Neurosurgical Management of *Bipolaris*-Specific Skull Base Allergic Fungal Sinusitis: Diagnostic Criteria and Outcome

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Skull base allergic fungal sinusitis is a rare but important neurosurgical entity that can be mistaken for a skull base tumor during preoperative assessment. Due to the significantly variable clinical presentation of and preoperative evaluation for this disease, clinicians are often surprised when the diagnosis becomes apparent during surgery or thereafter. However, SBAFS must be differentiated from malignancy and invasive fungal disease because this allergic disease does not require aggressive, complete resection or potentially toxic antifungal medications. We report six cases of SBAFS to illustrate the neurosurgical management of this rare disease.

Key Words: allergic fungal sinusitis, *Bipolaris*, skull base

Abbreviations Used: AFS, allergic fungal sinusitis; CT, computed tomography; GMS, Gomori methenamine silver; MR, magnetic resonance; SBAFS, skull base allergic fungal sinusitis

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Over the past decade, the incidence of fungal infections has increased dramatically. Fungal paranasal sinus disease, a large component of fungal infections, is common and is defined by the host and the host's response to the fungus. Invasive fungal sinusitis occurs in immunocompromised hosts and can manifest as acute, fulminant, and life-threatening or as a more manageable chronic/granulomatous indolent form. However, the hallmark of invasive disease is the presence of large amounts of the fungal element in the associated pathology without immune containment.

In contrast, noninvasive fungal sinusitis occurs in immunocompetent individuals. It exists in two forms, both characterized by the host's response to the fungal agent. With the first, mycetoma, the host's immune response is inadequate and the fungal agent proliferates as an encapsulated mass. The second, AFS, the subject of this report, occurs when the host provides an overly exuberant immune response to the antigens of the fungus.

Skull base allergic fungal sinusitis, a term first introduced by Kinsella et al., denotes the specific condition in which AFS extends intracranially.[10] Ten to 20% of patients with AFS have an intracranial extension.[13] Once SBAFS is encountered, neurosurgical intervention is required. Because of their variable presentation and rarity, these lesions are seldom expected preoperatively.[15] Consequently, SBAFS is often mistaken for a malignancy,[11,12,18,27] and patients may receive overly aggressive therapy. Because SBAFS is noninvasive, surgical debulkment is standard therapy; radical resection or toxic med-

Table 1. Clinical Summary of Six Patients with *Bipolaris* SBAFS

Case	Age/ Sex	Presenting Symptoms†	Presenting Signs	Medical History	Surgery	Bacterial Isolate‡	Neurological F/U
1	31/M	HA, OD vision loss, OS blurring	OD blindness/RAPD, Dysconjugate gaze	NP, asthma, chronic sinusitis	TNTS	*Staphylococcus*	resolved
2	25/F	OS vision loss	OS vision loss	NP, allergies, chronic sinusitis	SLTS	*Staphylococcus*	resolved
3	20/F	HA, N/V	OD proptosis and vision loss	NP, asthma	TNTS	*Staphylococcus*	resolved
4	36/M	Chronic nasal drainage	CN 6 paresis	NP, allergies, chronic sinusitis	SLTS§	*Haemophilus*	resolved
5	75/F	Tremor, falling, HA, decreasing memory	Head and upper extremity tremor	NP, allergies	TNTS	*Staphylococcus*	resolved
6	19/M	OD proptosis and blurring	Diplopia on left lateral upward gaze	NP, allergies, asthma	BCC	*Staphylococcus*	resolved

†No patient had presenting symptoms consistent with pituitary malfunction. ‡All cases cultured *Bipolaris* heavily; bacterial isolate represents coincident culture. §Complicated by aseptic meningitis. F/U = follow-up, HA = headache, N/V = nausea and vomiting, OD = right eye, OS = left eye, RAPD = relative afferent pupil defect (nonreactive pupil), NP = nasal polyps, CN = cranial nerve, TNTS = transnasal transsphenoidal, SLTS = sublabial transsphenoidal, BCC = bicoronal craniotomy.

ical regimens are unnecessary. We present six patients with *Bipolaris*-specific SBAFS to highlight the neurosurgical management of this rare clinical entity.

