CASE REPORT

Allergic Fungal Sinusitis presenting with Hypopituitarism: A Case Report and Literature Review

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Abstract
Allergic fungal sinusitis is a form of noninvasive chronic sinusitis. In this report, we describe the successful treatment of a patient with allergic fungal sinusitis and hypopituitarism. A 41 year old female presented with history of nasal obstruction, anosmia, right periorbital headache, and amenorrhea. The diagnosis of allergic fungal sinusitis was made using nasal endoscopy, CT scan and MRI of head and paranasal sinuses. There was nearly complete obliteration of the paranasal ethmoid, maxillary, and sphenoid sinuses with erosion of the medial wall of the right orbit. In addition, there was displacement of the right globe and medial rectus, and effacement of the pituitary gland. The sphenoid sinus showed fluid containing free hyphae, but no fungal invasion of mucosa was noted. Pituitary assessment revealed anterior pituitary insufficiency. Bilateral endoscopic ethmoidectomy and transnasal and transseptal bilateral sphenoidotomy were performed. After three months of follow up on hormone replacement and antifungal therapy, the patient's headache, anosmia, and nasal obstruction were completely relieved, menses resumed, and the patient's pituitary function had recovered.

Key words: Allergic fungal sinusitis; pituitary abscess; Aspergillus; paranasal sinuses; hypopituitarism; transseptal sphenoidotomy.

Introduction

Fungal infections of the paranasal sinuses are believed to be more frequent than previously thought and causally related to various degrees of anterior hypopituitarism (1). They usually manifest either as an invasive form of fungal sinusitis which occurs in immunocompromised individuals (characterized by its invasiveness, tissue destruction, rapid onset and high mortality if unattended), or in a more indolent and chronic pattern, seen more recently in the immunocompetent population. Two distinct forms are described in this latter category: Mycetoma and allergic fungal sinusitis (AFS) (2,3,4). We present an

interesting case of allergic fungal sinusitis occurring with hypopituitarism, along with a review of the literature.

Case presentation:

This is a 41 year old Emirati female who presented with a five to six month history of nasal obstruction, anosmia, right periorbital headache and intermittent right earache. There was also a one year history of lost menses but no galactorrhea, visual loss, or constitutional symptoms. There was no history of previous treatment for a sinus infection, allergic rhinitis, diabetes, immunosuppression, or steroid use. The patient was a housewife who lived in an arid region facing the desert on the Saudi border. Physical exam revealed right nasal polyposis, right proptosis and infraorbital anesthesia. Routine chemistry and hematology tests were normal. There was no evidence of leucocytosis or relative peripheral easinophilia.

The CT scan of the head and paranasal sinuses showed the paranasal ethmoid and maxillary airspaces almost completely obliterated by heterogeneous soft tissue densities, with areas of bony destruction over the medial wall of the right orbit, and a displacement of the globe and medial rectus (Fig 1). MRI T1- weighted sequences showed atypical low signal intensity of these densities. Also there was extensive sphenoid sinus involvement, which extended into and obliterated both cavernous sinuses and the sella turcica, with the carotid arteries displaced laterally. The pituitary gland was not visible; the optic chiasm was displaced superiorly. (Fig. 2 & 3).

Nasal endoscopy and right maxillary sinus puncture were performed for diagnosis. The maxillary sinus contained greenish thick, tenacious, glue-like fluid, and a few hyphae were seen microscopically consistent with fungal sinusitis, but without tissue invasion.

A preliminary diagnosis of chronic invasive fungal sinusitis with intracranial and intraorbital extension was entertained. The patient was returned to the operating room where a bilateral endoscopic ethmoidectomy and transnasal and transseptal bilateral sphenoidotomy were performed. Inflammatory polyps were identified in the ethmoid sinuses. The sphenoid sinus was filled with the same tenacious green fluid which was completely removed leaving behind only minimally edematous sphenoid mucosa. Pathologic examination of sphenoid contents revealed free hyphae in the fluid, but no fungal invasion of mucosa was noted. *Aspergillus fumigatus* was cultured within 24 hours.

