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Abstract

Importance: This report describes a new magnetic resonance finding in acute fulminant invasive fungal sinusitis that may aid in the diagnosis of orbital involvement.

Observations: The charts of two patients who presented with diabetic ketoacidosis and suspected acute fulminant invasive fungal sinusitis were retrospectively examined. Medical and surgical records, imaging studies, and histopathology specimens were reviewed. The two patients, a 58-year-old female and 54-year-old male each had a contrast-enhanced magnetic resonance of the paranasal sinuses and orbits. Acute fulminant invasive fungal sinusitis with suspected orbital involvement was associated with focal loss of contrast enhancement of the inferior rectus muscle and adjacent orbital tissues. Fungal involvement of the inferior rectus muscle was confirmed on pathologic evaluation in both patients after exenteration.

Conclusions and relevance: The finding of loss of contrast enhancement of an extraocular muscle on magnetic resonance may increase diagnostic confidence of orbital involvement in the setting of acute fulminant invasive fungal sinusitis and help guide surgical planning.

Keywords: Acute fulminant invasive fungal sinusitis; Imaging

Introduction

Acute fulminant invasive fungal sinusitis (AFIFS) is an uncommon, angioinvasive infection seen predominantly in immunocompromised patients [1]. In diabetic patients, roughly 80% of AFIFS is secondary to species from the class Zygomycetes and in neutropenic patients, Aspergillus species accounts for 80% of cases [1,2]. Infection generally begins in the nose and paranasal sinuses after the inhalation of fungal spores with spread to facial, orbital and intracranial structures through direct vascular invasion [3]. It is the most lethal form of fungal sinusitis, historically with a mortality up to 80% [1]. More recent studies report mortality rates under 20% likely because of earlier recognition and treatment [4,5].

Diagnosis of AFIFS is predicated on histopathologic confirmation of fungal hyphae invading bone or sinonasal tissue [1,2,6]. Treatment relies on a combination of surgical debridement of affected tissues, antifungal therapy and reversal of immune status if possible [4]. One of the more difficult concerns in the management of AFIFS is the determination of orbital involvement and whether this necessitates exenteration [7].

In light of this, noninvasive diagnostic techniques that allow accurate detection of the disease and provide guidance in surgical decision-making are essential. We present a new magnetic resonance imaging (MR) finding in AFIFS as highlighted by two cases that demonstrate loss of contrast enhancement (LoCE) of the inferior rectus muscle, representing extraocular muscle invasion by fungus confirmed on pathology. This radiologic finding may increase diagnostic accuracy of orbital involvement in the setting of AFIFS and help guide in surgical planning for debridement.

Case Report

Case 1

A 58-year-old female was transferred to our institution with suspected AFIFS. She originally presented to an outside institution with altered mental status, hyperglycemia, pancreatitis, and metabolic acidosis consistent with diabetic ketoacidosis. On admission, the patient had a visual acuity of 20/70 on the left side, chemosis, proptosis, and limitations of extraocular movements. In addition, significant premaxillary facial fullness and periorbital edema were noted with decreased sensation over the distribution of the left infraorbital nerve. A black eschar was appreciated on the roof of the mouth. Computed tomography (CT) study demonstrated opacification of the left ethmoid sinus, left maxillary sinus, and left nasal cavity, in addition to extensive inflammation of the left cheek. There was proptosis of the left eye without tenting of the nerve with subtle haziness of the retrobulbar fat. An MR with gadolinium was obtained in which T1 weighted images and fat saturation demonstrated loss of contrast enhancement of the left orbit (LoCE) of the walls of the maxillary sinus, the soft tissues anterior and posterior to the sinus, the nasal cavity lateral wall, inferior and middle turbinate, and the inferior aspect of the inferior rectus muscle (Figures 1A, 1B).

Endoscopic examination revealed necrosis of the left inferior turbinate with decreased sensation. Given the clinical and radiographic findings, aggressive debridement was recommended. The patient
which demonstrated complete opacification of the left maxillary sinus with effacement and LoCE of the left-sided premaxillary fat, pterygomaxillary fissure fat, the inferior and middle turbinates, and inferior aspect of the inferior rectus muscle of the left eye (Figures 3A, 3B). Enhancement and fluid around the left optic nerve was concerning for subarachnoid invasion.