Clinical Materials and Methods

Bipolaris-Specific SBAFS

The records of six patients (3 men, 3 women; mean age, 34 years; age-range, 19 to 75 years) who underwent resection with pathologic verification of AFS and culture-proven *Bipolaris* from January 1989 to August 2004 were analyzed retrospectively. The criteria for pathologic verification were allergic mucin-containing eosinophils, Charcot-Leyden crystals, cellular debris, and sparse hyphae. To evaluate the invasive nature of this disease, all cases of *Bipolaris*-specific AFS were identified by querying our microbiology database from January 1998 to August 2004.

Most patients became symptomatic with visual complaints or headache of gradually increasing intensity (Table 1). On examination, the most frequent sign was ocular defect. All patients had a history of atopy, including polyps and at least one other indicator of atopy.

Bipolaris-Specific AFS

Between January 1998 and August 2004, 28 cases of culture-proven *Bipolaris*-specific AFS were treated at our institution. There were 20 men and 8 women (mean age, 30 years; range, 13 to 80 years). Three patients had an intracranial extension consistent with SBAFS (invasion rate, 10.7%). Of these 28 cases, only 1 had fungal elements identified on a KOH preparation. Eleven had concomitant positive cultures for bacteria. Three patients who underwent surgery were not included in the microbiology database because they predated its establishment.

Results

Radiology

Bipolaris-specific SBAFS lesions were isointense on T1-weighted MR images relative to brain tissue (Table 2). T2-weighted MR images lacked lesional or perilesional hyperintensity, suggesting no inflammation. All but one lesion was isointense to brain parenchyma; the exception was hypointense (Table 2). Four cases showed intense uptake on gadolinium-enhanced MR imaging, and another lesion was considered ring enhancing. There was no gadolinium enhancement in the remaining case. In all cases CT showed increased attenuation and bony destruction with expansion of its associated sinus or sella without evidence of hyperostosis. The location of the pituitary in relation to the tumor varied across the cases.

Treatment

Five cases consisted of a primary sphenoidal extension and were treated through a transsphenoidal approach (Table 1). A tumor that originated from the frontal sinus and extended into the anterior cranial fossa was approached through a bicoronal craniotomy. In all cases a coincident positive culture of bacterial isolate (nasopharyngeal flora) was also treated (Table 1). Postoperatively, one patient was diagnosed with aseptic

Table 2. *Bipolaris* SBAFS Imaging Characteristics

Case	MRI†		Gadolinium Uptake	Attenuation†	CT Bone Destruction	Pituitary Location‡
	T1	T2				
1	Isointense	Isointense	Intense	Increased	+	Posterior
2	Isointense	Isointense	Intense	Increased	+	Elevated
3	Isointense	Isointense	Ring enhancing	Increased	+	Posterior
4	Isointense	Isointense	Intense	Increased	+	Anterior
5	Isointense	Isointense	No uptake	Increased	+	Posterior
6	Isointense	Hypointense	Intense	Increased	+	None

†Relative to brain parenchyma. ‡Relative to mass and sella.

meningitis. The resulting transient recurrent sixth cranial nerve palsy resolved with treatment. Whether this complication was related to surgery is unclear. After surgical decompression neurologic symptoms resolved in all cases (range of follow-up, 2 months to 15 years). All patients received postoperative steroids from 2 weeks to 4 months. Three patients also received 2 weeks of antifungal therapy. There were no recurrences.

