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Research Paper

Evidence for a 'preinvasive' variant of fungal sinusitis: Tissue invasion without angioinvasion

Hassan Paknezhad, Nicole A. Borchard, Greg W. Charville, Noel F. Ayoub, Garret W. Choby, Andrew Thamboo, Jayakar V. Nayak*

Division of Rhinology, Department of Otolaryngology — Head and Neck Surgery, Stanford University School of Medicine, USA

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Antifungal therapy

Abstract Clinical experience has suggested the existence of an intermediate form of fungal sinusitis between the categories of non-invasive fungal sinusitis (non-IFS) and invasive fungal sinusitis (IFS). This fungal sinusitis variant demonstrates unhealthy mucosa by endoscopy with fungal invasion, but lacks angioinvasion microscopically, representing what clinically behaves as a 'pre-invasive' subtype of fungal sinusitis. Unlike non-IFS disease, patients with pre-invasive fungal sinusitis were still felt to require anti-fungal medications due to histologic presence of invasive fungus. While sharing some clinical features of IFS, these 'intermediate' patients were successfully spared extended and repeated surgical debridements given the microscopic findings, and have been successfully treated with shorter courses of antifungal therapy. These select patients have had favorable outcomes when managed in a judicious and semi-aggressive manner, in an undefined zone between the treatments for routine fungal ball and aggressive IFS.

* Corresponding author. Division of Rhinology, Department of Otolaryngology — Head and Neck Surgery, Stanford University School of Medicine, 801 Welch Road, Stanford, CA 94305, USA.
E-mail address: jnayak@stanford.edu (J.V. Nayak).
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Introduction

Fungal sinusitis is classically divided into non-invasive (fungal ball, allergic fungal sinusitis, saprophytic fungal growth) and invasive forms (acute invasive fungal sinusitis, chronic IFS, chronic granulomatous fungal sinusitis) (Table 1).[1–6] Invasive fungal sinusitis (IFS) is a life-threatening entity involving fungal species such as *Mucor* and *Aspergillus* that, in the immunosuppressed host, become invasive, and extend beyond the bony boundaries of the sinuses and skull base.[1,2,6] The morbidity and mortality associated with IFS are high, especially for acute IFS.[3]

Histopathologic studies of IFS demonstrate both mucosal and submucosal invasion with angiovasion.[4] When successfully treated, patients with IFS require urgent surgical interventions, repeated surgical debridements, long-term antifungal therapy, and critically, reversal of the inciting cause of immunosuppression where possible.[1,2,5]

We share our experience with patients presenting with intermediate conditions of fungal sinusitis not entirely consistent with IFS nor non-invasive fungal sinusitis (non-IFS). While these patients demonstrate dusky tissue and intra-mucosal fungal infiltration characteristic of IFS, they failed to show direct angioinvasion and wide extension beyond the submucosa.[1,2] Although presenting clinically as IFS, these patients were managed successfully with limited surgical debridement and, in one case, short-term antifungal therapy. These data suggest the existence of an undescribed category of 'preinvasive' fungal sinusitis, supported by histologic analysis, which may be treated using distinct surgical and medical options.

Case series

Case 1

A 37-year-old male with acute lymphocytic leukemia presented shortly after bone marrow transplantation (BMT) with low-grade fever and sphenoid sinus opacification on a CT scan of the paranasal sinuses (Fig. 1A). Further examination revealed no abnormal findings on nasal endoscopy. MRI demonstrated left sphenoid opacification with heterogeneous material showing central hyperdensity and peripheral mucosal thickening, and signal loss on T2 MRI (Fig. 1B and C). Endoscopic sinus surgery (ESS) revealed purulence and central fungal debris surrounded by edematous, devitalized left sphenoid sinus mucosa. Frozen histology of the debrided tissue showed acellular tissue mixed with septated fungal hyphae without angioinvasion (Fig. 2).

A limited 'second look' operation was performed four days later which showed no new necrotic mucosa. Because of immunosuppression following BMT, the patient was prophylactically placed on longer term intravenous and oral antifungals postoperatively despite the resolution of symptoms and pathology findings. The patient has recovered well, without recurrence of fungal sinusitis over the past six years.

Case 2

A 70-year-old immunocompetent male presented with headaches and progressive vision loss OS over five days. No

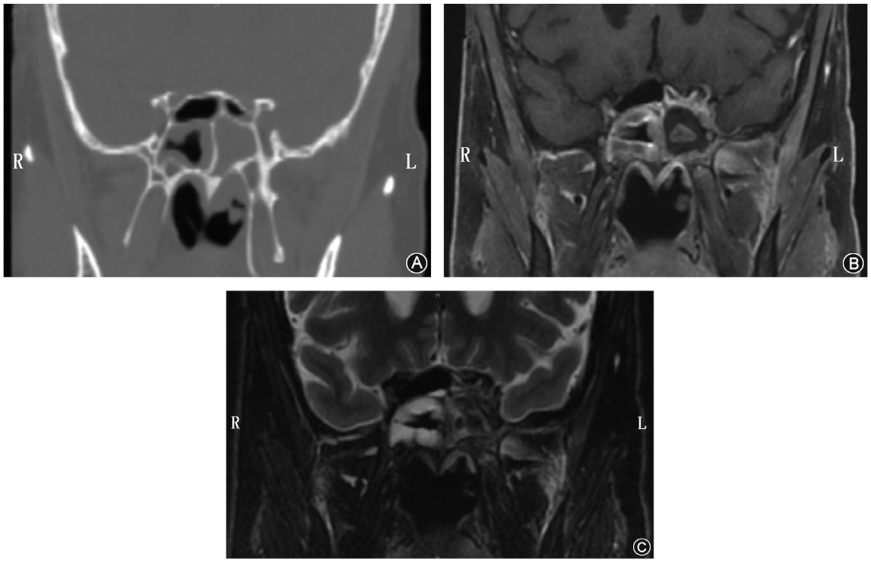

Fig. 1 CT and MRI imaging for Case #1. A: CT-scan coronal view without contrast demonstrating complete opacification of the left sphenoid sinus; no speckled calcifications noted; B: Coronal MRI T1 with contrast demonstrating left sphenoid central signal hyperintensity with surrounding rim of hypointensity; C: MRI T2 coronal view demonstrating loss of signal intensity within the left sphenoid, suggestive of fungal sinusitis and possible IFS.