ORIGINAL ARTICLE

Clinical Characteristics and Outcome in Patients with Sphenoid Allergic Fungal Disease

Hisham B. Alem, MS

Department of Otolaryngology, Faculty of Medicine
King Abdulaziz University, Jeddah, Saudi Arabia

Correspondence
Dr. Hisham B. Alem
Assistant Professor and Consultant
Dept. of Otolaryngology
Faculty of Medicine, King Abdulaziz University
P.O. Box 80215, Jeddah 21589, Saudi Arabia
e.M: halam@kau.edu.sa

Submission: 09 November 2014
Accepted: 20 December 2014

Citation
Alem HB. Clinical characteristics and outcome in patients with sphenoid allergic fungal disease. JKAU Med Sci 2015; 22(1): 17-23.

Abstract

Sphenoid Allergic Fungal Disease is an uncommon disease, usually non-aggressive course, as reported in the literature. It is usually undiagnosed because of its atypical presentation. This series reports four cases of Sphenoid Allergic Fungal Disease presenting with distinct symptoms. This article describes the clinician's experience in the diagnosis and treatment of Sphenoid Allergic Fungal Disease. This article also stresses the importance of competency and expertise of the clinician to be more suspicious of the Sphenoid Allergic Fungal Disease in their routine clinical practice as it is not a usual diagnostic condition. This four-case series will also explain the importance of various investigative procedures and radiological findings to be incorporated as required for diagnosing and treating the cases of Sphenoid Allergic Fungal Disease.

Keywords

Sphenoid sinus, Allergy, Fungal.

Introduction

Sphenoid Allergic Fungal Diseases (SAFD) are not common as part of pan-fungal sinusitis. The sphenoid sinus is otherwise known as the "neglected" sinus[1]. Isolated sphenoid fungal disease is rare and hard to diagnose[2,3]. However, as an under-diagnosed pathological entity, it is believed that only increased awareness among physicians to seek out the fungal involvement of this disorder will increase the diagnosis of SAFD. This article reports a series of four cases with different clinical manifestations from different age groups with final diagnoses of SAFD.

The present study was conducted at Otolaryngology (ENT) Department, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia. Four subjects participated in the study (1 male and 3 females), and written–informed consent was obtained from each subject.

Method

Case 1

A 9 year old girl presented to hospital with history of recurrent chest infection and productive cough. Complete Blood Counts (CBC) were normal and chest X-ray showed right middle lobe pneumonia. Her personal and family medical history were not significant and the patient had taken all immunizations since birth. The patient received medical treatment for chest infection but still complained intermittently of the same symptoms. A repeat X-ray of the chest was performed with discovery of a right sub-segmental consolidation collapse of the lung. However the patient did not completely recover from the lung symptoms, and a year later the patient complained of headache, for which a magnetic resonance imaging (MRI) of the brain was done. She was found to have a sphenoid fungal lesion. This was subsequently confirmed with a computerized

