

Allergic Fungal Sinusitis

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ABSTRACT

*Fungal sinusitis can present as one of four distinct clinico-pathologic entities: 1) fulminant or acute; and three types of chronic, 2) indolent, 3) mycetoma, and 4) allergic fungal sinusitis (AFS). The first three forms differ both clinically and pathologically from AFS. The first reported cases of AFS were associated with the fungus *Aspergillus*, but recently other fungal organisms have been implicated. Five different fungal organisms have been found to cause AFS in 14 patients. The prevalence of AFS among patients with chronic sinusitis may be as high as 7%. The diagnosis is made on the histologic findings of inspissated allergic mucin containing 1) numerous eosinophils, 2) scattered noninvasive fungal hyphae, and 3) Charcot-Leyden crystals. In addition, AFS patients have a characteristic clinical and immunologic profile. The clinical presentation, diagnosis, and management of AFS are discussed. Uniformity of the classification of fungal sinusitis is proposed.*

In the past decade, reports of sinusitis caused by fungal organisms have become commonplace in the literature. Cases of fulminant sinusitis in the immunocompromised host have been reported with increased frequency. *Mucor* mycosis in patients with diabetes and invasive *Aspergillus* in leukemic patients are well

known examples, although other fungal organisms have caused the same fulminant disease. A second type of fungal sinusitis, indolent or chronic invasive, has also been reported with increasing frequency in the literature. The fungus ball or mycetoma is another form that is well known and is analogous to the bronchopulmonary mycetoma.

A fourth presentation of fungal sinusitis is allergic fungal sinusitis (AFS). In 1981, Millar et al.¹ first suggested a relationship between "allergic aspergillosis of the paranasal sinuses" and allergic bronchopulmonary aspergillosis (ABPA). This entity was fully described by Katzenstein et al.^{2,3} in 1983 when they proposed the diagnosis of allergic *Aspergillus* sinusitis. Upon retrospective review of the surgical specimens of patients operated on for chronic sinusitis they found a number to contain thick, green inspissated mucus. The diagnosis of AFS was made in 7 of 113 patients based upon the finding of allergic mucin containing a histologic triad, namely: 1) numerous eosinophils, 2) noninvasive fungal hyphae, and 3) Charcot-Leyden crystals. These cases were all felt to be caused by *Aspergillus* species although the organisms were not identified by culture.

In 1987, Waxman et al.⁴, further described the clinical picture reporting eight additional patients with AFS felt to be caused by *Aspergillus*. As Millar et al. predicted, AFS seems to be analogous to the pulmonary disease ABPA. The thick, inspissated mucus found in the sinus of the AFS patient is almost identical grossly and histologically to the bronchial plugs seen in ABPA. It is felt that these two diseases have an allergic basis and are found to occur most often in young, immunocompetent, atopic hosts. Since first described, several other fungal organisms have been reported to cause both the pulmonary disease and AFS.⁵⁻¹⁰

This article describes 14 patients in whom AFS caused by five different fungal organisms was diagnosed. Evidence suggests that AFS is more common

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than generally appreciated and that the diagnosis is often overlooked. It is the purpose of this article to increase awareness of this entity and discuss the arguments for it being a distinct and separate sinus disease. The classification of fungal sinusitis is clarified.

METHODS

The Departments of Otolaryngology and Allergy/Immunology are caring jointly for a significant number of patients with the diagnosis of chronic sinusitis. In patients with a suspicious clinical history, initial screening tests include immediate cutaneous reactivity to multiple aeroallergens including molds, total peripheral eosinophil count, and total serum IgE level. Immune competence is determined by history and anergy panel. In five patients we additionally obtained total serum immunoglobulins, IgG subclasses, pre- and postantibody titer to polio and tetanus, isohemoagglutinins, complete blood count with differential, and CH50.

Patients who demonstrated evidence on the computed tomographic (CT) scan of chronic unremitting disease were treated either with conventional sinus procedures or functional endoscopic sinus surgery. Operative specimens were sent for fungal cultures and special stains to identify fungi and allergic mucin. Patients with cultures positive for fungus subsequently were tested for the presence of serum precipitins and specific IgG and IgE antibodies to the offending fungal organisms when these tests were available. The diagnosis of AFS was based upon the histologic presence of the typical allergic mucin containing 1) aggregates of necrotic eosinophils, 2) scattered fungal hyphae with absence of invasion, and 3) Charcot-Leyden crystals.

