidioides immitis, Blastomyces dermatitidis,* and *Paracoccidioides brasiliensis,* which are true pathogens and inherently virulent. Secondary mycotic organisms such as *Candida* and *Aspergillus* species, *Cryptococcus neoformans, Pneumocystis jirovecii,* and Mucorales fungi are opportunistic, less virulent pathogens. *Nocardia* and *Actinomyces* species are gram-positive bacteria that behave like fungi in terms of their growth pattern and cause fungal-like invasive indolent infections; thus, these organisms are included in this review. Fungal and fungal-like infections can affect a variety of organ systems and include conditions such as meningitis, sinusitis, osteomyelitis, and enteritis. As awareness of these infections increases, timely diagnosis and treatment will become even more important. Imaging has a critical role in the evaluation of disease activity, therapy response, and related complications. Using an organ-based approach with computed tomography, magnetic resonance imaging, and ultrasonography to gain familiarity with the appearances of these infections enables timely and accurate diagnoses.

KEYWORDS

invasive fungal, allergic fungal, granulomatous, sinusitis, *Aspergillus*, voriconazole

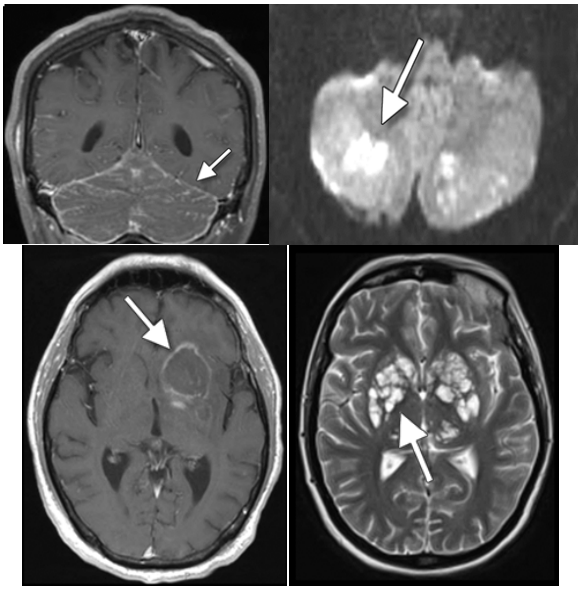
INTRODUCTION:

Fungi are pervasive microorganisms in the domain Eucarya, and the Fungi kingdom includes approximately 50 000 species. Only about 200 of these organisms are human pathogens, and about a dozen of them cause 90% of all human mycoses. (1)Fungi are classified on the basis of their morphology and include molds, yeasts, and dimorphic fungi. Molds are composed of mycelia, a conglomerate of fine white filaments (hyphae), whereas yeasts comprise a single cell. A dimorphic fungus has the morphology of yeast during its parasitic stage and the morphology of mold during its saprophytic stage, when it survives independently of a host and acquires nourishment from dead or decaying organic matter (1).

Invasive fungi such as *H capsulatum* and *C immitis* are true pathogens that cause virulent primary mycoses. Infections with these organisms often start in the lungs and become systemic in susceptible individuals. Secondary mycotic organisms such as *P jirovecii* and Mucorales fungi are opportunistic, less virulent pathogens that can wreak havoc in the immunocompromised patient (2). In addition to primary and secondary mycotic organisms, *Nocardia* and *Actinomyces* species are gram-positive bacteria that grow in the form of mycelia and behave like fungi; they are water and soil saprophytes.

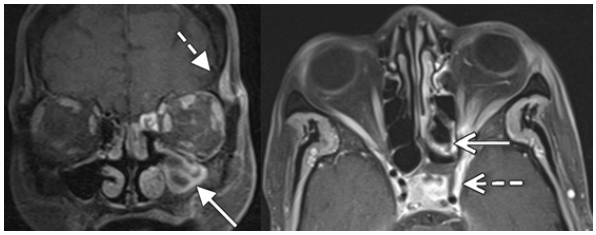
Invasive fungal and fungal-like infections result in mortality and substantial morbidity and are increasing in frequency as the population of immunocompromised individuals grows (3). Although the spectrum of these infections ranges from acute and aggressive to chronic and indolent disease, the condition of immunocompromised individuals is extremely tenuous. Early detection can optimize outcomes, and, therefore, radiologists should have a low threshold for recommending imaging examinations. Fungal infections can occur in immunocompetent individuals as well. Although fungal infections in this group are often not as serious, they tend to be symptomatic and may be clinically confusing. In this article, we describe the clinical features, natural history, and imaging findings of infections caused by invasive fungi and fungus-like organisms, with an emphasis on computed tomographic (CT) and magnetic resonance (MR) imaging assessment performed by using an organ-based approach.

Fungal and fungal-like infections of the CNS are uncommon and occur most frequently in immunosuppressed persons living in endemic areas—those with neutropenia and HIV in particular (4). These infections should be considered in immunocompromised individuals with new neurologic deficits. Routes of dissemination include direct extension, hematogenous spread, and cerebrospinal fluid seeding (4). The most common fungal pathogens associated with CNS infections include *Candida* and *Aspergillus* species, *C neoformans,* and Mucorales fungi (5). Meningitis and focal masses such as cerebral abscesses and granulomas are the most common CNS manifestations of invasive fungal and fungal-like infections (5).