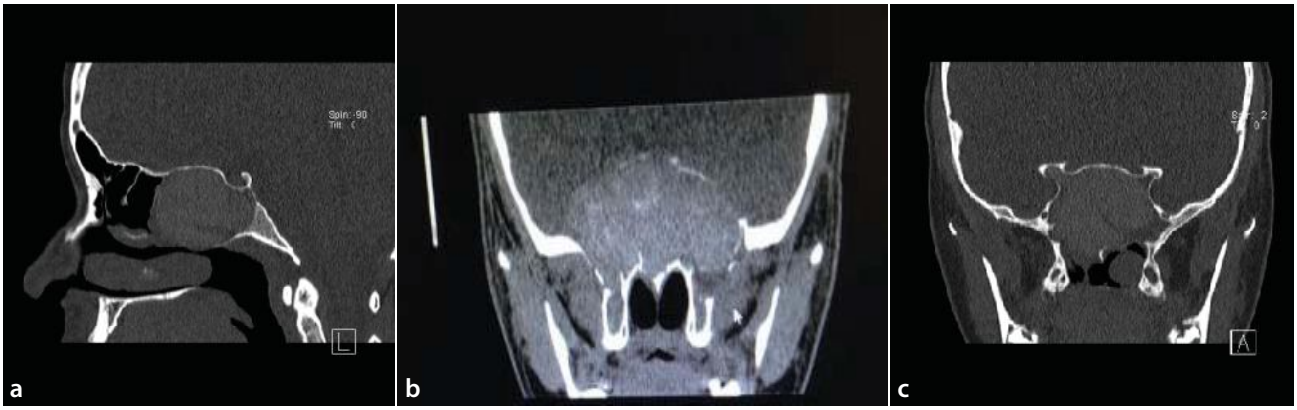

Figure 1. Non-enhanced CT scan of the paranasal sinuses. (a) mid-sagittal bone window, (b) coronal bone window and (c) coronal soft tissue window, showing expansion and remodeling of the sphenoid sinus by hyperdense content, causing mass effect on the inferior aspect of the brain. There is a hypo-attenuating rim seen at the left lateral aspect. There are multiple areas of osseous erosions. There is a polypoidal mucosal thickening in the posterior left ethmoidal sinus. No intra axial extension identified.

tomography (CT) scan (Fig. 1). On ENT consultation, signs and symptoms were all normal. CBC was normal but the level of immunoglobulin E (IgE) was elevated to 657 U/mL (normal is < 50 U/mL). Functional Endoscopic Sinus Surgery (FESS) was done and revealed extensive sphenoid fungal disease. Histopathology revealed numerous fungal hyphae and multiple fragments of inspissated mucus secretion with acute and chronic inflammatory cells with necrotic debris. Culture was positive for Asperigillus species. Post operative control of Allergic Fungal Sinusitis (AFS) was by topical steroid and a steroid oral maintenance dose was also given. Patient recovered from headache and the chest infection also cleared. She was followed up for two years.

Case 2

An 18 year old male patient presented with severe retro orbital pain and severe headache for 2 weeks. Ophthalmology consultation was done and it was normal. This was followed with a neurology consultation which was also normal. Patient was atopic and not known to have any allergies. MRI of the brain was requested by Neurologist and showed normal brain parenchyma with sphenoid lesion (Fig. 2). Patient was referred to ENT, findings were all normal apart from elevated IgE to 526 U/mL. FESS was also done and revealed isolated sphenoid fungal disease. Histopathological investigation showed hyphae with mucinous secretion. Culture was positive

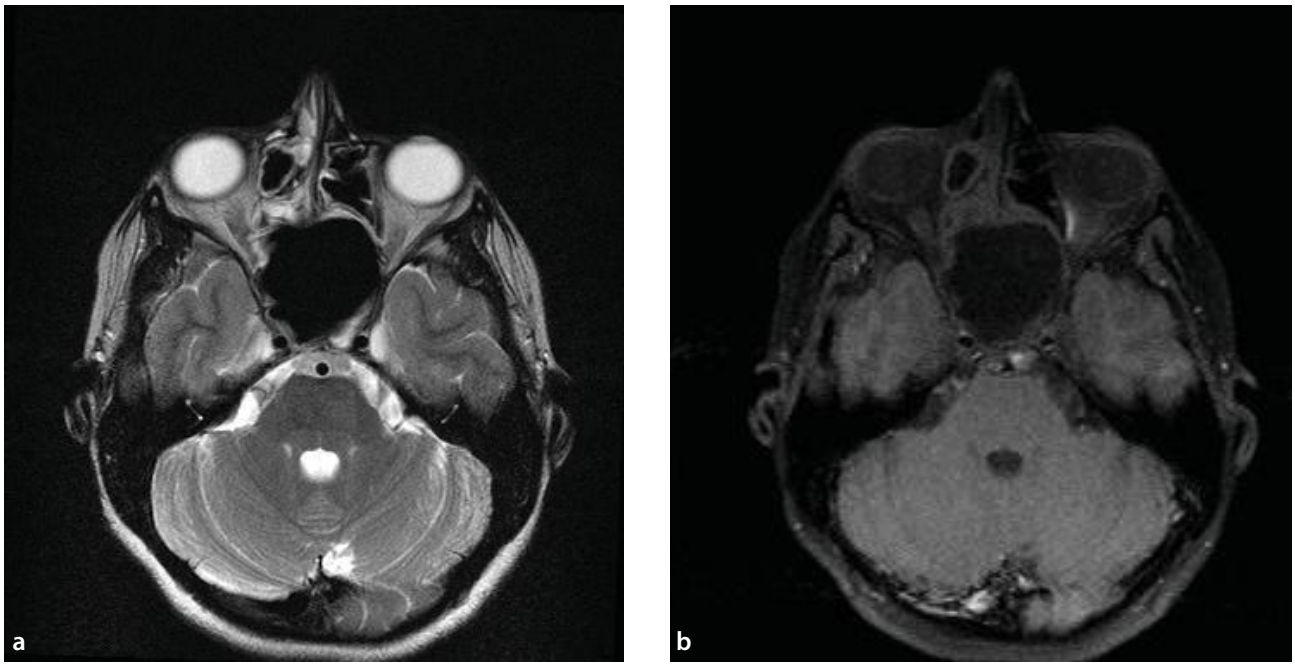

Figure 2. (a) Axial T2 and (b) axial FLAIR, showing homogeneous, diffuse hypointensity involving the expanded sphenoidal sinus.