Pathologic specimens of sinus contents from patients operated on for chronic sinusitis for the preceding 5 years were examined, recut, and restained, looking specifically for allergic mucin and fungal hyphae. This consisted of a total of 205 cases. Allergic mucin could be identified with standard hematoxylin and eosin (H&E) stain, while Gomori's methenamine silver (GMS) stain demonstrated the presence of hyphae. Charcot-Leyden crystals were demonstrated both with H&E and Brown and Brenn stains. As in the prospective cases, a meticulous search was made of the patients with positive results for allergic mucin to rule out fungal invasion into tissue or bone. Some of these patients were not available for long-term follow-up and extensive immunologic testing.

Finally, the *Bipolaris spicifera*-specific IgG and IgE levels of five patients with culture proven *B. spicifera* AFS were compared with the levels of two control (non-AFS) groups. The first group had positive cutaneous reactivity to *B. spicifera*, but no evidence of sinusitis by history or plain radiographs. The second group also had positive cutaneous reactivity to *B. spicifera*, but these

patients had chronic sinusitis that was subsequently documented by surgery as being non-AFS.

PATIENT REPORTS

Four cases are presented that exemplify the clinical presentation of the patient with AFS.

Case 1 (Patient 1, Table I)

A 35-year-old white woman had a 6-year history of nasal congestion, rhinorrhea, and chronic sinusitis. Her symptoms noticeably worsened during a recent pregnancy. Of interest is her past exposure to scuba diving in the Phillipines, which was immediately followed by the initial onset of symptoms. At presentation she was noted to have unilateral right nasal polyposis. A CT scan demonstrated soft tissue filling the right maxillary and ethmoid sinuses with destruction of the medial wall of the maxillary sinus (Fig. 1). Interestingly, the soft tissue exhibited a speckled hyperattenuation. On December 30, 1988, the patient underwent bilateral functional endoscopic sinus surgery and a right Caldwell-Luc procedure. On the right side thick, green, peanut butter-like mucin was encountered while on the left side only minimal polypoid disease was seen. Histologically, there was no evidence of tissue invasion and fungal cultures grew *Bipolaris australiensis*.

She was not treated with antifungal agents and 6 months later developed recurrence of her symptoms. CT scan showed recurrence of disease on the right side. She was then treated with systemic corticosteroids, the

TABLE I

Clinical Features*					
Case No.	Age/Sex	Asthma	Polyposis	Atopy	No. of Procedures
1	35/F	—	+	+	1
2	16/F	+	+	+	2
3	23/F	+	+	+	3
4	45/F	—	+	+	2
5	19/M	—	+	+	2
6	58/F	—	+	+	3
7	14/M	+	+	+	1
8	50/M	+	+	+	3
9	35/M	—	+	+	5
10	11/F	?	+	+	1
11	19/F	+	+	?	1
12	26/M	—	+	+	4
13	30/M	—	+	?	1
14	58/M	—	+	?	1

* 10–14 unavailable for follow-up.

