

Complications of Allergic Fungal Sinusitis

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ABSTRACT

PURPOSE: Allergic fungal sinusitis is a syndrome of chronic noninvasive fungal sinusitis that results in the accumulation of eosinophil-rich allergic mucin within the paranasal sinuses. This mucin may become an expansile mass leading to complications that have not been well characterized or classified.

METHODS: Inclusion criteria for this study required meeting previously published diagnostic criteria and complications greater than nasal polyps or sinusitis itself. Four patients from our cohort and 30 patients identified in a literature search formed the study group.

RESULTS: The majority of patients had pre-existing asthma or allergic rhinitis, or both, and 37% had nasal polyps before presentation. However, 27% had no previous history of rhinosinusitis or nasal polyposis. Complications of allergic fungal sinusitis fell into discrete categories: ophthalmic (n = 13), sinobronchial allergic mycosis (n = 9), bony erosion (n = 8), cavernous venous thrombosis (n = 3), and otic involvement (n = 1).

CONCLUSION: Visual symptoms, proptosis, headaches, and increased nasal symptoms, especially in association with bony erosions on sinus computed tomography, suggest allergic fungal sinusitis and its complications in patients with chronic rhinosinusitis and nasal polyps. Patients with allergic fungal sinusitis may present with a complication of the disease as the first symptom. Complications may be categorized into groups that facilitate surveillance and early identification.

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KEYWORDS: Allergic fungal sinusitis; Allergic mucin; Cavernous venous thrombosis

Allergic fungal sinusitis is a newly appreciated noninvasive form of chronic rhinosinusitis seen most often in atopic individuals who develop intractable sinusitis and nasal polyposis.^{1,2} The paranasal sinuses become filled with a characteristic eosinophil-rich “allergic mucin” that contains sparse, degenerating fungal elements to which the patients have fungal-specific immunoglobulin E (IgE).³ This mucin obstructs the osteomeatal complex of the sinuses and leads to chronic bacterial sinusitis and other complications. For instance, allergic mucin also may form an expansile mass capable of penetrating the cartilaginous walls of the sinuses

laterally into the orbits and superiorly or posteriorly into the cerebrum.⁴

There have been sporadic reports of complications of allergic fungal sinusitis, but most have been single case reports, and no report has included more than 6 patients. We are not aware of a systematic analysis of these complications or of risk factors for them. The clinical data on our patient cohort with complications of allergic fungal sinusitis and the reports available in the medical literature formed the basis of this study. We conclude that complications of allergic fungal sinusitis fall into at least 4 categories, any of which may present with nonspecific symptoms. Moreover, certain patients with allergic fungal sinusitis seem to be at high risk for serious complications and should be more closely followed to detect and address those early.

MATERIALS AND METHODS

We searched the medical literature in English with multiple search engines, including MEDLINE and PubMed, using

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the MeSH terms: allergic fungal sinusitis, sinobronchial allergic mycosis, and complications of allergic fungal sinusitis; reports in English, and not pediatrics. Diagnostic criteria for allergic fungal sinusitis published in 1995 were used as inclusion criteria for the diagnosis.³ The search included all cases identified in the literature since the publication of those criteria (1994 to 2010). Demographic and clinical information were tabulated for analysis. Complications forming inclusion criteria were adverse consequences of allergic fungal sinusitis other than nasal polyps, chronic rhinosinusitis, and the necessity of multiple sinus surgeries. Numerical results were reported as mean and standard deviation of the mean.

RESULTS

Study Group

Our computer-assisted searches identified 25 patients in 11 reports that met our inclusion criteria. Case histories from these patients were carefully reviewed. In the process of reviewing these 11 articles, we found 3 additional reports that identified 5 additional patients who met inclusion criteria. Similar data were tabulated on 4 patients from our cohort who met inclusion criteria. One of our 4 patients had been reported previously.⁵ The combination of these patients formed a study group of 34 individuals.

Findings in the Patients with Complications of Allergic Fungal Sinusitis Demographics. Patients ranged from 10 years to 69 years of age, with 39% younger than 25 years of age. The average age was 35 years (± 17) (Table 1). The race of study subjects was provided in only 2 patients in the literature search. One patient was of Chinese descent and the second was of Indian descent. Two of our patients are African American and 2 are of Caucasian descent. Thirteen patients were female (38%) and 21 (62%) were male.