for Asperigillus species. Post-operatively the patient was relieved from pain and headache. The patient was put on topical steroids / maintenance oral steroids and nasal irrigation with normal saline. The patient was followed up for two years with no signs and symptoms of the SAFD.

Case 3

A 68 year old female patient with well-controlled diabetes, presented to the Ophthalmology clinic at hospital complaining of decreased visual acuity, partial visual field impairment and headache over a period of one month. There were no nasal signs or symptoms. She was not receiving any medications and did not suffer from any food or drug allergies. She did not report any history of chronic disease. The patient had normal eye movement, and the central nervous system examination was normal. The ophthalmologist involved in the evaluation of the patient found that the patient had a decreased field of vision in both eyes. No optic nerve atrophy or papilloedema was observed. The patient's blood investigations showed normal CBC.

The magnetic resonance imaging (MRI) of the brain requested by the Neurosurgery consultant showed a sphenoid lesion which was pituitary in origin. Based on these findings, the patient was booked for transsphenoidal hypophysectomy and the patient was put on medication to decrease intracranial pressure. Intra-operatively, ENT surgeon was called to endoscopically provide access to the sphenoid sinus. Upon reaching the sphenoid it was found that the sphenoid sinus was full of fungal material. Since there was no intracranial extension or pituitary involvement, transsphenoidal hypophysectomy was aborted.

Histopathology and staining revealed numerous fungal hyphae and eosinophilic mucus. The culture showed Aspergillus flavus growth. Post-operatively the patient continued the antifungal treatment for 3 weeks and low-dose systemic steroids for 3 months, during which the ophthalmologists and otolaryngologists followed her up regularly. An improvement in the patient's vision was noted within one week after surgery. The ophthalmologist reported bilateral normal vision and an improvement in the visual fields and normal corneal and fundus reflexes. The patient remained symptom-free throughout the 2-year follow-up: Her condition had returned to normal.

Case 4

A 16 year old female patient was complaining of right side deep headache with retro orbital pain but had no decrease in visual acuity or proptosis. ENT examination revealed normal bilateral nasal mucosa and no secretion or polyps was seen. MRI scan was done, which revealed an extensive sphenoidal lesion mainly because of fungal sinusitis (Fig. 3). Blood investigation showed IgE is 800 U/mL, eosinophils 12 (normal 0-4). The patient underwent FESS with findings of extensive fungal material in