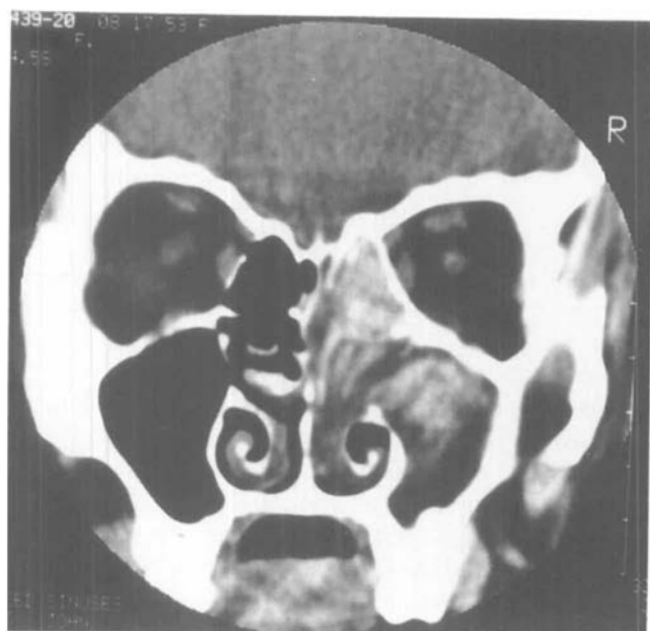


Figure 1. Coronal CT scan of patient 1 revealing opacification of the right maxillary and ethmoid sinuses. Note the hyperattenuation and the erosion of the medial wall of the maxillary sinus (window of 350).

dosage of which was tapered over 3 months with resolution of her symptoms and CT findings.

Case 2 (Patient 2, Table I)

A 16-year-old white woman from southern Texas had a history of frontal headaches and environmental allergies. She had received immunotherapy from 1976 to 1980 and had extrinsic asthma which currently required no medical therapy. She now complained of worsening symptoms and increased nasal obstruction during the preceding 12 months. Six months before admission she was noted to have laterally displaced medial canthi, epiphora, and nasal polyposis and was treated with intranasal steroids. A CT scan demonstrated that all sinuses were filled with a soft tissue which exhibited increased attenuation. There was bowing of the lamina papyracea and obliteration of the nasolacrimal duct. There was also destruction of the medial wall of the maxillary sinus (Fig. 2).

On July 20, 1987, she underwent right external ethmoidectomy, sphenoidotomy, and a Caldwell-Luc procedure. The sinuses were filled with polyps and a thick, green, peanut-butter-like material. Fungus cultures grew *B. spicifera* (Fig. 3). Five weeks later she underwent a left external ethmoidectomy and a Caldwell-Luc procedure with similar intraoperative findings. Postoperatively, she was not treated with antifungal agents because there was no histologic evidence of invasion.

She did well for 1 year at which point her symptoms recurred. A CT scan demonstrated recurrent soft tissue



Figure 2. Coronal CT scan of patient 2 demonstrating complete opacification of maxillary and ethmoid sinuses. The hyperattenuation is 100–125 Hounsfield units.



Figure 3. *Bipolaris spicifera* identified by characteristic geniculate conidiophores with attached conidia grown on Sabouraud glucose agar.

in all the sinuses and transnasal cultures of inspissated mucus again grew *B. spicifera*. She was treated with oral prednisone and over 3 months her symptoms and her CT findings markedly improved.

Case 3 (Patient 5, Table I)

A 20-year-old white man raised in southern Texas had a long history of allergic rhinitis, headaches, and chronic sinusitis. There was no history of asthma, immunotherapy, or intranasal steroids. One week before elective surgery for polyposis he had a subperiosteal abscess secondary to a bacterial frontal sinusitis. On November 21, 1986, he was treated with a trephination

and drainage of the abscess followed by intravenous cefoperazone. Cultures grew *Staphylococcus epidermidis* and *B. spicifera*. CT scan after initial therapy showed that all sinuses were filled with soft tissue that again demonstrated hyperattenuation. There was also the suggestion of erosion of the right lamina papyracea and the right posterior maxillary wall (Fig. 4).

On December 18, 1986, he underwent frontal sinus obliteration, right transfrontal partial ethmoidectomy, and left external sphenoethmoidectomy. One month later he underwent right external ethmoidectomy and bilateral Caldwell-Luc procedures. The sinuses were filled with thick, green, tenacious material and polyps. Cultures again grew *B. spicifera* as well as *Pseudomonas aeruginosa*, *Streptococcus viridans*, and *Haemophilus parainfluenzae*. There was no evidence of tissue invasion by the fungus, so antifungal therapy was withheld. The patient has done well and has not had a recurrence after 24 months of follow-up.

