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Skull base erosion and associated complications in sphenoid sinus fungal balls

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ABSTRACT

Background: Sphenoid sinus fungal balls (SSFB) are rare entities that can result in serious orbital and intracranial complications. There are few published reports of complications that result from SSFB.

Objective: To review the incidence of skull base erosion and orbital or intracranial complications in patients who present with SSFB.

Methods: A retrospective review was performed of all the patients with SSFB who were treated at the Massachusetts Eye and Ear Infirmary from 2006 to 2014. Presenting clinical data, radiology, operative reports, pathology, and postoperative course were reviewed.

Results: Forty-three patients with SSFB were identified. Demographic data were compared between patients with (39.5%) and those without (61.5%) skull base erosion. Two patients underwent emergent surgery for acute complications of SSFB (one patient with blindness, one patient who had a seizure). Both patients with acute complications had evidence of skull base erosion, whereas no patients with an intact skull base developed an orbital or intracranial complication ($p = 0.15$). All the patients were surgically managed via an endoscopic approach.

Conclusion: SSFBs are rare but may cause significant skull base erosion and potentially severe orbital and intracranial complications if not treated appropriately. Endoscopic sphenoidotomy is effective in treating SSFB and should be performed emergently in patients who presented with associated complications.

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Fungal rhinosinusitis (FRS) can be divided, by histopathologic evaluation, into invasive and noninvasive types. Noninvasive FRS can be further classified as eosinophilic (including allergic FRS) and sinus fungal balls (FB).¹ The clinical course for these disorders is varied and ranges from indolent to potentially fatal. Management differs based on the diagnosis, although surgical intervention is necessary for diagnosis and treatment. The pathologic evaluation of paranasal sinus FB reveals fungal hyphae that fill the sinus interior but lack mucosal invasion. The most common reported location for FB is the maxillary sinus,^{2,3} followed by the sphenoid sinus.⁴ Presenting symptoms for FB are dependent on the location of the pathology and can also be incidentally identified on imaging studies in pa-

tients who are asymptomatic.³ When the sphenoid sinus is affected, headache, nasal obstruction, and visual disturbances are the most common presenting symptoms.^{2,3}

The proximity of the sphenoid sinus to surrounding critical structures, including the internal carotid artery and the optic nerve, can result in significant complications from sphenoid sinus disease. Several studies describe sphenoid sinus wall erosion and SSFB^{5–9}; however, reported complications from SSFB are limited in the literature.^{4,8,10–12} Previous case series demonstrate that endoscopic sinus surgery (ESS) for removal of SSFBs is an effective treatment and that systemic antifungal therapy is not necessary.^{4,5,8,11,12} However, the incidence and management of patients who present with complications of SSFB has not been specifically studied. Given the limited nature of published reports, the purpose of this study was to review our institution's experience with SSFBs, including the incidence and management of intracranial or orbital complications.

METHODS

A retrospective review was performed of all the patients who underwent ESS for SSFB from 2006 to 2014 at Massachusetts Eye and Ear Infirmary. Clinical data, including age, sex, the presence of orbital or intracra-

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nial complications, radiologic data, surgical management, microbiologic and pathologic results, and the postoperative course were extracted from the medical record. Skull base erosion was defined as radiographic evidence of loss of bone within the sphenoid sinus. The institutional review board at the Massachusetts Eye and Ear Infirmary approved this study. J.C. Meier and G.A. Scangas contributed equally to the manuscript.

Evaluation and Management

All the patients underwent preoperative evaluation with rigid nasal endoscopy and computed tomography (CT) imaging. Magnetic resonance imaging was ordered in four patients in whom there was concern for a possible neoplasm, patients who presented with an orbital or intracranial complication, or if there was extensive orbital involvement or skull base erosion. The patients underwent ESS with a wide endoscopic sphenoidotomy (transnasal or transethmoid), with removal of the fungal debris. All the specimens were sent for histopathologic evaluation. Bacterial and fungal cultures were sent in 78.0 and 42.0% of cases, respectively. Patients with evidence of purulence in the sphenoid sinus during surgery were discharged home on broad-spectrum antibiotics. Nasal saline solution irrigations were instituted on postoperative day 1. Endoscopic debridement was performed 1 week after surgery and repeated if necessary.

Statistical Analysis

The Fisher exact test with two tails was used to compare demographic categorical data between pa-

tients with and patients without skull base erosion. Unpaired *t*-tests were used to compare continuous data. A *p* value of <0.05 was deemed significant.