Classification by Presenting Complication. Patients were arbitrarily placed in subgroups on the basis of their presenting complication in order to determine if there were particular findings that might be associated with specific complications (Table 1). The most common presenting complications of allergic fungal sinusitis were *ophthalmic* and represented 38% (13 of 34) of the complications.⁶⁻¹¹ Nine patients had both allergic fungal sinusitis and allergic bronchopulmonary mycosis, a syndrome previously termed *sinobronchial allergic mycosis* syndrome.^{5,12-14} One of these patients also had a frontal lobe abscess composed of eosinophils, Charcot Leyden crystals, and fungal elements. Culture grew *Aspergillus* species.¹² Eight patients had *erosion of the sinus walls* on imaging studies.^{15,16} These erosions were more than compression-induced thinning of the

sinus walls commonly seen on computed tomography in patients with allergic fungal sinusitis. To be placed in this category, bowing of the sinus walls caused impingement on vital structures that resulted in clinical symptoms, or rupture of the sinus walls resulted in extrusion of allergic mucin out

of the confines of a sinus.¹⁷ Four of the 8 patients with such erosions had no previous medical diagnosis of rhinosinusitis. Seven of these patients had proptosis on initial examination, of which 2 had no previous history of rhinosinusitis. An additional 8 patients in other groups also had erosions as part of their evaluation. Three patients presented with *cavernous venous thrombosis*, all of whom had visual symptoms.¹⁸⁻²⁰ One of these patients also had associated eosinophilic meningitis. Finally, one of our patients had *tympanic membrane perforation* with aller-

gic mucin in the middle ear, a new finding in allergic fungal sinusitis.

Clinical Features of the Study Group

Presenting Symptoms. Detailed clinical case histories were available on 30 patients. Among all groups, the most common symptoms coexisting with the complication at presentation were headaches and worsening nasal complaints. The majority of patients had preexisting allergic rhinitis and asthma, and many had nasal polyposis before complications of allergic fungal sinusitis (Table 1). Specifically, 18 patients (60%) had preexisting asthma or allergic rhinitis (or both), 11 patients (37%) had a history of nasal polyps, and 3 (8%) had nasal polyposis at presentation. Eight patients (27%) had no previous history of rhinosinusitis when they presented with a complication of allergic fungal sinusitis.

Patients with ophthalmic syndromes or cavernous venous thrombosis had visual symptoms, and 7 patients in the sinobronchial allergic mycosis syndrome group had proptosis at presentation. Thus, ophthalmic findings, including proptosis, decreased visual acuity, blurry vision, and diplopia, were the most common findings in the study group as a whole. New-onset nasal polyposis or a recurrence of nasal polyposis also was common among the groups.

Comparisons among patient subgroups are difficult because of the small number of patients reported to date (Table 1). The mean age of the patients in the bony erosion (28 ± 15) and ophthalmic involvement groups (26 ± 17) were younger than the cavernous sinus thrombosis (55 ± 10) and the sinobronchial allergic mycosis syndrome groups (41 ± 13) (Table 1). Some data on IgE levels and eosinophil counts were available (Table 2). The mean IgE for patients with the sinobronchial allergic mycosis syndrome was $4176 (\pm 2544 \text{ SD})$ ($n = 9$ patients), compared with a mean of $815 (\pm 637 \text{ SD})$ ($n = 4$ patients) for the

CLINICAL SIGNIFICANCE

- The possibility of allergic fungal sinusitis should be considered in patients with intractable chronic sinusitis.
- Allergic fungal sinusitis may present with severe complications.
- Complications of allergic fungal sinusitis include visual changes, cavernous venous thrombosis, and expansion of allergic mucin into the brain.

Table 1 Demographics and Clinical Features of Patients with Complications of Allergic Fungal Sinusitis