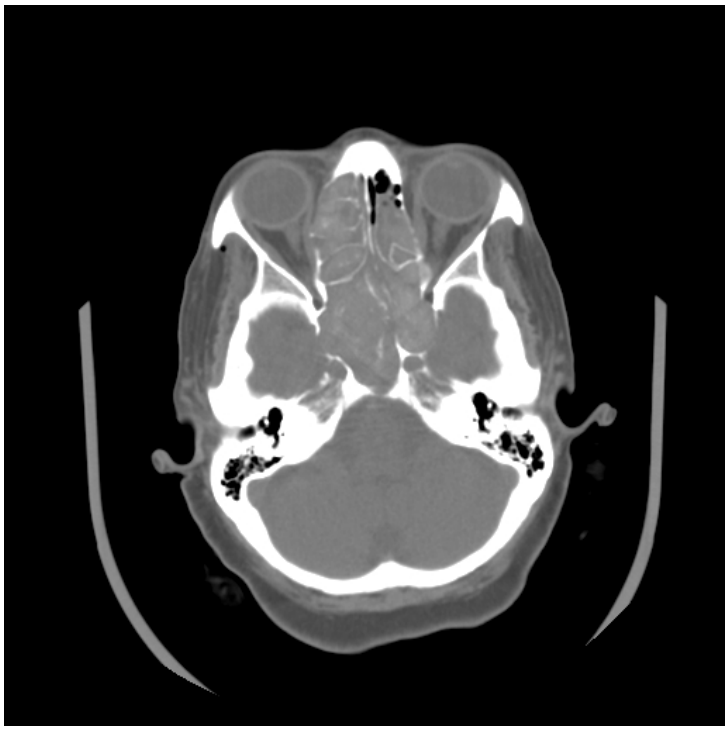
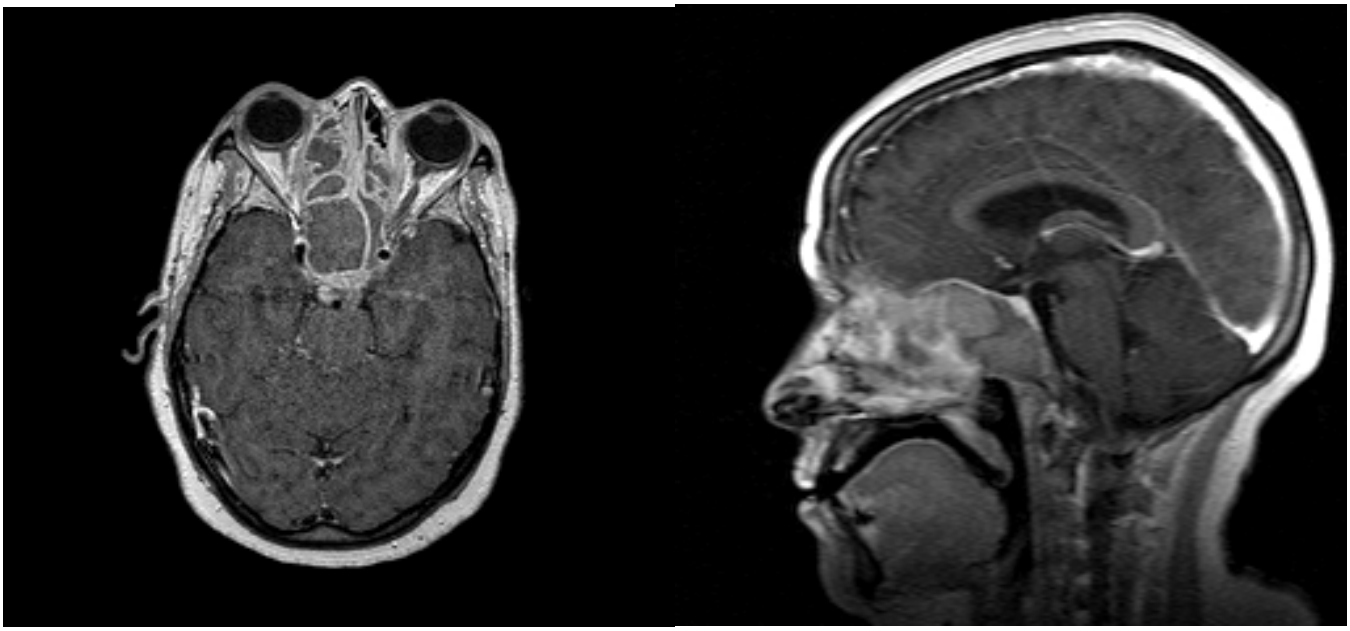


Figure 1: CT scan of the head and paranasal sinuses showed the paranasal ethmoid and maxillary airspaces nearly completely obliterated by heterogeneous soft tissue densities (straight thin arrow)with area of bony destruction over the medial wall of the right orbit and a displacement of the globe and medial rectus (thick black arrow).