Illustrative Case

Patient History

A 31-year-old African-American man was transferred from an outside hospital with the radiographic diagnosis of a skull base tumor for further evaluation. The patient reported an 8-month history of headache and progressive loss of vision. The headache consisted of constant throbbing frontal pain. It gradually progressed from low-grade pain to an intensity of 10 on a 1 to 10 scale. Photophobia was present, but there was no evidence of nausea, vomiting, transient visual scotoma, or flashing lights. With the right eye, the patient could only see shadows. Vision in his left eye was beginning to blur. His history included evidence of significant atopy, nasal polyposis, chronic sinusitis with eight previous sinus surgeries, and childhood asthma.

Physical Examination

On neurologic examination the patient was alert and oriented. His right pupil was nonreactive to light; his left pupil was miotic but briskly reactive. Vision was full to confrontation in the left eye. Extraocular movements were intact bilaterally; however, gaze was dysconjugate. Evaluation of pituitary function was unremarkable.

Radiological Examination

Noncontrast head CT showed a hyperattenuating mass occupying the sphenoid sinus and sella (Fig. 1). The bony confines were expanded, and multiple calcified foci were present within the lesion without evidence of hyperostosis or perilesional edema. On T1- and T2-weighted MR images, the lesion was isointense relative to brain parenchyma (Fig. 2). Gadolinium-enhanced MR images showed a large, avidly enhancing lesion with its isocenter in the sphenoid sinus. It extended to the planum sphenoidale inferiorly and abutted the clivus posteriorly. Furthermore, there was evidence of an intracranial extension into the anterior cranial fossa beneath the frontal lobes. Moreover, involvement of the optic nerve suggested chiasmopathy and involvement of the perichiasmal segment (Fig. 3).

Treatment

The patient began steroid therapy and his vision subsequently improved. He then underwent frameless stereotactic transnasal-transsphenoidal debulking of the lesion. A firm white mass intermingled with fibrous tissue, which had eroded the planum sphenoidale and anterior and basal sellar floors, was encountered. Its adherence to the sellar diaphragm and frontal fossa dura made its removal difficult. An intraoperative frozen-section biopsy was consistent with an inflammatory process. The lesion was debulked without complication.

Histopathology

Hematoxylin and eosin staining revealed inflammatory infiltrate without dysplasia. Sparse fungal elements with the rare yeast were present on Fontana and GMS stains. By Day 10, intraoperative cultures were positive for *Bipolaris*.

Outcome

The patient recovered on steroid therapy without complications. At discharge his visual function had normalized, and his headaches had improved significantly.

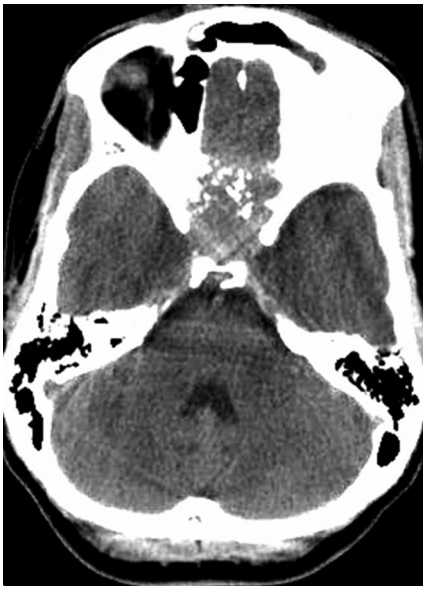

Figure 1. Noncontrast head CT shows a hyperattenuating lesion occupying the sphenoid sinus and sella, with evidence of expansion of these fossae and bony destruction.