RESULTS

A total of 43 patients with SSFB were treated from 2006 to 2014. Thirty-three patients were women and 10 were men; the average age was 62.1 years old (Table 1). The average follow-up time was 14.8 months. The most common presenting symptom was headache (56.8%), followed by nasal obstruction (18.1%). Sphenoid sinus opacification was noted incidentally in 13.1% of the patients. Sixteen patients (37.2%) had undergone previous sinonasal surgery, including four patients who had undergone transsphenoidal pituitary surgery and seven who had undergone previous ESS. The patients who had undergone previous sinonasal surgery had a reduced rate of skull base erosion compared with those who had not undergone surgery previously (17.6 versus 50%; *p* = 0.05) (Table 1). Radiologic findings on preoperative CT (Fig. 1) included the following: heterogeneous hyperdensity within the sinus (72.9% of patients), hyperostosis of the walls of the sphenoid sinus (74.4%), and skull base erosion (39.5%). Evidence of heterogeneous hyperdensity on CT (88.2 versus 57.7%; *p* = 0.045) was seen in patients with skull base erosion when compared with patients without skull base erosion (Table 1). Four patients underwent magnetic resonance imaging to further evaluate the sphenoid opacification before surgical exploration (Fig. 2). Two of the SSFB demonstrated T2 hypointensity, with variable T1 intensities, without enhancement of the SSFB.

Table 1 Clinical data of patients with and patients without skull base erosion

	All Patients (<i>n</i> = 43)	Patients with Skull Base Erosion (<i>n</i> = 17)	Patients with No Skull Base Erosion (<i>n</i> = 26)	<i>p</i> Value
Average age, y	62.1	62.7	61.7	0.859
Follow-up, mo	14.8	13.7	15.6	0.729
Sex, %				
Men	23	35.2	18.1	0.158
Women	77	64.8	71.9	0.158
Previous nasal surgery, %	37.2	17.6	50	0.053
Hyperostosis, %	74.4	76.5	73.1	0.999
Hyperdensity, %	72.9	88.2	57.7	0.045
Complications from SSFB, %	4.7	11.7	0	0.151
Presenting symptoms, %				
Headache, %	56.8	64.7	50	0.369
Obstruction, %	18.1	17.6	19.2	0.999
Incidental finding, %	13.1	17.6	11.5	0.665

SSFB = Sphenoid sinus fungal ball.

Demographics and clinical data of 44 patients with SSFB. There was a significant differences between patients with and without skull base erosion in terms of CT findings of hyperdensity.

Bold denotes *P* value < 0.05 indicating a difference between patients with and without skull base erosion.

Figure 1. Computed tomography of a right sphenoid sinus fungal ball. Computed tomographies without contrast (coronal, left; sagittal, right) of a patient who presented with an acute onset of right-sided blindness. Right optic nerve and sellar dehiscences are evident.