Figures 2 & 3: MRI T1- weighted sequences axial & sagital images showed atypical low signal intensities of those densities (thick straight arrow). There also is extensive sphenoid sinus involvement (thin straight arrow), which extended into and obliterated both cavernous sinuses and the Sella turcica (white square), with the carotid arteries displaced laterally (curved arrow). The pituitary gland was not visible; the optic chiasm was displaced superiorly

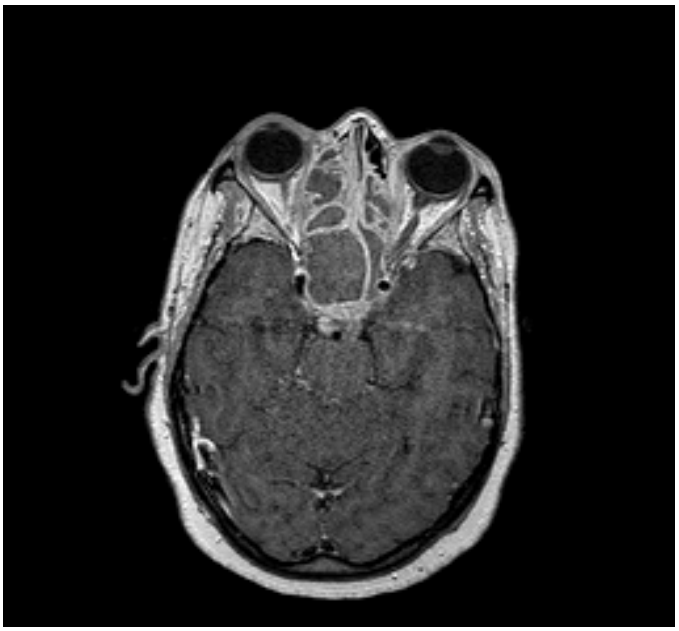


Figure 4: Post op MRI - Post IV Gadolinium T1 weighted Axial images showed only minimal thickening of the mucosa and polypoid change confined to the right middle turbinate

In the interim, an endocrine evaluation was performed. Baseline hormonal testing was as follows: thyroid stimulating hormone (TSH) 0.293 (0.5-4.65 mIU/l), Free T4 9.79 (9.1-23.8 pmol/l), estradiol <73 (143-694 pmol/l), luteinizing hormone (LH) 2.97 (1-18 mIU/l), follicular stimulating hormone (FSH) 9.21 (4-13 mIU/l), serum cortisol <30 (165-830 nmol/l), adrenocorticotropin hormone (ACTH) <2.2 (0-10 pmol/l), human growth hormone (GH) 0.4 (0-13 mIU/l), serum insulin growth factor 1, (IGF-1) 28.86 (adjusted for age 16.20-40.51 nmol/l).

The patient received IV Caspofungin preoperatively which was continued during her four day post operative stay. She was then discharged home on corticosteroids and oral Voriconazole 200 mg twice daily for six weeks. After three months follow up, the patient's headache, anosmia, and nasal obstruction were completely relieved. Repeat CT and MRI scans at six months (Fig. 4) showed only minimal thickening of the mucosa, and polypoid change confined to the right middle turbinate. The ethmoids were clear and the mass in the right orbit had resolved. The sella, pituitary gland, and optic chiasm had returned to normal.

Repeat hormonal testing included an insulin-induced hypoglycemia: serum cortisol rose adequately from a baseline level of 139.6 to 563.6 nmol/l at 60 minutes, and baseline serum ACTH level from 3.5 to 22.9 pmo/l at 120 minutes. In the interim, the patient's menses resumed spontaneously, and her thyroid hormone and prolactin levels were normal. One year later, the patient was still clinically and biochemically asymptomatic on no hormone replacement therapy.