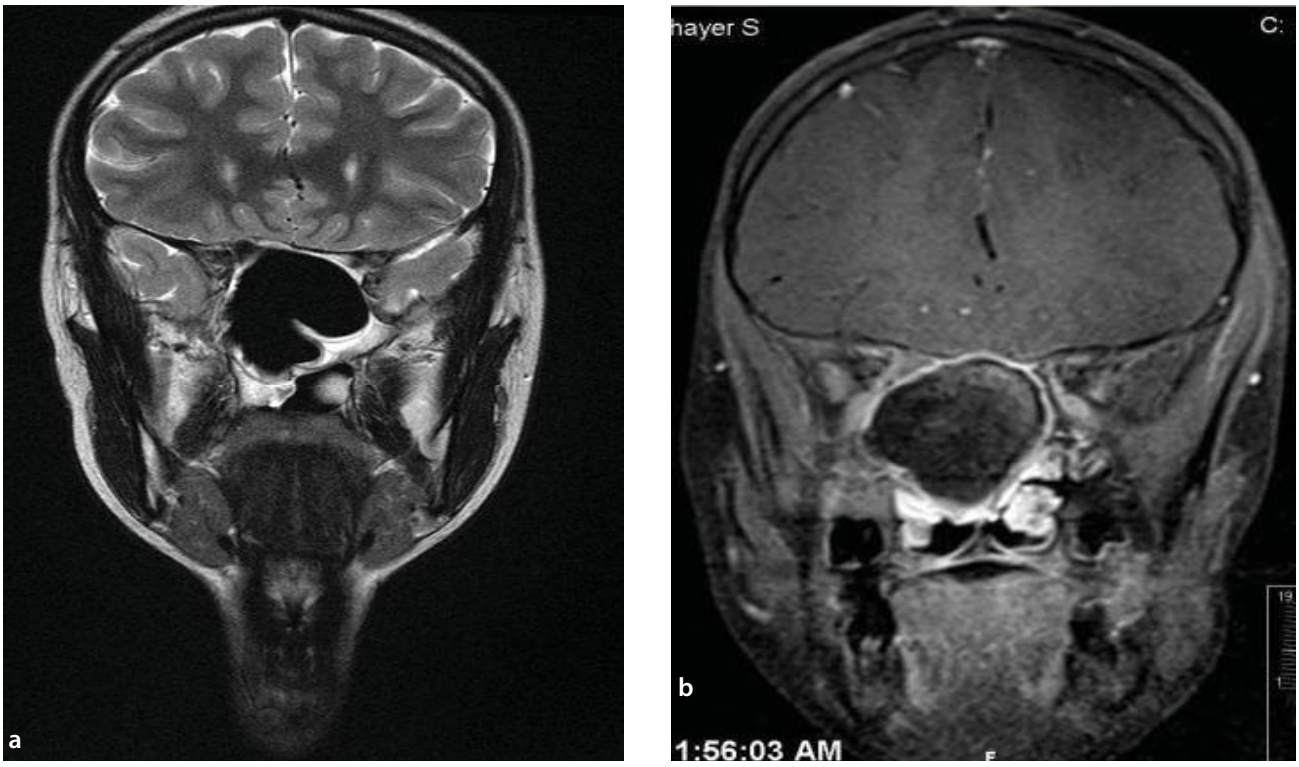

Figure 3. (a) Coronal T2 and (b) coronal FLAIR showing enhanced fat saturated at the level of the sphenoidal sinus showing non-enhancing, heterogeneous, predominantly hyperintense content and a peripheral rim of enhancement representing inflamed mucosa, typically seen in allergic fungal sinusitis. The brain parenchyma is normal. No evidence of intra axial extension.

the sphenoid sinus and a widened sphenoid ostium. Histopathology showed numerous fungal hyphae and multiple fragments of mucus secretion. Post-operatively the patient was continued on topical steroids and a short period of oral steroids. The patient was followed up for 2 years. No evidence of recurrence and no signs or symptoms of SAFD were found.

Discussion

Sphenoid Allergic Fungal Disease (SAFD) is unusual and its incidence is very negligible among all the sinus infections. It is frequently misdiagnosed or undiagnosed because its presentation is atypical and the sphenoid sinus' anatomical relations with many intracranial structures can cause serious complications[1]. This sinus has some typical features: It is lined with ciliated pseudo stratified epithelium with less mucous secreting cells as compared to the other paranasal sinuses. This can lead to less drainage problems and may be the reason why there is low incidence of isolated sphenoid disease[4].

In this series was discussed four different cases of SAFD, each from different age groups ranging from childhood to older adulthood. This shows that SAFD can affect any age group. The chief complaints of each case were different: Each patient was showing isolated clinical symptoms which direct the clinician to think widely during the process of diagnosis. Cases two and four, even though of different sex, complained of common symptoms of retro orbital pain and headache but the other two cases presented entirely different symptoms. However, the most common symptom among all patients was headache, mainly due to sinus aeration. Symptoms in SAFD are atypical and vague, while headache and visual problems are the very common symptoms. As in these four cases, the absence of nasal symptoms does not exclude sphenoid disease. These patients were not complaining of fever, and laboratory tests done initially did not confirm any bacterial infection[1,4-6].

There was no other associated disease or systemic disease could be found for any of these patients except in case 3, where she had a known case of diabetes since 12 years prior. Another important finding is that, even though it was also one of the sinus diseases, none of them were complaining of any nasal symptoms like runny nose, nasal obstruction, allergic rhinitis, or chronic sinusitis that includes nasal congestion, purulent rhinorrhea, postnasal drainage; which makes this disease entirely different from Allergic sinusitis[7]. This is the reason why many times it has not been diagnosed early by clinicians, unless they do not think widely and deeply as it was explained in the literature that the allergic fungal disease is difficult to diagnose.