Case 4 (Patient 12, Table I)

A 26-year-old white man had a history of refractory pansinusitis, allergic rhinitis that had been treated recently with nasal steroids, and multiple sinus procedures including Caldwell-Luc procedures, ethmoidectomies, sphenoidotomies, and transnasal polypectomies. He was noted to have bilateral nasal polyps, which were worse on the left side. On May 2, 1986, he underwent a left external ethmoidectomy, sphenoidectomy, frontal sinusotomy, and a Caldwell-Luc procedure. One week later he underwent a right external ethmoidectomy and sphenoidotomy. A thick, yellow-green mucus was found filling the frontal and ethmoid



Figure 4. Axial CT scan of patient 5 demonstrating complete opacification of the ethmoid and sphenoid sinuses. Note the bowing of the lamina papyracea.

sinuses. Fungal cultures grew *Curvularia lunata*. Histologic review demonstrated fungal hyphae without any evidence of invasion. The patient did well and was free of disease at 6 months when he was lost to follow-up. No antifungal therapy was given.

RESULTS

The clinical features of our 14 patients are summarized in Table I. In nine patients the diagnosis was made prospectively and in five patients from the retrospective review. The average age was 31 years (range, 11–58). Seven were men (50%) and seven were women. Six patients (43%) had asthma. All patients (100%) had nasal polyposis, and all of those tested (11) were atopic with reactivity to multiple aeroallergens. The average number of surgical procedures for each patient was 2.14 (range, 1–5) although the five patients lost to follow-up had only one procedure at our institution.

Radiologic review included CT scans of all patients with each patient having an average of 4.5 of 8 sinuses involved. Bony erosion was demonstrated on 50% of the scans with the medial wall of the maxillary sinus and the intraethmoid septae being the most common sites followed by the lamina papyracea. None of the patients showed contiguous or noncontiguous invasion into adjacent structures such as brain or orbital soft tissue. All scans demonstrated hyperattenuation of the opacified sinuses.

Table II contains the immunologic and laboratory data for the patients. Cultures for five patients grew *B. spicifera*, two grew *Alternaria alternata*, two grew *C. lunata*, one grew *B. australiensis*, and one grew both *Aspergillus fumigatus* and *B. spicifera* from different sinuses. One patient had negative fungal cultures, and culture specimens were not taken from two patients. Serum precipitins and fungus-specific IgE and IgG antibodies were elevated in serum from those patients growing *B. spicifera*.

Table III compares the *Bipolaris*-specific IgG and IgE levels of AFS patients to the two control groups. The levels of IgE and IgG in the AFS patients were uniformly elevated; however, only *Bipolaris*-specific IgG elevations were statistically significant ($P < 0.05$).

Of the 205 patients reviewed retrospectively, five demonstrated AFS. When combined with the nine patients above, this yielded 14 patients with AFS from 214 patients with surgically treated chronic sinusitis for an prevalence of 6.5%.

DISCUSSION

The classification systems for fungal sinusitis have been both confusing and inconsistent. Most do not account for all of the cases reported in the literature. When McGill et al.¹¹ first described fulminant *Aspergillus* sinusitis in 1980 they suggested the presence of

TABLE II

Laboratory Data*							Organism†
Case No.	T. Eosin	IgE	Skin Test	PPT	sIgE	sIgE	
1	716	150	n/a	n/a	n/a	n/a	<i>B. australiensis</i>
2	229	3310	+	+	250	112	<i>B. spicifera</i>
3	n/a	n/a	+	+	11.5	75	<i>B. spicifera</i>
4	405	762	+	+	11	125	<i>B. spicifera</i>
5	352	254	+	+	19	12	<i>B. spicifera</i>
6	560	2107	+	+	226	55	<i>Aspergillus</i> , <i>B. spicifera</i>
7	352	1026	+	n/a	n/a	n/a	<i>Alternaria</i>
8	344	56	+	n/a	n/a	n/a	<i>Alternaria</i>
9	447	109	+	n/a	14	65	
10	n/a						<i>B. spicifera</i>
11	n/a						n/d
12	n/a						<i>C. lunata</i>
13	n/a						<i>C. lunata</i>
14	n/a						n/d

* Cases 10–14 not available (n/a) for immune testing.