Given these MR findings, the patient was started empirically on caspofungin and amphotericin B. A biopsy of the necrotic left nasal ala demonstrated rare nonseptate hyphae on potassium hydroxide smear consistent with AFIFS. The patient then underwent emergent debridement of necrotic tissue, including left-sided orbital exenteration, maxillectomy, ethmoidectomy, and inferior and middle turbinectomy. Intraoperative frozen pathology of the left orbit demonstrated nonseptate hyphae consistent with AFIFS. Histopathalogy with H&E stain confirmed involvement of the left inferior rectus muscle (Figure 4). Final cultures grew *Rhizopus oryzae*. The patient received two months of IV caspofungin and ambisome B and was then transitioned to oral posaconazole for two additional months. He underwent facial reconstruction one month after the primary debridement.

Case 2

A 54-year-old male with a history of poorly controlled diabetes was initially admitted to an outside hospital in diabetic ketoacidosis for management of facial cellulitis and sinusitis that developed after a left upper canine tooth infection. He then developed proptosis of the left eye, necrosis of the left nasal ala, and early necrosis of the hard palate that prompted transfer to the authors’ institution. MR with gadolinium underwent a left total maxillectomy with posterior debridement into the infratemporal fossa and left orbital exenteration. Mucormycosis involvement of the left inferior rectus muscle was identified by hematoxylin and eosin (H&E) stain and confirmed by Gomori’s methenamine silver stain (GMS) (Figure 2). Two weeks after presentation, nasal discharge culture grew *Rhizopus microsporius* varian microsporius. The patient was treated with caspofungin, and amphotericin B for eight weeks and then was transitioned to oral fluconazole. Two months after the initial surgery, the patient returned to operating room for facial reconstruction.

Figure 1: MR imaging of a 58-year-old female (Case 1) with AFIFS. (A) Axial T1 MR with gadolinium and fat saturation demonstrates soft tissue swelling of the left cheek and opacification of the left maxillary sinus. Note, however, loss of contrast enhancement (LoCE) of the wall of the sinus, of the soft tissues anterior and posterior to the sinus (arrows), and of the nasal cavity lateral wall (curved arrow). LoCE of tissues is believed to correlate with tissue necrosis. (B) Coronal T1 MR with gadolinium and fat saturation shows extensive LoCE of the left maxilla and perimaxillary tissues, but also LoCE of the inflamed retrobulbar fat and periphery of the inferior rectus muscle (arrow). Normal extracocular muscles enhance on gadolinium-enhanced T1 MR.

Figure 2: Histopathology of the exenteration specimen from a 58-year-old female (Case 1) with AFIFS. A section through the inferior rectus demonstrates marked, acute inflammation with an abscess of the muscle (asterix) (Hematoxylin-eosin; original magnification 2x). The inset shows aseptate hyphae characteristic of mucormycosis (Gomori’s methenamine silver; original magnification 40x).

Figure 3: MR imaging of a 54-year-old male (Case 2) with AFIFS. (A) Axial T1 post-contrast fat-saturated MR image demonstrates loss of enhancement of the inferior turbinate (arrow) and of most of the walls of the left maxillary sinus (arrowheads), but also of the retromaxillary (asterisk) and premaxillary (open arrow) fat. (B) Coronal T1 post-contrast fat-saturated MR demonstrates loss of enhancement of orbital fat (arrow) and the inferior rectus muscle (arrowhead) on the left side.

Figure 4: Histopathologic sections of the exenteration specimen from a 54-year-old male (Case 2) with AFIFS. An abscess of the inferior rectus muscle is demonstrated (asterix) (Hematoxylin-eosin; original magnification 4x) with the inset showing infiltration of the tissue with hyphae (arrows) (Hematoxylin-eosin; original magnification 20x).
Discussion

Imaging plays a critical role in the diagnosis and management of AFIFS. The most consistent early CT finding of AFIFS is marked, unilateral, nasal soft-tissue thickening, although this is a non-specific finding [5]. More extensive changes such as retroantral and premaxillary fat pad inflammation, unilateral sinus opacification with adjacent focal osseous erosion, and intracranial or orbital extension are more specific, but are very late imaging features [5]. Furthermore, bony erosion occurs comparatively late in the disease process with extra-sinus vascular spread frequently present before bone destruction is evident on imaging [8]. Delayed clinical or imaging suspicion may have historically contributed to higher mortality rates.