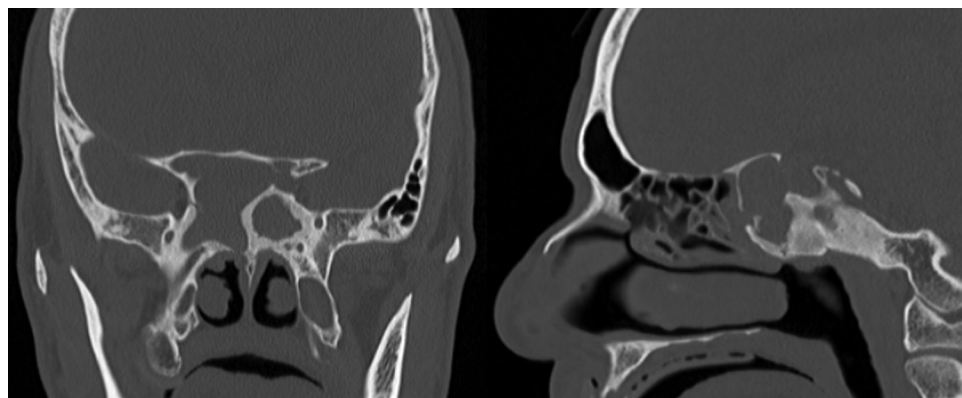
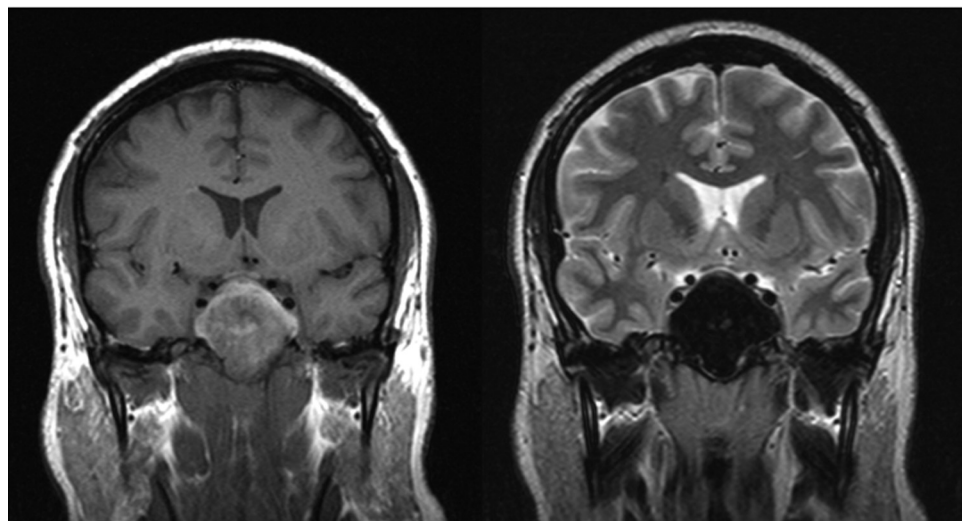


Figure 2. Magnetic resonance images of sphenoid sinus fungal ball (SSFB). Magnetic resonance images without gadolinium contrast enhancement of a patient with SSFB. The T1 sequence (left) reveals mild hyperintensity of the SSFB to muscle. The T2 sequence (right) shows a complete lack of signal, characteristic of a fungal ball.



Two patients (4.7%) presented with complications that resulted from the SSFB, and both had skull base erosion. No patient with an intact skull base presented with an orbital or intracranial complication ($p = 0.15$). The patients with complications included one patient with complete unilateral blindness (who presented 4 days after the onset of vision loss), and one patient who had a new-onset seizure. Both underwent emergent ESS. The patient with vision loss did not have any recovery of vision after surgery. The patient with new onset seizure had no recurrence of seizures after removal of the SSFB. All the patients underwent a purely endoscopic approach for removal of the SSFB. Transnasal sphenoidotomy was performed in 10 patients (23.3% of cases), and transethmoid sphenoidotomy was performed in 33 patients (76.7% of cases). Seven patients (16.2%) underwent drilling of the sphenoid face or sphenoid nasalization to ensure a wide sphenoidotomy. Three patients (7%) developed perioperative complications. Two patients developed epistaxis, which required endoscopic control of the sphenopalatine artery in the operating room. One patient required prolonged ventilation in the postoperative acute care

unit due to a previously undiagnosed acetylcholinesterase deficiency. No intraoperative complication, *e.g.*, cerebrospinal fluid leak, was encountered.

Histologic evaluation showed fungal hyphae without evidence of mucosal invasion in all the patients. *Aspergillus* was identified in 70% of the patients. A specific species of fungus was not identified in the remaining 30% of patients. Fungal cultures were obtained in 21 patients; only 4 (19%) demonstrated positive growth after 28 days of incubation. Forty patients had bacterial cultures performed (Table 2). The most-common pathogenic species isolated were methicillin-sensitive *Staphylococcus aureus* (25% of all the patients), α -hemolytic *Streptococcus* (15%), and *Pseudomonas aeruginosa* (12.5%). Four patients required revision surgery, for a re-operation rate of 9.3%. Two revision surgeries were performed shortly after the original surgery to assess for residual accumulated debris noted on postoperative examination. One patient had recurrence of the FB approximately 1 year after the original surgery, for a recurrence rate of 2.3%. One patient developed asymptomatic scar tissue over the sphenoidotomy; revision surgery was performed to lyse scar tissue.