† n/d, not determined.

three forms of *Aspergillus* sinusitis: 1) aspergilloma, 2) indolent, and 3) fulminant. As late as 1988, Washburn et al.¹² considered fungal sinusitis as acute, chronic invasive, and chronic noninvasive. Since the work of Katzenstein et al.^{2,3} suggesting a new type of *Aspergillus* sinusitis in 1983, the medical and allergy literature has discussed four types: 1) invasive, 2) indolent, 3) mycetoma, (4) allergic.^{13,14} This terminology tends to be misleading since indolent *Aspergillus* sinusitis, well described in Sudan in the 1960s, is known to be invasive and potentially fatal.^{15–17}

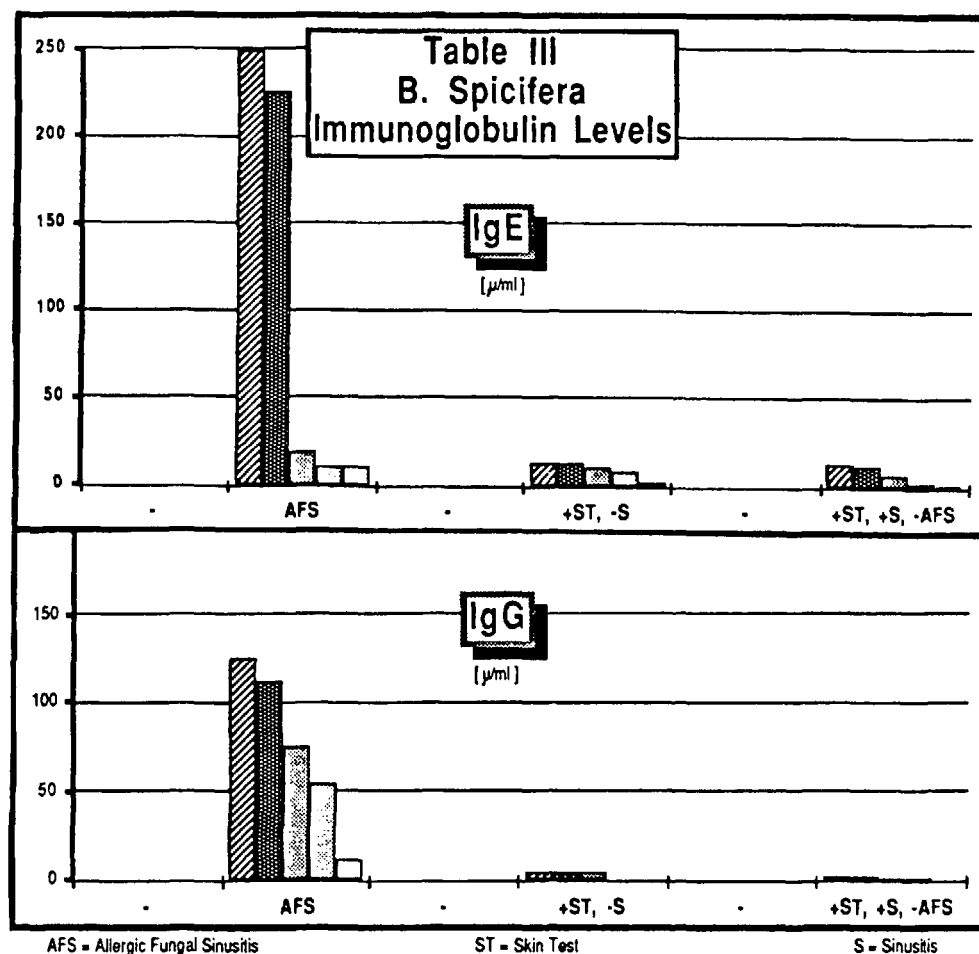
We propose the following classification system in order to facilitate both interdisciplinary communication and the further study of fungal sinusitis. We feel that this terminology most clearly and accurately accounts for the cases currently in the literature. Fungal sinusitis should be considered one of four types: 1) fulminant or acute, and three types of chronic, 2) indolent, 3) mycetoma, and 4) allergic. It is appropriate to define and describe briefly the clinical characteristics, pathophysiology, and histology of each category (Table IV).

It is apparent that the same fungal organism, such as *A. fumigatus*, can be the pathogenic organism in all four types. Recent reports suggest that most if not all forms can also be caused by a number of other fungal organisms such as the dematiaceous or black molds. Variables that may affect the type of fungal sinusitis include the local sinonasal environment, the host's immune response, the inoculum size of the fungus, and iatrogenic factors such as previous antibiotic and pos-

sibly topical steroid use. The host immune response seems to be the most likely factor that affects or determines the type of fungal sinusitis that develops.