Complication Category	Pt #	Age (yrs)/Sex	Presentation	History	Ref
Ophthalmic	1	35/M	4 m of neck pain and stiffness, altered mental status, fever, loss of vision, proptosis	Allergic rhinitis on allergen immunotherapy for 2-3 y before presentation	This report
	2	69/M	Recurrent nasal polyposis, right sided lacrimal duct obstruction	3 previous polypectomies, 1 FESS, asthma	6
	3	18/M	5 m of nasal congestion, frontal HA, proptosis, nasal polyps	No past history of rhinosinusitis	7
	4	18/M	Frontal sinus tenderness, periorbital pain, nasal polyps, proptosis	Allergic rhinitis, multiple polypectomies	7
	5-8	21-29/2 M; 2 F	All 4 had papilledema, unilateral nasal obstruction, unilateral visual loss	None given	8
	9	30/F	15 m of nasal discharge and obstruction, 3 m of decreased vision, numbness over lip	No past history of rhinosinusitis	9
	10	23/M	2 w of eye pain, blurry vision, diplopia, nasal obstruction, nasal discharge, and proptosis	Allergic rhinitis, sinusitis 1 m prior that never resolved	10
	11	13/M	2 m of left-sided proptosis	Asthma, sinusitis	11
	12	21/M	Left-sided proptosis, CT revealed sinus opacification, encroachment on the medial left orbit	Asthma	11
	13	10/M	Several m of HA and nasal obstruction, right sided proptosis, CT demonstrated sinus opacification with encroachment on right orbit	Allergic rhinitis, sinusitis	11
	Mean $\pm$ SD	26 $\pm$ 17			
SAM Syndrome	1	17/M	Chronic sinusitis, nasal obstruction, intermittent purulent discharge, nasal polyps	Asthma, allergic rhinitis on allergen immunotherapy 1 y	5
	2	32/M	Grand mal seizure, exophthalmus, HA (1 w), worsening nasal congestion (6 m)	Asthma, chronic nasal obstruction	12
	3	57/M	Nasal congestion, wheezing, productive cough	Asthma, chronic sinusitis, bronchiectasis, multiple polypectomies, 1 FESS	13
	4-9	36/M 41/M 58/F 38/F 47/F 45/F	All reported to present with purulent nasal discharge, cough and expectoration of sputum	Nasal polyps, asthma	14
	Mean $\pm$ SD	41 $\pm$ 13			
Cavernous sinus thrombosis	1	49/M	9 d of HA, nausea and vomiting, blurry vision, diplopia on lateral gaze, proptosis	Chronic rhinosinusitis, hypertension	18
	2	68/F	2 w of ophthalmoplegia, bilateral purulent rhinorrhea, visual impairment, fever	No past history of rhinosinusitis	19
	3	49/F	2 w of diplopia, HA, abducens nerve palsy	No past history of rhinosinusitis	20
	Mean $\pm$ SD	55 $\pm$ 10			

Table 1 Continued

Complication Category	Pt #	Age (yrs)/Sex	Presentation	History	Ref
Bony erosion	1	17/F	5 y of progressive bilateral nasal congestion, HA, anosmia, nasal polyps found on initial examination	No past history of rhinosinusitis	This report
	2	34/F	7 y of nasal obstruction, rhinorrhea, frontal HA	1 prior polypectomy, 1 FESS	15
	3	59/M	Sensorineural hearing loss, nasal obstruction	No past history of rhinosinusitis	15
	4	37/M	5 y of nasal obstruction, rhinorrhea, facial pain, HA, aspirin intolerance	1 prior polypectomy	15
	5	21/F	2 w of diplopia, HA	Allergic rhinitis	15
	6	20/M	Nasal polyps protruding from both nostrils	1 prior polypectomy	15
	7	13/M	HA, hyposmia, nasal obstruction, massive polyposis	No past history of rhinosinusitis	15
	8	26/M	11 m forehead mass, nasal obstruction, polyps	No past history of rhinosinusitis	16
Mean ± SD	28 ± 15				
Otic	1	56/F	Otitis media, tympanic membrane perforation with drainage of allergic mucin, conductive hearing loss	AFS, asthma, atrophic rhinitis, eczema, chronic nasal polyposis, 1 prior FESS	This report

Abbreviations: AFS = allergic fungal sinusitis; CT = computed tomography; d = day; F = female; FESS= functional endoscopic sinus surgery; HA = headache; M = male; m = month; Pt # = patient number; Ref = reference; SAM = sinobronchial allergic mycosis; SD = standard deviation; w = week; y = year.

ophthalmic group. The mean eosinophil count for the bony erosion group was 580 (± 437 SD) (n = 7 patients), compared with a mean of 3741 (± 4189 SD) (n = 9 patients) in the sinobronchial allergic mycosis syndrome group.

Fungi Identified on Culture

Twenty-two of 34 patients had a specific fungus cultured from the sinus (Table 2). Several reports also noted that fungal elements were present in allergic mucin. Eleven patients grew *Aspergillus* species (7 *Aspergillus fumigates*, 3 *Aspergillus flavus*), with an additional report of *Aspergillus* on the basis of visual identification. Sinus cultures grew *Curvularia* species from 5 patients and *Bipolaris* species from 5. Of the 4 culture results available from patients with sinobronchial allergic mycosis syndrome, all 4 of these grew *Aspergillus fumigatus*.