Diagnostic criteria for the patients with suspicious SAFD includes: Total serum IgE level; antigen specific IgE for fungal inhalants; fungal antigen specific IgG; precipitating antibodies; microscopic evaluation; and fungal culture of allergic mucin evacuated during the operation[3,8]. However, the investigation methods performed for all the subjects in this case series were a complete blood examination which was found to be normal, whereas the IgE level was raised among all patients. It was assumed that the normal values of IgE are below 50 U/mL but in all these four subjects the total IgE values are raised above 500 U/mL[9].

Even though SAFD is caused by many types of fungi such as dematiaceous fungi (consisting of the genera *Bipolaris, Curvularia, Exserohilum, Alternaria, Drechslera, Helminthosporium,* and *Fusarium),* the most common organism identified in allergic fungal sphenoid disease is Aspergillus species. The fungal culture revealed in these cases that Aspergillus flavus growth was found in all the patients. Histopathological examination revealed numerous fungal hyphae and abundant eosinophilic mucus with an intact sinonasal mucosa[10].

The ophthalmological symptoms of sinus fungal disease include proptosis, blepharoptosis, diplopia, epiphora, orbital abscesses, opthalmoplegia and rarely visual loss. Loss of vision associated with SAFD is an uncommon finding[11]. In the third case among this series the cause of the observed visual impairment secondary to SAFD was unusual. In this case the proposed mechanism of the visual impairment associated with SAFD includes expansion of the sphenoid sinus due to the infectious process, followed by involvement of the suprasellar area, leading to compression on the optic chiasma. The patient described here is immunocompetent adult presenting with visual disturbance due to allergic fungal disease involving the sphenoid sinus. This report demonstrates the potentially serious implications of sphenoid sinus disease and highlights the rarity of allergic fungal disease induced visual impairment from compression of the optic chiasma. Although the allergic fungal disease associated visual impairment was observed in this patient, the patient improved post-operatively and immediately began regaining her vision.

The usual radiological investigations performed in these patients are CT scan and MRI in order to confirm the diagnosis. And in this case series, case 1 underwent CT scan whereas case 2, 3, and 4 did MRI. The literature suggests that a high rate of misdiagnosed cases are reported because of its atypical presentation[1]. The best radiological diagnostic study of choice for detecting the lesion is CT scan and MRI of the paranasal sinus. In CT scan the normal physiological pneumatization of the sphenoid sinus leads to formation of recesses that are variably prominent; these include the opticocarotid recess, an aerated greater wing of the sphenoid, and the pterygoid recess. The other findings include: Thickening of mucosal wall; opacification of sphenoid; and erosions

or sclerosis of surrounding bones (Fig. 1). The MRI findings suggestive of fungal disease include low signal intensity on T1 weighted images and/or mixed signal intensities[11]. Such findings on MRI are most likely due to fungus and calcium deposition (Fig. 2 and 3). Routine radiographs usually fail to detect fungal disease because it is seated deep[12].

A high index of suspicion of SAFD is essential for early diagnosis and the right treatment. Pre-operative diagnosis will help the clinician on the surgical approach, extent of surgery and adjuvant medical therapy as well[11,13]. A wide consensus on the appropriate treatment of allergic fungal disease has not been reached, and both medical and surgical procedures are used. Long-term medical therapy includes oral or topical corticosteroids, antifungal agents and/or immunotherapy. The use of antifungal agents for the treatment of allergic fungal disease has shown variable results, and thus their role is controversial. Sullivan and Bent[10] reported that systemic antifungal therapy in allergic fungal disease has no role since the fungal sinus disorder is extra mucosal. In contrast, Khattar and Hathiram[9] affirmed that oral itraconazole seems to be beneficial. Finally, topical fluconazole nasal spray was used with positive results and, although there is no adequate evidence for its efficacy, some authors have performed nasal and paranasal amphotericin B washes to reduce the luminal load of the fungus[3].

Imaging is mandatory before surgical treatment, and therapy is similar in both children and adults. Surgical debridement of the lesion and cleaning of involved sinuses by an endoscopic sinus approach is the gold standard of treatment[3,14]. Finally, the surgeon must keep this in mind and closely follow patients for early diagnosis and prompt adequate therapy. Treatments given to all the patients in this series were intranasal steroid spray and oral steroid (20 mg prednisolone), tapering to small maintenance dose (5 mg prednisolone once daily for three months) along with the nasal FESS.

During the postoperative follow-up, all the patients were totally relieved of retro orbital pain and headache. Close follow-up of these patients are warranted due to the chance of having a recurrence. The prognoses among all the subjects were very promising and all of them were completely relieved of the symptoms of which they were complaining. All the subjects were followed up to find out the recurrence of the disease and to know the current status of the patients until 2 years, and it was a satisfactory response from all four patients.