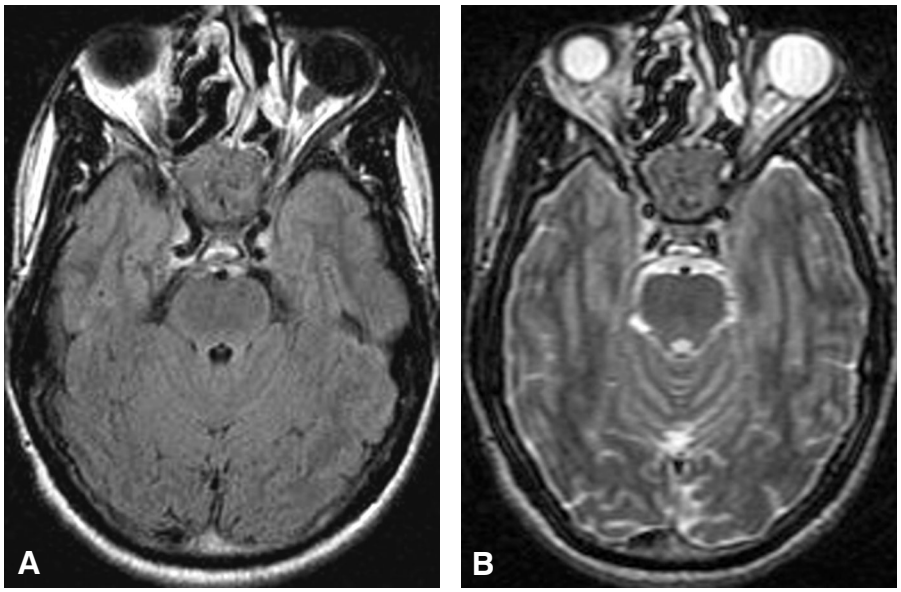

Figure 2. (*A*) T1- and (*B*) T2-weighted MR images show an isointense lesion occupying the sphenoid sinus and sella.

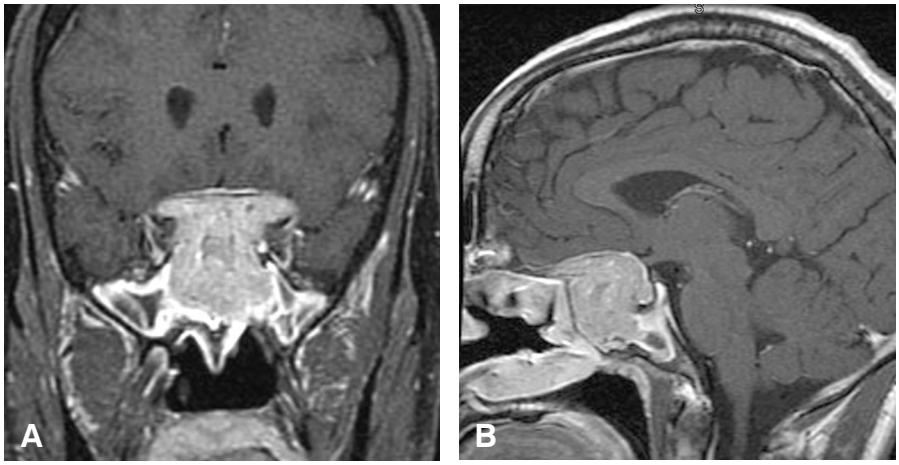

Figure 3. T1-weighted gadolinium-enhanced (*A*) coronal and (*B*) sagittal MR images show chiasmopathy and impressive expansion of the sella. On the sagittal MR image (*B*), an intracranial extension into the anterior cranial fossa resembles a dural tail.

Discussion

Natural History

AFS accounts for 7% of all fungal sinus disease. Dematiaceous fungi, most prominently *Bipolaris*, account for 81% of AFS. The remaining cases are primarily caused by *Aspergillus*. *Bipolaris* is found in dust and soil and on plants. Many cases of *Bipolaris* occur in hot, arid climates with mild winters such as the southern United States and Middle East.[10,17,24,25]

AFS caused by *Aspergillus* and fungal agents of the dematiaceous family, *Bipolaris*, represent different entities. Many *Aspergillus*-associated cases of AFS have been associated with immunodeficiency such as chemotherapy for acute lymphoblastic leukemia, renal failure, or long-standing diabetes. Therefore, we excluded such cases. However, all cases reviewed and all cases reported as *Bipolaris* SBAFS fit the atopic pattern of young, immunocompetent patients, suggesting that this group is homogeneous. Patients with aspergillosis AFS may have elements of invasive disease and should not be considered to have AFS.[19]