Reports of allergy skin tests for fungi were available in 15 patients (Table 2). Patients usually had IgE specific for multiple fungi, and among these individuals, 6 had IgE to other allergens, most commonly grass, weed, and dust mite.

Findings on Imaging

Patients had a variety of imaging procedures that demonstrated evidence of allergic mucin and polyps within the sinuses and extension of allergic mucin out of the sinuses into contiguous spaces. There were detailed descriptions of sinus imaging available in all reports, and most provided images. There were common findings among the groups. Increased intrasinus attenuation on non-contrast-enhanced computed tomography, a common finding in this syndrome, was usually present.²¹

In the group of patients with ophthalmic complications, computed tomography demonstrated complete opacification of at least one sinus, and in the majority of cases, multiple sinuses. The sinus computed tomography on our patient revealed expansion of allergic mucin into a sphenoid sinus and left ethmoid sinus, with erosion into the cavernous sinus and the left orbital apex (Figure 1).

Radiologic evidence of bony erosion was common (Table 3). Six patients with bony erosions as the only complication of allergic fungal sinusitis were described in a single report.¹⁵ Bony erosions also were seen in combination with other complications in some patients (Figure 1).

The sinus computed tomography in patients with sinobronchial allergic mycosis syndrome revealed findings characteristic of allergic fungal sinusitis, including pansinusitis, opacification, and hyperattenuation of the heterogeneous material by microcalcifications within the sinuses.²¹ Bony erosion was present in 3 of the 8 patients reported with sinobronchial allergic mycosis syndrome (Table 3).^{12,14} Chest computed tomography demonstrated central bronchiectasis in 7 patients or fixed or transient pulmonary infiltrates.¹²⁻¹⁴ The sinus and chest images from our previously reported patient with sinobronchial allergic mycosis syndrome demonstrated the range of complications resulting from the accumulation of allergic mucin in the airways and

Table 2 Laboratory Findings in Patients with Complications of AFS

Complication Category	Pt #	Total Eos (mean ± SD)	Total IgE (mean ± SD)	Fungus to which IgE was demonstrated by allergy skin test or RAST and results of culture of sinus content if performed	Ref
Ophthalmic	1	286-570	248-671	IgE: <i>Alternaria</i> , <i>Epicoccum</i> , <i>Helminthosporium</i> , <i>Aspergillus</i> , <i>Curvularia</i> ; culture: <i>Bipolaris spicifera</i>	This report
	2	na	na	IgE: na; culture: none	6
	3	↑	364*	IgE: <i>Helminthosporium</i> , <i>Alternaria</i> ; culture: <i>Curvularia spicifera</i>	7
	4	↑	1720*	IgE: <i>Helminthosporium</i> , <i>Alternaria</i> , <i>Aspergillus</i> , <i>Hormodendrum</i> ; culture: <i>A. flavus</i>	7
	5-8	na	↑	IgE: na; culture: <i>A. flavus</i>	8
	9	na	na	IgE: <i>A. fumigates</i> ; culture: <i>A. fumigates</i>	9
	10	na	726-2000*	IgE: <i>A. fumigatus</i> , <i>A. niger</i> , <i>Bipolaris</i> , <i>Fusarium</i> , <i>Helminthosporium</i> , <i>Alternaria</i> ; culture: Fungal elements	10
	11	na	na	IgE: na; culture: <i>A. flavus</i>	11
	12	na	na	IgE: na; culture: <i>Curvularia spicifera</i>	11
	13	na	na	IgE: na; culture: <i>Bipolaris spicifera</i>	11
	Mean ± SD	390 ± 106	815 ± 637		
	SAM syndrome	434-16,000	1920-8154*	IgE: <i>Alternaria</i> , <i>Deschleria</i> , <i>Curvularia</i> , <i>Aspergillus</i> , <i>Stemphylium</i> , <i>Cladosporium</i> ; culture: <i>A. fumigatus</i> , sinus and lung	5
	2	120	6048*	IgE: <i>A. fumigates</i> ; culture: <i>A. fumigatus</i> , sinus and lung	12
Bony erosion	3	67	1987*	IgE: na; culture: na	13
	4	408	1250	IgE: <i>A. fumigates</i> ; culture: na	14
	5	230	8306	IgE: <i>A. fumigates</i> ; culture: na	14
	6	627	127	IgE: <i>A. fumigates</i> ; culture: <i>A. fumigates</i>	14
	7	1035	3003	IgE: <i>A. fumigates</i> ; culture: <i>A. fumigates</i>	14
	8	2220	2359	IgE: <i>A. fumigates</i> ; culture: nd	14
	9	149	1928	IgE: <i>A. fumigates</i> ; culture: nd	14
	Mean ± SD	3741 ± 4189	4176 ± 2544		
	1	126-1380	65-255	IgE: <i>Alternaria</i> , <i>Penicillium</i> , <i>Curvularia</i> , <i>Epicoccum</i> , <i>Stemphylium</i> , <i>Fusarium</i> ; culture: <i>Curvularia lunata</i>	This report
	2	864	na	IgE: na; culture: <i>Exserohilum rostratum</i> , <i>Bipolaris spicifera</i>	15
	3	890	na	IgE: na; culture: <i>Bipolaris spicifera</i>	15
	4	670	na	IgE: na; culture: Fungal hyphae	15
	5	485	na	IgE: na; culture: <i>Bipolaris spicifera</i>	15
	6	644	na	IgE: na; culture: Fungal hyphae	15
	7	603	na	IgE: na; culture: <i>Curvularia spicifera</i>	15
	8	na	na	IgE: na; culture: <i>Curvularia lunata</i>	16
	Mean ± SD	580 ± 437	167 ± 59		
CST	1	na	na	IgE: na; culture: <i>A. fumigatus</i> , staph	18
	2	na	na	IgE: na; culture: <i>A. fumigates</i>	19
	3	78	Nml	IgE: na;† culture: <i>Aspergillus</i> hyphae	20
Otic		296-731	71-192	IgE: <i>Curvularia</i> , <i>Penicillium</i> , <i>Dreschleria</i> ; culture: Fungal elements	This report
Mean ± SD		505 ± 180	127 ± 45		