Table 2 Microbiology of operative cultures

Bacterial Strain	No.	Strains, %	Cases, %
Coagulase-negative <i>Staphylococcus</i>	26	28.3	65.0
<i>Propionibacterium acnes</i>	13	14.1	32.5
Methicillin-sensitive <i>Staphylococcus aureus</i>	10	10.9	25.0
<i>Diphtheroids</i>	9	9.8	22.5
α -Hemolytic <i>Streptococcus</i>	6	6.5	15.0
<i>Pseudomonas aeruginosa</i>	5	5.4	12.5
<i>Klebsiella oxytoca</i>	3	3.3	7.5
<i>Serratia maracens</i>	3	3.3	7.5
Other	17	18.4	42.5

Operative culture results from a total of 92 strains from 40 operative cases. The most common pathogenic organisms cultured were methicillin-sensitive *Staphylococcus aureus*, hemolytic *Streptococcus*, and *Pseudomonas aeruginosa*. No. = Number of cultures.

DISCUSSION

Sphenoid sinus disease can result in significant morbidity due to the proximity of adjacent structures, including the cavernous sinus, carotid artery, and optic nerve. Sphenoid sinusitis can be due to bacterial or fungal infection, and the possibility of invasive fungal sinusitis should always be considered, especially in patients who are immunocompromised and present with acute complications of sinusitis. Visual symptoms, including vision loss and diplopia, can often be the initial presenting symptom of a sphenoid process. In a report of 13 patients with visual disturbance secondary to isolated sphenoid sinus disease (including four patients with SSFB), the optic nerve was the most commonly affected cranial nerve (54%), followed by the sixth cranial nerve (40%).¹³ Only three of eight patients who presented with visual loss in that study had improvement after surgical management of the sphenoid disease.¹³ Pagella *et al.*⁴ reported eight patients with SSFB who presented with blurred vision, blindness, and diplopia. Six patients recovered after surgery; however, there was only 60% recovery in patients with optic nerve involvement; the one patient who presented with unilateral blindness did not recover.⁴

Another series of patients with SSFB identified five patients with orbital complications, including two patients with vision loss and three patients with diplopia.⁸ Although the diplopia resolved in all the patients, the two patients with vision loss did not have any recovery in visual function.⁸ In our series, the patient who presented to our institution four days after complete loss of vision did not recover vision after surgical intervention. Thus, prompt diagnosis and treatment are imperative in the hope that the presenting visual complication can be reversed. Although less common than orbital complications, other sequelae of SSFB have been reported. Schlosser *et al.*¹¹ reported one patient with internal carotid artery thrombosis, and, similar to the patient in our study, deShazo *et al.*¹⁰ reported two

patients with new onset seizure in the context of newly diagnosed SSFB.¹⁰ In this series, after surgical intervention, the patient who presented with a new onset seizure had complete recovery, with no further seizure activity and a completely normal neurologic workup. Interestingly, in our study, 13.1% of SSFB were discovered incidentally, comparable with other reported studies (8.9%,³ 20.7%⁵). It is important to consider that, given the severity of potential complications of untreated SSFB, surgical exploration and removal are warranted, even in asymptomatic cases of SSFB. The potential development of orbital and intracranial complications should be specifically discussed with patients when considering treatment options once this disorder has been identified on imaging studies.

The pathogenesis of sinus FB remains unclear. In cases of maxillary sinus FB, several studies implicated the transgression of dental material into the maxillary sinus *via* an endodontic procedure as a potential instigator of mucosal damage and subsequent fungal growth.¹⁴⁻¹⁷ Nicolai *et al.*³ noted that 104 of 120 patients (86.7%) with maxillary FB in their study had previously undergone endodontic treatment of a maxillary tooth. However, this history was not noted in patients with SSFB.³ Lee *et al.*¹³ presented a case series of patients with sphenoid sinus disease with visual disturbances (4/13 with SSFB). Of these, five had previously undergone sinus surgery (four *via* Caldwell Luc, one *via* endoscopy) and one patient had undergone transseptal sphenoidotomy for resection of a pituitary adenoma.¹³ Interestingly, in our current study, 16 patients (37.2%) had undergone previous sinonasal surgery. Of these 16 patients, 11 underwent previous sphenoidotomy (4 underwent transsphenoidal pituitary surgery and 7 underwent ESS). The high percentage of patients with SSFB who had undergone previous sinonasal surgery may be a risk factor for SSFB, although, at this point, the exact mechanism remains unclear.