The mean age of patients with AFS ranges between 21 to 26 years. Our patients, however, averaged 30 to 34 years old.[4,14] There was no difference in the incidence of SBAFS patients by gender, but the 2:1 male-to-female ratio in our AFS population is consistent with published reports.[14] All had nasal polyps with at least one other atopic finding, which is also consistent with previous reports. None of our patients had stigmata of immunoincompetency. Many patients with SBAFS have proptosis or visual defects.[5,22,28] Five of our six surgical patients had an ocular defect. Almost 11% of the 28 AFS patients we treated had an intracranial extension, a finding consistent with the literature.[13]

In addition to those proposed by Kinsella et al.,[10] we support the following criteria for the diagnosis of *Bipolaris* SBAFS (Table 3). (1) Evidence of intracranial extension by radiographic, surgical, or pathologic means must be present. (2) Histopathologically, the lesion must be consistent with AFS. *Aspergillus* should be excluded. (3) Finally, many reports suggest that species such as *Drechslera* and others are separate microbial agents, but this is not the case.

Curvularia, *Brachycladium*, *Drechslera*, and *Helminthosporium* are obsolete synonyms of *Bipolaris*. *Cochliobolus* is also a teleomorph. Therefore, all of these microbes should be reported as *Bipolaris*.

Diagnostic Imaging

The most remarkable aspect of SBAFS is the consistency with which findings on preoperative imaging are considered to be a malignancy, as occurred in our patient. Preoperative radiographic diagnoses often include chordoma, meningioma, chondrosarcoma, and head-and-neck squamous cell carcinoma. Such misdiagnoses can result in an overly aggressive surgical and/or medical intervention. However, reported imaging characteristics are relatively uniform. In early case reports, sinus expansion was uniformly noted on CT.[3,30] As in our patient, bony erosion with residual bony spiculation without hyperostosis has been reported in all cases of SBAFS.[6]

The finding of a hyperattenuating lesion (45-60 Hounsfield units) is also uniform. Sinus expansion and bony destruction may be related to pressure atrophy, and hyperattenuation may be related to the high residual content of metallic ions in the lesion. Moreover, these lesions appear as areas of diminished signal intensity on both T1- and T2-weighted MR images. As in our patient, the lesions often enhance with the administration of gadolinium.[2,16,23] CT evidence of a lesion extending from a paranasal sinus associated with bony expansion, erosion, and hyperattenuation should prompt suspicion of an SBAFS. When this diagnosis is doubtful, MR imaging can be useful. The lesion should appear iso- to hypointense on both T1- and T2-weighted MR imaging. Transnasal sampling under CT guidance is possible.[20]

Treatment

Because the pathophysiology of AFS is of an allergic nature and the disease is noninvasive,[14] complete removal is unnecessary. The goals of surgery should be to provide tissue for pathologic verification (via intraoperative frozen section, permanent section, and microbial culture), debulkment, and aeration of sinuses. Several authors describe aggressive approaches such as facial degloving. Such radical approaches reflect preoperative uncertainty about malignancy. Aggressive surgical approaches can be associated with complications such as granulomatous encephalitis or cerebrospinal fluid leakage. No case of dural invasion in histiologically confirmed SBAFS has been described. No postoperative complications were associated with conservative treatment in our patients.