Abbreviations: A. = *Aspergillus*; AFS = allergic fungal sinusitis; CST = cavernous sinus thrombosis; Eos = eosinophils; IgE = immunoglobulin E; na = not available; nd = not done; Pt # = patient number; RAST = radioallergosorbent test; Ref = reference; SAM = sinobronchial allergic mycosis; SD = standard deviation.

↑ = increased but no exact number given.

*Also had positive precipitins to fungus.

†Stated IgE strong positive to *Aspergillus fumigatus*.

sinuses of these individuals.⁵ There was central sacular bronchiectasis, a distinctive finding in patients with allergic bronchopulmonary mycosis, on the chest computed tomography (Figure 2).

All 3 patients with cavernous sinus thrombosis had multiple imaging procedures.^{18,19} No bony erosion was described. Nonenhancement of the cavernous sinus on con-

trasted studies suggested cavernous sinus thrombosis that was confirmed with magnetic resonance imaging or angiography. Dural enhancement adjacent to the left sphenoid sinus and proximal left tentorium, as well as a slight hypodensity within the left cavernous sinus, also was seen in one patient.¹⁹ Magnetic resonance imaging in the one patient showed thrombosis of the right transverse cavernous



Figure 1 Sinus computed tomography of our patient in the ophthalmic complications group after removal and debridement of a destructive mass of allergic mucin originating from the sphenoid sinus and the left ethmoid sinus with erosion into the cavernous sinus and the left orbital apex. There has been left globe exorbitation (white arrow), resection of the left frontal sinus, left lamina papyracea, and left middle turbinate along with bilateral maxillary antrectomies. Mucosal thickening of the maxillary sinuses remains (2 small black arrows) as does extensive opacification of the right ethmoid air cells with presence of hyperdense material (black arrow with white point). There is also mucosal thickening of the sphenoid sinuses with opacification of the right frontal sinus.

sinus and the sigmoid venous sinuses associated with bilateral sphenoid and ethmoid sinusitis.²⁰

Treatment

Before the diagnosis of their allergic fungal sinusitis complications, only 7 of the 34 patients (21%) in this cohort had sinus surgery, including polypectomies. After diagnosis, 27 were treated with oral corticosteroids, most were treated with intranasal corticosteroids, and 13 were treated with oral or intravenous antifungal antibiotics. Five of the patients were started on allergen immunotherapy to fungal allergens.

The patient with otic involvement was treated with a left tympanoplasty and mastoidectomy, oral prednisone and montelukast, and nasal irrigations with budesonide. Patients with cavernous sinus thrombosis most often were treated with intravenous heparin and intravenous vancomycin. Two of these patients also received treatment with antifungal antibiotics.