Discussion

The present case fits the description of the recently defined entity of allergic fungal sinusitis. Patients commonly present with a history of nasal obstruction, polyposis, or a history of multiple sinus procedures. Nasal endoscopy reveals polyposis, allergic mucin, and thick tenacious debris. The diagnosis can be made if it fits the most widely accepted diagnostic criteria which were initially described by Bent and Kuhn (3) and supported later by deShazo (5). These types are:

1. Hypersensitivity (IgE mediated) confirmed by history, skin testing, or serology
2. Nasal polyposis
3. Characteristic radiological findings by CT and MRI (decrease signal on T1 or T2 with peripheral enhancement)
4. Histologic evidence of eosinophilic mucus without evidence of fungal invasion into sinus tissue
5. Positive fungal stain or culture of the sinus contents removed intraoperatively or during office endoscopy
6. Absence of contributing factors such as diabetes or immunodeficiency.

Allergic fungal sinusitis is believed to occur as an allergic reaction to fungi in which the fungus causes, in certain predisposed immunocompetent atopic individuals, an immune reaction, producing mucosal thickening, formation of allergic mucin, fungal concretions, and polyps. The same scenario in a nonatopic host may result in a fungal ball or no sinus disease (4).

Incidence and etiology of AFS appears to be impacted by geographical distribution. In North America, Bipolaris species were dominant in the western and inland regions whereas *Curvularia* species was found in the Southeast, and the Aspergillus *agent* in the Southwest region. Similarly, Aspergillus species was the dominant agent recovered in India and Saudi Arabia and occurs more frequently in hot and dry regions. The male to female ratio varies and may be age and geographically dependent, and different in children and adults (6-11).

Erosion into the adjacent structures may occur if the condition is left untreated leading to proptosis, or possibly that which mimics a pituitary tumor. (7,12,13,14). Kinsella and colleagues (13) described a series of 28 cases of allergic fungal sinusitis of which six cases were initially suspected to have a neoplastic process, had radiographic evidence of skull base erosion, and histological diagnostic criteria of allergic fungal sinusitis. All patients were managed with surgery and anti-fungal antibiotics. A diagnostic entity was proposed "skull base allergic fungal sinusitis" which incorporates the radiographic findings of bone erosion and the histological diagnostic criteria for allergic fungal sinusitis. Postulated hypothesis for bone erosion are local pressure effects and local production by inflammatory cells of cytokines with resulting lytic effects.

To date, there are more than 210 cases of pituitary abscesses reported in the literature (15) representing less than 1% of all cases of pituitary disease (16). Pituitary involvement is seen in more than 70% of the cases as an extension from adjacent sinus infections (17). Primary pituitary abscesses were reported in 27 cases over the last six years (16,18,19) and Aspergillus infection is noted in three out of those 27 (11%). Only one case was labeled as a case of allergic

fungal sinusitis (19) involving the sella turcica with no sinus involvement and no pituitary function assessment. To our knowledge, pituitary function assessment was only appropriately documented for biochemical cure in our case. Nasal endoscopy is used to establish diagnosis, staging, and to follow the response to medical therapy (4,7).

The treatment of AFS is mainly surgical to remove all fungal hyphae and spores, and to restore proper ventilation of the sinuses, in addition to corticosteroids and or immunotherapy to prevent recurrences. These surgical goals can be accomplished through a number of approaches and techniques, the choice of which ultimately is influenced by the experience and training of the surgeon. Endoscopic powered instrumentation has demonstrated its effectiveness; this technique allows for removal of soft tissue and thin bone while maintaining good visibility. However, one should exercise great care when using powered instrumentation because the well-recognized bone dissolution associated with AFS increases the potential risk of inadvertent orbital and/or intracranial penetration. In retrospect, the transseptal approach in our patient was not indicated and probably dangerous.

The use of antifungal therapy is disputable but may be considered when the disease takes a more expansive pattern, similar to what was seen in our case (20, 21).

In conclusion, proper recognition of the allergic fungal sinusitis entity in immunocompetent patients is essential to prevent unnecessary delays in the institution of proper therapy. The entity of allergic fungal sinusitis can best be thought of as a chronic fungal affectation (not an infection) to which the body's immune system hyperreacts. Hypopituitarism is usually reversible with proper surgical cavity aeration. Prevention of the condition is also made feasible by the proper identification of the inciting infectious organism, or the predisposing condition, and the use of inhaled corticosteroid or relevant immunotherapy. Finally, surgical drainage is the main therapeutic modality to consider for cure.

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