A noncontrast CT should be the initial imaging modality to evaluate FRS. Findings on CT that are suspicious for FB include the following: hyperdensity or calcifications within the sinus, and hyperostosis or erosion of the surrounding bone.^{18,19} In our series, a hyperdensity or calcification within the sinus was seen in 72.9% of the patients, and hyperostosis of the walls of the sphenoid sinus was noted in 74.4% of the patients. In addition to reviewing the imaging studies to predict the diagnosis of SSFB, the CT should be closely reviewed in preparation for surgical exploration. A history of endoscopic sphenoid sinus procedures, including ESS or transsphenoidal pituitary surgery, remains imperative because the anatomy can be significantly altered. The presence of skull base erosion should also be noted. Forty percent of the patients in our study were noted to have skull base erosion on initial imaging studies. There was a higher rate of complications from SSFB seen in patients with skull base erosion compared with patients without skull base erosion, although it did not reach significance (11.7 versus 0%, respectively; $p = 0.151$).

Both of the patients in our series who presented acutely with intracranial or orbital complications were noted to have skull base erosion on initial CT. This finding was seen in another series, in which there was a significantly higher rate of sphenoid sinus wall erosion in patients with orbital complications compared with those without orbital complications (100 versus 36.3%).⁸ Only one previous study of SSFB specifically commented on the incidence of skull base erosion¹¹; however, other studies did note percentages of patients with erosion of sphenoid sinus walls, which were 13%,⁵ 16%,⁶ 25%,⁷ 48%,⁸ and 52%.⁹ Although skull base erosion can be suggestive of a more ominous diagnosis, in our series (39.5%) and in others, it was commonly seen with SSFB. Magnetic resonance imaging can be obtained as an ancillary study in patients with acute orbital or intracranial complications of sinusitis or if the diagnosis is not certain. FBs can have variable T1 intensity; however, they predominantly have a low T2 signal, which can aid in identifying this disorder.²⁰

Once SSFB was suspected, the treatment algorithm for these patients involved prompt surgical exploration. The two patients with intracranial and orbital complications underwent surgery emergently. An important principle of surgical management remains adequate exposure for complete removal of all fungal debris. In cases of isolated sphenoid sinus involvement, endoscopic transnasal sphenoidotomy alone can often achieve adequate exposure and was performed in 23.3% of the patients in our study. In patients with limited transnasal access or involvement of the ethmoid sinuses, an endoscopic transethmoid sphenoidotomy approach can be performed (76.7% of cases in our study). Seven patients (13.7%) underwent a more-

extensive surgical sphenoidotomy, with either drilling of the face of the sphenoid or sphenoid nasalization¹² to ensure adequate exposure of the sphenoid sinus with complete removal of fungal debris. Although no cases of intraoperative cerebrospinal fluid leak were noted in our cohort, surgeons should be prepared to address this possibility at the time of surgery, especially in patients in whom skull base erosion has been noted on preoperative imaging studies. In this series, the patient who presented with unilateral blindness recovered uneventfully after surgery but did not regain any vision. The patient who presented with an acute seizure recovered uneventfully, without further neurologic sequelae.

Histopathologic evaluation to confirm FB and to rule out invasive FRS is imperative for the final diagnosis of this disorder. In patients with a history of immunosuppression or diabetes, the diagnosis of invasive fungal sinusitis is especially important to ascertain in a timely fashion. In all cases in our series, histopathologic evaluation showed a large volume of fungal hyphae without evidence of sinonasal mucosal invasion. Operative cultures were much less sensitive for identifying fungus, with only 4 of 21 cases that resulted in a positive culture, as has been noted in other studies.^{3,21} Ultimately, the diagnosis is dependent on the histopathologic presence of fungal forms rather than microbiologic evaluation. Limitations of the study included the retrospective nature of this review and the small number of patients with complications of SSFB in our series. Large series of SSFB are not commonly reported, and this review added to the body of literature on this uncommon disorder. It is important to recognize that skull base erosion is frequently seen in this disorder and that orbital and intracranial complications of SSFB can occur and can result in permanent deficits if not recognized and treated.

CONCLUSION

SSFB is a rare entity, which often presents with non-specific symptoms or which is identified incidentally on imaging studies but can cause potentially severe complications, including permanent visual loss, given the critical structures that surround the sphenoid sinus. Skull base erosion is frequently seen as a consequence of SSFB and should be specifically assessed before surgical exploration. Endoscopic surgical removal of the SSFB is necessary for management and should be performed in an emergent fashion for patients who present with significant complications, especially when the optic nerve is involved because visual loss is often not reversible.

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