Conclusion

Sphenoid allergic fungal disease is rare and not a common condition in any age group. The description of this case series experience in the diagnosis and treatment of SAFD underlines the importance of a high index of suspicion in order to diagnose and treat early, and this need to be an active process. In the modern advanced health care era, even though the clinicians depend more on the investigative procedures to arrive at the diagnosis and treatment, it is still advisable to be suspicious clinically based on the signs and symptoms. CT scan and diagnostic nasal endoscopy can be considered as the best choice of diagnostic examination tools. MRI can also be taken into consideration if required for the early diagnosis of Sphenoid allergic fungal disease.

Acknowledgement

The author wishes to thank Dr. Mohamed Faisal CK of Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah for his excellent technical assistance.

Declaration of Source of Funding

The author declares that no funding was received for the present study

References

[1] Monti A, Katsanoulas C, Farini M. Acute isolated sphenoid sinusitis in a 4-year-old child: a rare case with an atypical presentation. Signa Vitae 2008; 3(1): 51–54.

[2] Ng YT, Butler IJ. Sphenoid sinusitis masquerading as migraine headaches in children. J Child Neurol 2001; 16(12): 882-884.

[3] Berlucchi M, Pedruzzi B. Allergic fungal sinusitis in children. J Aller Ther 2012; S5(004): 1-5

[4] Tan HK, Ong YK. Acute isolated sphenoid sinusitis. Ann Acad Med Singapore 2004; 33(5): 656-659.

[5] Saitoh A, Beall B, Nizet V. Fulminant bacterial meningitis complicating sphenoid sinusitis. Pediatr Emerg Care 2003; 19(6): 415-417.

[6] Herrmann BW, White FV, Forsen JW Jr. Visual loss in a child due to allergic fungal sinusitis of the sphenoid. Otolaryngol Head Neck Surg 2006; 135(2): 328-329.

[7] Al-Swiahb JN1, Al-Ammar A, Al-Dousary SH. Allergic fungal sinusitis in children in Saudi Arabia. Saudi Med J 2007; 28(11): 1711-1714.

[8] Ciprandi G, Silvestri M. Serum Specific IgE: a biomarker of response to allergen immunotherapy. J Investig Allergol Clin Immunol 2014; 24(1): 35-39.

[9] Khattar VS, Hathiram BT. Allergic fungal rhinosinusitis. Otorhinolaryngol Clin Int J 2009; 1(1): 37-44.

[10] Sullivan DP, Bent JP. Allergic fungal sinusitis: diagnosis and management. Oper Tech Otolaryngol-Head Neck Surg 2001; 12: 2-6.

[11] Chaaban MR, Pinto JM, Poon CS, Hong C, Aw J. Allergic fungal rhinosinusitis in the lesser and greater wngs of the sphenoid with resultant optic neuropathy: a case report and review of the literature. J Curr Surg 2012; 2(4-5): 149-153.

[12] Aribandi M, McCoy VA, Bazan C 3rd. Imaging features of invasive and noninvasive fungal sinusitis: a review. Radiographics 2007; 27(5): 1283-1296.

[13] Manjula BV, Nair AB, Balasubramanyam AM, Tandon S, Nayar RC. Isolated sphenoid sinus disease - a retrospective analysis. Indian J Otolaryngol Head Neck Surg 2010: 62(1): 69-74.

[14] Dykewicz MS, Hamilos DL. Rhinitis and sinusitis. J Allergy Clin Immunol 2010; 125(2 Suppl): S103-115.

الخصائص السريرية ونتائجها في علاج مرضى حساسية الأمراض الفطرية

هشام بكر عالم
قسم الأنف والأذن والحنجرة ، كلية الطب، جامعة الملك عبدالعزيز
جدة - المملكة العربية السعودية

المستخلص. المرض التحسسي الفطري للجيوب الوتدية هو مرض غير شائع، وعادة ما يكون غير عدواني، كما ورد في المراجع. ويصعب تشخيصه وذلك لظهوره بشكل لا نمطي. وفي هذه المقالة، نقدم أربع حالات من المرض بأعراض واضحة. وتوضح هذه المقالة أهمية وخبرة وكفاءة الطبيب للقدرة على تشخيص وعلاج ذلك المرض. وعلاج هذه الحالات تفسر أيضا أهمية مختلف الفحوصات والنتائج الإشعاعية لإدراجها على النحو المطلوب لتشخيص هذا المرض.