Whether postoperative antifungal therapy should be used is also uncertain. No differences have been reported in recurrence rates between cases of SBAFS treated with or without antifungal medications.[26,31] In most early cases of SBAFS, culture of a fungus was followed by treatment with systemic amphotericin B, ketoconazole, or itraconazole. These agents were initiated despite limited in vitro or in vivo activity of these drugs against *Bipolaris*. If treatment for the fungal agent was warranted, systemic corticosteroids, which are usually prescribed with the antifungal agent, would be contraindicated. However, patients usually respond to systemic steroid therapy rather than to antifungal medication. Several cases of recurrent AFS after antifungal therapy alone have been reported.[9,31] No cases of AFS appear to have recurred after appropriate corticosteroid therapy. However, cases of recurrent AFS treated with corticosteroids have resolved.[1,7,8,21,26,29] Although three of our patients with SBAFS received antifungal therapy after surgery, it is most likely not useful and may even be harmful due to the toxicity of systemic antifungal agents. Moreover, postoperative corticosteroid therapy may be necessary for complete resolution.[10] Definitive treatment for SBAFS is surgical debridement with adjunctive steroid therapy.

The prognosis of SBAFS is good. After adequate surgical debridement and aeration of the sinuses, complete neurologic resolution can be expected, as in our 6 cases. Close follow-up care is important. CT, MR imaging, or both are adequate for following SBAFS. The long-term use of topical steroids controls relapses, and systemic steroids may be warranted for a recurrence.

Table 3. Diagnostic Criteria for SBAFS

Skull base involvement
Radiographic evidence of sellar or anterior cranial fossa invasion.
Surgical evidence of intracranial spread
Pathologic abutment of dura
Pathology
Inflammatory reaction to fungus with "sporadic fungal elements"
No fungus ball collection (i.e., mycetoma)

Conclusions

Although *Bipolaris* SBAFS associated with a skull base extension is rare, this diagnosis should be considered when a paranasal sinus mass is present in a young atopic patient. CT findings of a hyperattenuating mass extending from the paranasal sinuses with bony erosion and isointense to hypointense lesions on T1- and T2-weighted MR images are consistent with *Bipolaris* SBAFS. These findings should raise suspicions of this entity in patients living in hot, arid climates. Definitive treatment consists of conservative surgical debulkment with aeration of the sinuses and pre- and postoperative use of corticosteroids. Postoperatively, antifungal medications are not required and complete neurologic recovery can be expected.