All patients required sinus surgery to remove mucin and promote drainage subsequent to their complication, and 9 required additional later sinus surgeries (Table 4). Three received corticosteroids postoperatively. One patient was treated with itraconazole for 2 months. All patients with sinobronchial allergic mycosis syndrome were treated with oral corticosteroids, and 7 of the 9 also

were treated with antifungal agents including amphotericin B, itraconazole, or voriconazole. All 13 patients with ophthalmologic complications were treated with corticosteroids, 5 were treated with antibiotics, and 3 were treated with itraconazole.

Outcomes

None of the patients in this series succumbed to their complications. The longest follow-up of any patient was 15 years.¹⁴ The follow-up of the 4 patients from our clinic ranged from 4 to 10 years. All are living and have had no further complications after removal of polyps and allergic mucin and surgical clearance of the osteomeatal complex. All receive frequent surveillance rhinoscopy. We also use a regimen of fungal allergen immunotherapy, nasal washes with topical nasal steroids, montelukast, and rare corticosteroid bursts for exacerbations of nasal polyposis. Many of our patients with allergic fungal sinusitis have developed atrophic rhinosinusitis, a complication of allergic fungal sinusitis not traditionally included in reports of this disease.²²

CONCLUSIONS

Allergic fungal sinusitis is an allergic disease caused by fungal-specific, IgE-driven, eosinophilic inflammation within the sinuses.²³ The release of cytokines associated with allergic inflammation from the inflammatory cells participating in this process is a reasonable explanation for a hypersecretory state that produces eosinophil-rich allergic mucin, a putty-like material with the ability to obstruct the osteomeatal complex of the paranasal sinuses.^{24,25} This obstruction establishes a milieu for chronic bacterial sinusitis, inflammatory nasal polyposis, and the creation of an expansile mass in the paranasal sinuses. This mucoid mass has the potential to compromise the thin cartilaginous walls of the sinuses and expand into structures within the calvarium. A similar process occurs within the bronchi in allergic bronchopulmonary mycosis. However, decompression of mucus impaction through the bronchi appears to protect vital structures in the chest.^{26,27}

We anticipate that our arbitrary classification of patients into groups on the basis of presenting complications will increase the awareness of these consequences and form the basis for treatment trials in the future. Ophthalmic findings and bony erosion on imaging, headaches, worsening nasal complaints, and visual symptoms were pervasive among all groups. Moreover, regardless of the category, all complications had the potential for serious outcomes. These included destruction of the middle ear, cerebrovascular accidents, intracranial invasion, loss of vision, diplopia, and ophthalmoplegia.

Estimates of the prevalence of bony erosion in allergic fungal sinusitis vary from 20% to 90%.¹⁷⁻²⁸ Bony erosion seems to occur most commonly from the ethmoid sinus into the orbit.¹⁷ Inspissated allergic mucin with or with-

Table 3 Anatomic Locations of Bony Erosions and Associated Complications in Allergic Fungal Sinusitis

Location of Erosion	Complications	Ref
Posteriorly out frontal sinus into cranial area	Extension into the brain requiring anterior craniotomy with insertion of metal plate	This report
Medial walls of both maxillary sinuses, lamina papyracea, lateral walls and roof of the clivus and sphenoid and posterior ethmoid roof	Headache, obstruction, polyps	15
Anterior cranial fossa, lateral wall and roof of sphenoid, and clivus	Dura resection which was patched with fascia lata	15
Posterior table of frontal sinus and lamina papyracea	Headache, facial pain	15
Sphenoid bone	Right 6 th cranial nerve palsy	15
Orbital and cribriform plate erosion and marked expansion of left frontal sinus posteriorly	Polyps	15
Left cribriform plate and left orbit	Hyposmia, headache, nasal obstruction	15
Right side of frontal sinus displacing frontal lobe posteriorly	Forehead mass, bicoronal flap, temporoparietal fascial flap with flexible titanium mesh	16
Walls of right sphenoid and left ethmoid sinus and adjacent sella, apex.	Orbital exenteration, subdural empyema	This report
Medial orbit	Lacrimal sac involvement	6
Right orbital roof	Proptosis, headache, nasal congestion	7
Left orbital roof and lamina papyracea	Frontal sinus tenderness, periorbital edema, left proptosis	7
Lateral sphenoid wall in region of optic nerve	Vision loss from compression of optic nerve and papilledema	8
Sphenoid wall	Decreased vision in left eye	9
Right frontal sinus into right orbit	Proptosis, headache, blurry vision and eye pain	10
Left orbit	Vision loss and papilledema	11
Encroachment of medial left orbit	Left proptosis	11
Right orbit	Left proptosis	11
Ethmoidal septa and right lamina papyracea	Right proptosis	12
Unlisted location of bony erosion in 2 patients	Sinobronchial allergic mycosis (SAM) syndrome	14