A spectrum of immune response to fungal pathogens most likely exists. One end of the spectrum is seen in the leukemic bone marrow transplant patient who is severely immunocompromised. When a fungal infection develops, it is fulminant and rapidly progressive due to lack of functioning immune cells. Despite aggressive surgical debridement and therapy with systemic antifungal agents, the mortality rate may be as high as 80%.¹⁸ Histologic examination demonstrates both tissue and angioinvasion with massive necrosis. These patients typically have no previous history of atopy or sinusitis. The opposite end of the spectrum may be the excessive immune response of AFS with indolent and mycetoma somewhere in between. When one of the remaining three types of fungal sinusitis develops, the routine immunologic screening is entirely appropriate. However, this does not exclude isolated immune defects that are yet unknown or are not tested for.

The indolent form often is invasive but may be noninvasive early in its course. Histologically, there is a chronic inflammatory reaction with giant cells and granuloma formation within the tissue. The allergic mucin and inflammatory cells which fill the sinus cavity in AFS are absent. Some of these patients may lack the immune mechanism to prevent invasion. Like patients with AFS, they have chronic sinusitis for which long-term medical management and multiple surgical procedures have failed. Unlike patients with AFS, most of



these patients do not have a history of atopy. Recurrence of disease is not uncommon despite systemic antifungal therapy following surgery. This disease can invade neighboring structures such as the orbit and brain and may be fatal.^{12,19}

The mycetoma is noted by the marked absence of a significant inflammatory cell infiltrate and the abundance of tightly packed fungal hyphae, suggesting a proliferation within the melee of the inspissated mucous. However, invasion into tissue is lacking. These patients do not seem to have a characteristic clinical presentation other than chronic sinusitis of a single sinus that has failed to respond to conventional medical therapy and antral lavage. Surgical debridement and aeration seem to be curative.²⁰

The hypersensitivity-like reaction seen in AFS with an outpouring of inflammatory cells, especially eosinophils with their high content of the very toxic major basic protein, may inhibit significant fungal proliferation and tissue invasion. This may account for the paucity of fungal hyphae seen within the allergic mucin. It is documented that major basic protein is toxic to respiratory mucosa and may lead to tissue necrosis.²¹

Whether one type of fungal sinusitis can progress into another type is not known at this time. It seems possi-

ble, but to date no case of AFS documented in the literature has progressed to invasion.²²

It is hoped that by classifying fungal sinusitis as one of these four entities, further research and interdisciplinary communication will be facilitated. The remaining discussion will be limited to allergic fungal sinusitis.

Clinical Presentation of AFS

A clear clinical pattern has been demonstrated both in our experience and in the cases reported in the literature. AFS seems to occur in the young, immunocompetent patient who is atopic and has nasal polyposis. Patients have a history of chronic sinusitis of multiple sinuses that has not been responsive to conventional medical therapy. Most have undergone a variety of surgical procedures. Up to one-half of the patients have a history of asthma.

In contrast, patients in the literature with mycetoma, indolent, and fulminant disease show much less tendency to be atopic or have nasal polyposis.

Pathophysiology

The disease mechanism of AFS is unknown but is proposed to be very similar to that of ABPA, which is caused by a hypersensitivity reaction (Gelland and

TABLE IV

Classification of Fungal Sinusitis				
Type	Host	Clinical	Pathology	Treatment
1. Fulminant	Immunocompromised	Acute (days)	Angioinvasion tissue invasion	Surgical resection/antifungal therapy
2. Indolent	Immunocompetent	Chronic (weeks to months)	Granulomas and possible tissue invasion	Surgical debridement/antifungal therapy
3. Mycetoma	Immunocompetent	Chronic (months)	Noninvasive tightly packed hyphae	Surgical debridement
4. Allergic	Immunocompetent Atopic	Chronic (months)	Noninvasive allergic mucin	Surgical debridement/stenoids