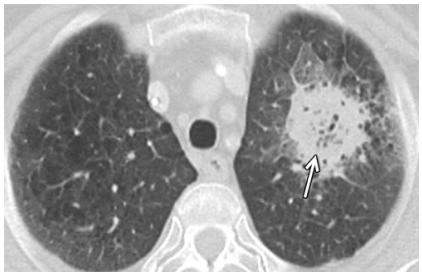


Acute invasive fungal or fungal-like sinusitis is a rapidly progressive infection that is associated with a mortality rate of up to 18% . Acute invasive fungal sinusitis is rare in immunocompetent individuals and most commonly seen in immunocompromised persons. Up to 93% of these infections occur in individuals with an underlying malignancy . Diabetes mellitus is another classic predisposing condition. Zygomycetes fungi, including *Rhizopus, Rhizomucor,* and *Mucor* species, are the most common infectious fungi in persons with diabetes mellitus. Conversely, *Aspergillus* species are more common in other immunocompromised individuals in whom neutropenia is the dominant condition—especially persons with hematologic malignancies, hematopoietic stem cell transplant recipients, and solid-organ transplant recipients . Patients present with fever, facial tenderness, and nasal congestion. Although fungal sinusitis can mimic bacterial sinusitis, fungal infections are often more locally invasive, causing osseous destruction, extending into adjacent soft tissues, and invading the pterygopalatine fossa, cavernous sinus, and intracranial

cavity. Vascular invasion with hematogenous dissemination also may develop. After intracranial extension, signs and symptoms can progress to include mental status changes, exophthalmos, cranial nerve deficits, headache, and death. Treatment includes prompt surgical débridement, systemic antifungal therapy, and, if possible, reversal of the underlying immunosuppression.



The human respiratory system is frequently the site of first contact with environmental fungal and fungal-like antigens owing to their ubiquity in nature. Many environmental fungal species are nonpathogenic or only important and invasive in immunocompromised individuals. Invasive fungal and fungal-like pulmonary infections are most frequently diagnosed or suggested on the basis of chest radiographic findings and CT findings in particular. These infections have a wide spectrum of phenotypic characteristics, which range from nodules to lobar consolidations to chest wall invasion (16). There may be features of airway-centered bronchopneumonia with associated tree-in-bud nodules. Some fungal pneumonias may manifest predominantly as ground-glass opacities. Ancillary features, including lympha denopathy and pleural effusions, also may be present. The overt nature of many of the findings belies the challenge in distinguishing the characteristic patterns associated with particular organisms. There is substantial overlap in findings, and it may take days to weeks for cultures to yield results. However, the radiologist may add clinical value by suggesting infections caused by certain organisms on the basis of distinguishing features and, in turn, facilitating targeted therapy.



DISCUSSION

Acute invasive fungal or fungal-like sinusitis is a rapidly progressive infection that is associated with a mortality rate of up to 18%. Acute invasive fungal sinusitis is rare in immunocompetent individuals and most commonly seen in immunocompromised persons. Up to 93% of these infections occur in individuals with an underlying malignancy. Diabetes mellitus is another classic predisposing condition. Zygomycetes fungi, including *Rhizopus, Rhizomucor,* and *Mucor* species, are the most common infectious fungi in persons with diabetes mellitus. Conversely, *Aspergillus* species are more common in other immunocompromised individuals in whom neutropenia is the dominant condition—especially persons with hematologic malignancies, hematopoietic stem cell transplant recipients, and solid-organ transplant recipients. Patients present with fever, facial tenderness, and nasal congestion. Although fungal sinusitis can mimic bacterial sinusitis, fungal infections are often more locally invasive, causing osseous destruction, extending into adjacent soft tissues, and invading the pterygopalatine fossa, cavernous sinus, and intracranial cavity. Vascular invasion with hematogenous dissemination also may develop. After intracranial extension, signs and symptoms can progress to include mental status changes, exophthalmos, cranial nerve deficits, headache, and death. Treatment includes prompt surgical debridement, systemic antifungal therapy, and, if possible, reversal of the underlying immunosuppression.

Imaging should be considered for symptomatic patients, and radiologists should have a low threshold for imaging the sinuses in febrile immunocompromised patients with no obvious infectious source. Early recognition of the fungal infection is crucial for initiating therapy and avoiding potentially devastating complications. CT is often the initial imaging examination of choice and is the preferred method for evaluation of possible osseous destruction. Common CT findings include mucosal thickening and soft-tissue attenuating material in the sinus cavities. Inflammatory changes in the orbital fat and exophthalmos are signs of orbital invasion.

CONCLUSION

The incidence and awareness of invasive fungal and fungal-like infections continue to rise as the population of immunocompromised persons grows and medical treatments improve. These organisms often cause more indolent infections in immunocompetent individuals, but they have a propensity to quickly disseminate and can rapidly become fatal in immunosuppressed hosts. Some fungal and fungal-like infections have specific imaging appearances, while others manifest with more nonspecific findings. Therefore, it is imperative that clinicians have a low threshold for requesting imaging and that radiologists have a low threshold for suspecting a fungal cause of disease in patients at high risk of developing these infections. The radiologist should be familiar with the manifestations of these infections throughout the body and be able to suggest the presence of certain organisms on the basis of their unique disease patterns.

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