out polyps enlarges the sinus cavity as the bone is remodeled in response to the pressure of the expanding disease process. This causes thinning (pseudoerosion),

bulging, or actual destruction of the sinus wall (erosion).⁴ Globe displacement in proptosis reflects expansion of allergic mucin from the paranasal sinuses into the affected orbit through the poorly calcified sinus walls that compose the bony margins of the orbits.¹⁰ Diplopia is thought to occur from a sixth cranial nerve palsy caused by compression of the nerve from the expansion of the allergic mucin.¹⁰

Our patient with tympanic membrane rupture from allergic fungal sinusitis, not previously reported, to our knowledge, had allergic mucin confirmed by histopathologic staining removed from the middle ear. There are 2 possible mechanisms that could have caused mucin to appear in the middle ear. First, retrograde flow of purulent material through the eustachian tube occurs in infants, as the eustachian tube in younger children is shorter and more horizontal. This appears less likely in adults. More likely, the allergic mucin was produced primarily in the middle ear, functioning as a sinus. The middle ear has mucus-producing epithelium containing cilia that extend beyond it into the mastoid bone. This combination of ciliated epithelium and mucus-secreting elements makes the middle ear lining true mucosa similar to respiratory mucosa.²⁹ Fungal DNA is

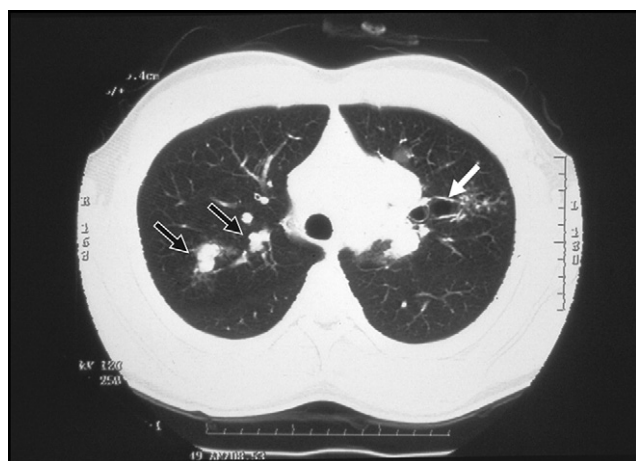


Figure 2 Chest computed tomography of the patient from our cohort with sinobronchial allergic mycosis (SAM) syndrome showing central bronchiectasis of a segmental bronchi on the left (white arrow) and 2 pulmonary nodules on the right (black arrows).

Table 4 Treatments in Addition to Functional Endoscopic Sinus Surgery and Outcomes