Coombs Types I and III).^{23,24} Ubiquitous fungal spores are inhaled and trapped in the nasal cavity and sinuses. Sensitized mast cells then release a host of inflammatory mediators. This begins the cascade of immunologic events that leads to chronic inflammation and subsequent tissue destruction and bony erosion. The marked influx of eosinophils and thick inspissated mucus traps fungal hyphae and provides for continued antigenic stimulation. As eosinophils degenerate, they release enzymatic granules which are rich in major basic protein (MBP). MBP is known to be tissue-toxic and may be the cause of tissue necrosis and the bony destruction when found. Despite the speculation that AFS and ABPA have similar mechanisms, only a few cases have been reported of both occurring in the same patient at different times or concurrently.^{25,26} None of our 14 patients demonstrated evidence of ABPA. The reason for the localization of the disease process to the sinuses instead of the lungs is not known.

Immunology

Patients with AFS are immunocompetent by humoral and cellular screening. They demonstrate cutaneous reactivity to the offending fungal organism. Serum precipitans to the fungus are present. An elevation of the total peripheral eosinophil count is seen as well as an elevation of the total IgE level. When testing for fungus-specific IgE and IgG is available, levels are uniformly elevated. When immune testing demonstrates this pattern, the diagnosis should be suspected even before surgical biopsy and cultures. It is not known at this time whether serum antibody levels may serve as markers for disease activity as in ABPA.

Radiology

Recently Naul et al.²⁷ discussed the hyperattenuation noted on the CT scans of two patients with polyposis and inspissated mucus. The density was higher than is typically seen with nasal and sinus polyposis. Zinreich et al.²⁸ reviewed the CT and magnetic resonance imaging (MRI) scans of patients with documented fungal sinusitis. They found the CT scans to demonstrate increased attenuation with a mean of 122.2 Hounsfield units, which is significantly higher than that seen in chronic bacterial sinusitis with polyposis. The MRI scans demonstrated isointense or slightly decreased intensity on T1-weighted images while the T2-weighted images were decreased. They suggested that this could be related to the presence of calcium, air, or ferromagnetic elements. Spectrometric analysis demonstrated higher levels of magnesium, manganese, and iron in fungus-infected mucin than were found in bacteria-infected mucin.

These findings were seen uniformly on CT scans in our patient population. We had a number of patients

with bony erosion, most commonly of the intraethmoid septae and the medial wall of the maxillary sinus. We also had two patients in whom remodeling and erosion of the lamina papyracea were seen. Some authors have stated that the presence of bony erosion was diagnostic of invasive disease.¹² Spector and Katzenstein have both treated patients with AFS with bony erosion and no histologic evidence of tissue invasion.²² The mechanism for bony erosion in AFS is not known but could be the pressure from the expanding mass of polyps and inspissated mucin or the toxic effect of locally released inflammatory enzymes and mediators such as MBP.

These radiographic findings are not pathognomonic for fungal sinusitis, but certainly are suggestive of the diagnosis. It is not known how CT and MRI scans might differentiate between the forms of fungal sinusitis except that significant invasion into tissue or extension beyond the confines of the sinuses can often be identified when present.

Intraoperative Findings

Intraoperatively, the surgeon usually encounters thick, green, peanut butter-like mucin. This is removed in conjunction with polyps and, when seen, should alert the surgeon to the possibility of fungal disease. To confirm the diagnosis both the inspissated mucus and mucosal biopsies need to be sent for fungal stains and cultures. In addition, the entire surgical specimen should be reviewed by the pathologist to rule out invasive disease.

Histology

The diagnosis of AFS is made by histologic evaluation. In our experience, many pathologists are not aware of this newly described disease entity. Unless appropriate stains are obtained, the classic triad of allergic mucin containing numerous eosinophils, non-invasive fungal hyphae, and Charcot-Leyden crystals may be overlooked all together. Surgical specimens from our patients demonstrated inspissated allergic mucin laden with eosinophils when stained with the routine H&E preparation (Fig. 5). Many of the eosinophils are found to be degenerate and other inflammatory cells may be present as well. When stained with GMS, the mucin is found to contain scattered fungal hyphae (Fig. 6). A careful search of the mucosal tissue and bony trabeculae shows no evidence of invasion. H&E stain demonstrates Charcot-Leyden crystals, but these are seen even more profoundly with the Brown and Brenn stain (Fig. 7). These crystals are formed from the membrane of released granules within eosinophils and are made up almost exclusively of lysophospholipase. They appear hexagonal in cross-section and spindle-shaped in longitudinal section. The presence of these three histologic features and the absence of any fungal