References

1. Allphin AL, Strauss M, Abdul-Karim FW: Allergic fungal sinusitis: Problems in diagnosis and treatment. **Laryngoscope 101:**815-820, 1991
2. Bent JP, III, Kuhn FA: Diagnosis of allergic fungal sinusitis. **Otolaryngol Head Neck Surg 111:**580-588, 1994
3. Berry AJ, Kerkering TM, Giordano AM, et al: Phaeohyphomycotic sinusitis. **Pediatr Infect Dis 3:**150-152, 1984
4. Corey JP, Delsupehe KG, Ferguson BJ: Allergic fungal sinusitis: Allergic, infectious, or both? **Otolaryngol Head Neck Surg 113:**110-119, 1995
5. Friedman GC, Hartwick RW, Ro JY, et al: Allergic fungal sinusitis. Report of three cases associated with dematiaceous fungi. **Am J Clin Pathol 96:**368-372, 1991
6. Glass RB, Hertzanu Y, Mendelsohn DB, et al: Paranasal sinus aspergillosis. A case report with computed tomogram findings. **J Laryngol Otol 98:**199-205, 1984
7. Goldstein MF, Atkins PC, Cogen FC, et al: Allergic *Aspergillus* sinusitis. **J Allergy Clin Immunol 76:**515-524, 1985
8. Khan DA, Cody DT2, George TJ, et al: Allergic fungal sinusitis: An immunohistological analysis. **J Allergy Clin Immunol 106:**1096-1101, 2000
9. Killingsworth SM, Wetmore SJ: *Curvularia*/*Drechslera* sinusitis. **Laryngoscope 100:**932-937, 1990
10. Kinsella JB, Bradfield JJ, Gourley WK, et al: Allergic fungal sinusitis. **Clin Otolaryngol 21:**389-392, 1996
11. Larranaga J, Fandino J, Gomez-Bueno J, et al: Aspergillosis of the sphenoid sinus simulating a pituitary tumor. **Neuroradiology 31:**362-363, 1989
12. Lee JH, Park YS, Kim KM, et al: Pituitary aspergillosis mimicking pituitary tumor. **AJR Am J Roentgenol 175:**1570-1572, 2000
13. Liu JK, Schaefer SD, Moscatello AL, et al: Neurosurgical implications of allergic fungal sinusitis. **J Neurosurg 100:**883-890, 2004
14. Manning SC, Holman M: Further evidence for allergic pathophysiology in allergic fungal sinusitis. **Laryngoscope 108:**1485-1496, 1998
15. Manning SC, Mabry RL, Schaefer SD, et al: Evidence of IgE-mediated hypersensitivity in allergic fungal sinusitis. **Laryngoscope 103:**717-721, 1993
16. Manning SC, Merkel M, Kriesel K, et al: Computed tomography and magnetic resonance diagnosis of allergic fungal sinusitis. **Laryngoscope 107:**170-176, 1997
17. McGinnis MR, Campbell G, Gourley WK, et al: Phaeohyphomycosis caused by *Bipolaris spicifera*: An informative case. **Eur J Epidemiol 8:**383-386, 1992
18. Mehta SA, Kaul S, Mehta MS, et al: Phaeohyphomycosis of the paranasal sinuses masquerading as a neoplasm: A case report. **Head Neck 15:**59-61, 1993
19. Parker KM, Nicholson JK, Cezayirli RC, et al: Aspergillosis of the sphenoid sinus: Presentation as a pituitary mass and postoperative gallium-67 imaging. **Surg Neurol 45:**354-358, 1996
20. Phadke R, Saha M, Prasad K, et al: Transnasal access for sampling a skull base lesion. **AJNR Am J Neuroradiol 22:**745-747, 2001
21. Rinaldi MG, Phillips P, Schwartz JG, et al: Human *Curvularia* infections. Report of five cases and review of the literature. **Diagn Microbiol Infect Dis 6:**27-39, 1987
22. Robson JM, Hogan PG, Benn RA, et al: Allergic fungal sinusitis presenting as a paranasal sinus tumour. **Aust N Z J Med 19:**351-353, 1989
23. Roth M: Should oral steroids be the primary treatment for allergic fungal sinusitis? **Ear Nose Throat J 73:**928-930, 1994
24. Schubert MS: Medical treatment of allergic fungal sinusitis. **Ann Allergy Asthma Immunol 85:**90-97, 2000
25. Schubert MS, Goetz DW: Evaluation and treatment of allergic fungal sinusitis. I. Demographics and diagnosis. **J Allergy Clin Immunol 102:**387-394, 1998
26. Sobol SM, Love RG, Stutman HR, et al: Phaeohyphomycosis of the maxilloethmoid sinus caused by *Drechslera spicifera*: A new fungal pathogen. **Laryngoscope 94:**620-627, 1984
27. Tan KT, Ong PL, Poh WT, et al: Aspergillosis of sphenoid sinus presenting as a pituitary tumour. **Singapore Med J 29:**410-412, 1988
28. Washburn RG, Kennedy DW, Begley MG, et al: Chronic fungal sinusitis in apparently normal hosts. **Medicine (Baltimore) 67:**231-247, 1988
29. Waxman JE, Spector JG, Sale SR, et al: Allergic *Aspergillus* sinusitis: Concepts in diagnosis and treatment of a new clinical entity. **Laryngoscope 97:**261-266, 1987
30. Young CN, Swart JG, Ackermann D, et al: Nasal obstruction and bone erosion caused by *Drechslera hawaiiensis*. **J Laryngol Otol 92:**137-143, 1978
31. Zieske LA, Kopke RD, Hamill R: Dematiaceous fungal sinusitis. **Otolaryngol Head Neck Surg 105:**567-577, 1991