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Multimodal management for acute invasive fungal rhinosinusitis

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Acute invasive fungal rhinosinusitis (IFRS) is an aggressive sinonasal infection that is associated with a high risk of morbidity and mortality. Acute IFRS typically affects individuals with a deficient immune system and is characterized by a fulminant proliferation of tissue invasion by opportunistic fungal species. The early diagnosis and management of acute IFRS play important roles in improving the disease prognosis. The management of acute IFRS requires a multimodal approach that relies on both medical and surgical interventions. This article highlights general considerations for both the medical and surgical strategies for treatment of acute IFRS as a rhinologic emergency.

Introduction

Acute invasive fungal rhinosinusitis (IFRS) is an aggressive and potentially fatal infection characterized by direct invasion of sinonasal tissues by virulent fungi. The progression of infection, caused most commonly by *Aspergillus* and *Mucor* species, rapidly occurs within a matter of hours or days. In advanced stages, the infection may extend from the nasal cavities and paranasal sinuses into the surrounding hard palate, orbital cavity, or intracranial compartment.[1,2] Acute IFRS typically occurs in individuals with significant quantitative or functional neutropenia. Etiologies for immunologic compromise include poorly controlled diabetes mellitus, acquired immunodeficiency syndrome, organ transplantation, and hematologic malignancies. Iatrogenic immunosuppression via the use of chemotherapeutic agents and chronic systemic corticosteroids also predisposes individuals to acute IFRS.

The treatment for acute IFRS requires a multimodal approach utilizing both medical and surgical interventions to improve disease outcomes. Historically, acute IFRS has been associated with mortality rates as high as 50%-80%, but with increased recognition and early aggressive treatment of the disease, more recent studies report overall mortality rates at 18%-50%.[3-6] Medical therapy for acute IFRS generally includes reversing the immunocompromised state and also initiating systemic antifungal medications. Surgical therapy, which is increasingly completed through the endoscopic endonasal route, is intended to debride all tissue with evidence of fungal invasion. In this article, we highlight the workup and management of acute IFRS and discuss the surgical goals that affect the ultimate patient outcomes.

Clinical and imaging assessment

From a clinical standpoint, acute IFRS is most commonly suspected when immunocompromised patients develop signs and symptoms suggestive of rapidly progressive sinusitis. Facial swelling, fever, and nasal congestion are regarded as the usual presenting symptoms, while rhinorrhea, epistaxis,

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periorbital swelling, headaches, facial pain, and anesthesia of the facial soft tissues also raise concerns for acute IFRS.[6] The clinical suspicion for acute IFRS in immunocompromised patients is especially relevant if fevers and localized sinonasal symptoms persist even after 48 hours of appropriate broad-spectrum antibiotics have been initiated. Diplopia, changes in visual acuity, mental status changes, and seizures signify advanced stages of possible acute IFRS with orbital or intracranial extension.

Besides a clinical history, nasal endoscopy plays an essential part of the initial workup of acute IFRS. The most consistent intranasal findings for acute IFRS involve alterations in the color and appearance of the nasal mucosa. During the early stages of acute IFRS, mucosal pallor may indicate tissue ischemia due to ongoing angiocentric fungal invasion, while black discoloration suggests late stages of disease with overt tissue necrosis (Figure 1). Crusting, ulcerations, decreased bleeding, and hypoesthesia of the nasal mucosa are complementary findings. Mucosal abnormalities are most commonly found on the middle turbinate, followed by the septum, hard palate, and inferior turbinate.[4] Suspicious intranasal mucosal abnormalities, combined with the appropriate patient risk factors, require urgent biopsies in order to confirm the histopathologic diagnosis of acute IFRS and to facilitate cultures for fungal identification. While the use of frozen section analysis commonly expedites the diagnosis, negative results on frozen section analysis do not necessarily rule out acute IFRS, and early therapeutic management for acute IFRS is indicated if the clinical suspicion remains high.[7]

Both computed tomography (CT) and magnetic resonance (MR) imaging are utilized to assess patients with concerns for acute IFRS and can provide vital information regarding the location and extent of infectious involvement. CT findings are generally nonspecific for acute IFRS, usually consisting of unilateral sinus opacification that suggests soft tissue thickening within the nasal and sinus cavities. In advanced cases of acute IFRS, CT may provide evidence of bony erosion with extension of sinus opacification into the oral, intracranial, or orbital compartments. Compared to CT, MR imaging provides improved delineation of soft tissue abnormalities and thus better assists in defining infectious extent. On MR, infiltration and obliteration of the periantral fat planes represent the earliest radiographic evidence of acute IFRS.[8]

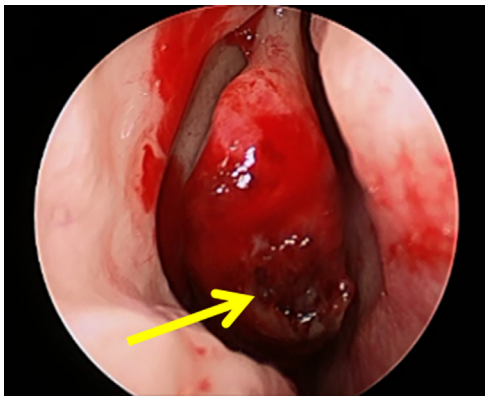

Figure 1 The view of the right nasal cavity provided by rigid nasal endoscopy demonstrates black mucosal discoloration on the middle turbinate *(indicated by the yellow arrow)*. These mucosal changes in an immunocompromised patient with symptoms of ipsilateral facial pain are suggestive of tissue necrosis in acute invasive fungal rhinosinusitis. (Color version of figure is available online.)

Medical therapy

When acute IFRS is clinically suspected, the different treatment strategies for disease control should be promptly initiated in order to achieve favorable disease prognosis. One of the mainstays of acute IFRS treatment includes the reversal of the underlying immunodeficiency. The successful reversal of immunodeficiency in acute IFRS is specifically correlated with disease-specific survival rates. This task is more easily accomplished if the immunodeficiency is secondary to poorly controlled diabetes mellitus or medication-induced immunosuppression. In the case of diabetes mellitus, efforts should be made to maintain strict glycemic control and to provide adequate fluid hydration. Temporarily withholding immunosuppressive agents should also be considered if they are the source for the immunodeficient state. Neutropenia due to hematologic malignancies, on the other hand, provides a greater challenge in improving immunocompetence. For these patients, white blood cell transfusions and administration of granulocyte colony-stimulating factor may be considered, as increasing the absolute neutrophil count to above 1000/mm^3 has been shown to provide better local control of acute IFRS.[1]

Medical therapy for acute IFRS additionally consists of the initiation of systemic antifungal medications. Deoxycholate amphotericin B serves as the drug of choice for systemic antifungal therapy, although its use in critically ill patients may be limited by the drug's nephrotoxic side effects. Liposomal amphotericin B is an alternative to deoxycholate amphotericin B due to its more favorable adverse effect profile, but the wide use of this formulation is limited by its cost. Intravenous voriconazole also serves as a highly effective antifungal therapy for acute IFRS, although the use of voriconazole as monotherapy should be employed only if *Aspergillus* has been established as the causative microorganisms. In cases of mucormycosis, the utility of voriconazole is limited by *Mucor* species that have developed resistance to the antifungal agent. With either amphotericin B or voriconazole, nonetheless, topical antifungal therapies, as applied through nasal irrigations or nebulizers, may provide adjunctive roles to systemic antifungal therapies.

The management of patients with acute IFRS furthermore requires a multidisciplinary strategy that utilizes the expertise of not only otolaryngologists, but also specialists