Complication Category	Pt #	Treatment	Outcome	Ref
Ophthalmic	1	Left orbital radical exenteration, craniotomy w/ removal of subdural empyema, oral prednisone, NCS, budesonide irrigation, montelukast, Abx	Lost to follow-up for 5 y when he presented with acute rhinosinusitis and nasal polyps requiring surgery	This report
	2	Dacrocystorhinostomy, lacrimal stent, oral prednisone, NCS, irrigations, nasal itraconazole	No recurrence at 2 y	6
	3	Oral prednisone, NCS, amoxicillin/clavulanate	Asymptomatic at 1 y and 3 y	7
	4	Oral prednisone, NCS, irrigation, amoxicillin/clavulanate	Asymptomatic at 3 y	7
	5-8	Oral prednisone, NCS, IV steroids, amphotericin B, itraconazole	Post-op vision recovered in 3 pts; partially in 1; all pts free of recurrence at 10 m	8
	9	Amphotericin B, itraconazole, oral prednisone	Slow improvement in vision, sphenoid clear on endoscopy (unknown time frame)	9
	10	Itraconazole, IV steroid, NCS, amoxicillin/clavulanate	Asymptomatic at 3 m, when steroids were ↓, pt had ↑ in HA, congestion, ↑ IgE, was restarted on prednisone then lost to follow-up	10
	11	Oral prednisone, NCS	Asymptomatic at 21 m	11
	12	Oral prednisone for 3 w, NCS	Asymptomatic at 36 m	11
	13	Oral prednisone for 3 w, NCS, Abx	Asymptomatic at 12 m	11
SAM Syndrome	1	Oral prednisone, NCS, lavage, budesonide rinse, montelukast, ICS/LABA, SABA, 6 m itraconazole	Recurrence of AFS at 1 y, nasal polyps treated w/ oral prednisone at 2 y, nasal polyps at 3 y, recurrence of AFS w/ polyps requiring surgery at 6 y	5
	2	Oral prednisone, NCS, nasal cromolyn, SABA, amphotericin B, drain purulent mucocele from frontal & ethmoid sinus, decompression, excision of frontal lobe abscess	Asymptomatic at 1 y	12
	3	Oral prednisone 20 mg (flare <15 mg), 2 m itraconazole, 2 m voriconazole, SABA, ICS/LABA, chest PT, Abx	After tx w/ voriconazole and 2.5 mg oral prednisone, asymptomatic at 20 m and 2 y	13
	4-9	Oral prednisone taper over 3 m to 2 y, 4 pts received oral antifungals	15 y follow-up all cases; resolution in 3 cases; clinical improvement in 1 case; failure in 2	14
Bony Erosion	1	Anterior craniotomy, insertion of metal plate, removed floor of ethmoid sinus w/ uncinectomy, NCS, montelukast, irrigations, oral prednisone	Nasal polyps treated w/ oral prednisone at 2 y	This report
	2	Oral prednisone after requiring revision surgery	Required revision surgery after initial improvement, nasal polypectomy at 1 and 3 y, nasal polyps but w/o neurological changes at 7 y	15
	3	Dura resection then patched with fascia lata	Asymptomatic at 3 y	15
	4	Bicoronal osteoplastic flap approach to frontal sinus	Asymptomatic at 3.5 y	15
	5	NCS	6 th nerve palsy improved within 24 h, asymptomatic at 1 w	15
	6	NCS	Asymptomatic at 3 m	15
	7	NCS, oral prednisone	Recurrence of polyps (time frame unknown)	15
	8	Bicoronal flap, lateral rhinotomy, temporo-parietal fascial flap, flexible titanium mesh, 2 m itraconazole	Asymptomatic at 2 y	16
CST	1	IV heparin, IV Vancomycin, IV voriconazole, Coumadin amoxicillin/clavulanate	HA at 3 m, complete resolution in 6 m	18

Table 4 Continued

Complication Category	Pt #	Treatment	Outcome	Ref
Otic	2	IV heparin, IV Abx	Recovery of exophthalmos within 48 h, clear CT in 1 m, asymptomatic at 2 y	19
	3	IV Abx, oral metronidazole, oral prednisone, itraconazole, antihistamine	Recovered ability to abduct eye within 6 m	20
	1	Oral prednisone, montelukast, budesonide rinses, ICS/LABA, SABA, repair TM, tympanoplasty, mastoidectomy	Asymptomatic at 2 y, nasal polyps requiring polypectomy at 5 y	This report

Abbreviations: Abx = antibiotics; AFS = allergic fungal sinusitis; CT = computed tomography; h = hour; HA = headache; ICS = inhaled corticosteroid; IV = intravenous; LABA = long acting beta-agonist; m = month; mg = milligram; NCS = nasal corticosteroid; PT = physical therapy; Pt # = patient number; pts = patients; post-op = post operatively; Ref = Reference; SABA = short acting beta-agonist; SAM = sinobronchial allergic mycosis; TM = tympanic membrane; tx = treatment; w = week; w/ = with; y = year.

↑ = increased.

↓ = decreased.

present in 34% of middle ear effusion samples, a prevalence similar to the paranasal sinuses.³⁰

Most patients who presented with complications of allergic fungal sinusitis had not had previous sinus surgery or polypectomies to decompress their sinuses and had relatively low-grade symptoms before the onset of their complication. This suggests that allergic inflammation was robust in these patients, leading to a shorter course that precluded early diagnosis and treatment. Whether or not high total serum IgE levels and marked eosinophilia may be a useful risk factor for prediction of complications of allergic fungal sinusitis is unclear but has potential importance.

There is no consensus on the appropriate treatment of allergic fungal sinusitis. Our experience, and that of others, suggests that with removal of fungal debris, establishment of sinus aeration and intranasal corticosteroid treatment are the place to start.³¹ However, with this approach, the disease reactivates in the majority of patients and often is associated with ongoing symptoms and the need for further sinus surgeries. Our own treatment approach includes daily nasal lavage with saline and topical corticosteroids, and allergen immunotherapy to fungi to which the patient has specific IgE. Our experiences and that of others suggest that allergen immunotherapy to fungi may be helpful in decreasing allergic inflammation and recurrence of disease.³²

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