MR has superior contrast resolution as compared to CT, with greater sensitivity for detection of subtle changes in soft tissues. For this reason it is believed to be significantly better at demonstrating the early findings of AFIFS. Previously described MR findings include sinus opacification, variable intensity within the sinuses on T1- and T2-weighted images, inflammatory changes in the extracranial fat and muscles, and leptomeningeal enhancement [9-11]. The latter two findings are more common in advanced disease. More recently, the unique MR finding of loss of normal nasal mucosal enhancement with AFIFS was described, with the absence of enhancement proposed to represent necrosis of tissue [12]. This non-enhancing, hypointense mucosal appearance, most commonly involves the nasal turbinates in early AFIFS and is also referred to as the "black turbinate sign." [11].

Fungal organisms infiltrate and track along blood vessels. Histopathologic examination has demonstrated growth along the internal elastic lamina of blood vessels resulting in dissection away from the media as well as growth into the vessel lumen, further promoting endothelial damage and causing thrombosis [13]. Additionally, hyphae may also form embolic microthrombi and cause a fibrin reaction further promoting ischemia. From this vascular occlusion, the remaining vessels may develop congestion, resulting in spillover edema, which may also accentuate the other forms of soft tissue infiltration seen on MR.

Recent studies have described more subtle MR findings that occur outside of the sinuses, particularly in the soft tissue adjacent to the maxillary sinus including infiltration of the periantral fat and obliteration of nasopharyngeal tissue planes [9]. A new case-control study by one of the authors (CMG) of 17 immunocompromised patients with confirmed AFIFS found MR to be more sensitive and have a higher negative predictive value in detecting early changes of AFIFS [12]. Both modalities had similar specificities and positive predictive values.

Loss of contrast enhancement (LoCE) of the sinus and nasal mucosa in AFIFS has only recently been described- a finding that has not been seen in the setting of acute viral or bacterial rhinosinusitis [12]. Similarly, LoCE of the extracranial muscles can be observed on contrast enhanced T1 weighted images. In AFIFS, we believe that LoCE represents the hyphal invasion of the smaller blood vessels supplying the mucosa and rectus muscles with the resulting infarction preventing enhancement. Extracranial muscles and sinonasal mucosa normally intensely enhance with gadolinium on T1 MR, while nearly all other facial tissues including fat and striated muscles show some small degree of enhancement. In this same manner, small focal areas of LoCE on MR have previously been described in other organ systems such as in cases myocardial and pancreatic ischemia [14,15]. Clinically, LoCE in AFIFS appears to correlate with devitalized tissue, which begins as dusky, pale, or edematous mucosa and progresses to a necrotic, black eschar.

Ultimately, the diagnosis of AFIFS rests on the clinician who has a high index of suspicion, as early presentation may be difficult to discern from other more common forms of rhinosinusitis [1]. Immunocompromised patients with symptoms of sinusitis should undergo early radiographic imaging consisting of both CT and MR studies and nasal endoscopy by an otolaryngologist. Should orbital involvement of AFIFS be identified, the critical decision of whether to perform an orbital exenteration can be difficult, especially when there are no definitive guidelines to assist physicians [7]. Accordingly, multidisciplinary conferences and discussions with the patient and/or family members are essential. In our cases, the surgical recommendation of exenteration was made because the MR findings gave confidence of AFIFS with orbital involvement and that the affected tissue burden was too great for medical management alone.

In conclusion, we have demonstrated that the MR finding of LoCE in the extraocular muscles correlates with angioinvasive fungal infection within the orbit. Histopathologic confirmation of hyphal elements is the current gold standard for diagnosis, and thus tissue confirmation substantiates this new observation. LoCE may, therefore, be a useful finding to provide appropriate patient counseling and surgical planning.

References