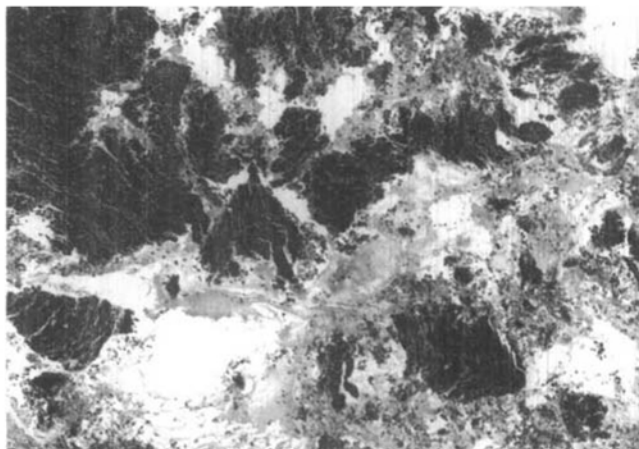


Figure 5. Allergic mucin from patient with AFS demonstrating numerous degenerating eosinophils and cellular debris in a background of laminated, dense, mucoid material (H&E, original magnification $\times 100$).

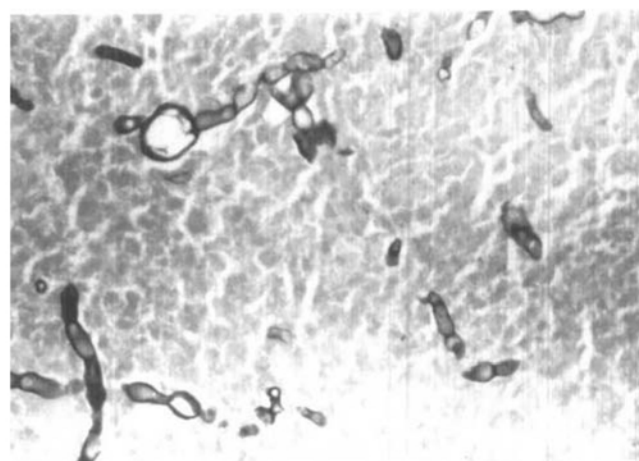


Figure 6. Allergic mucin from AFS patient demonstrating septate hyphae within the mucoid background (GMS stain, original magnification $\times 700$).

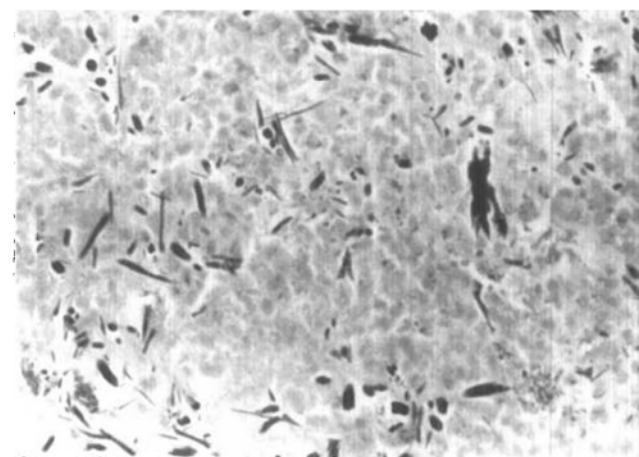


Figure 7. Charcot-Leyden crystals are well demonstrated as darkly staining prisms or hexagons in cross-section (Brown and Brenn stain, original magnification $\times 600$).

invasion into mucosa or bone confirms the diagnosis of allergic fungal sinusitis.

Many of the early reports describing allergic *Aspergillus* sinusitis were retrospective studies of cases where cultures were not done. Most mycologists agree that fungal organisms cannot be reliably identified by tissue H&E or GMS stain only. It is only when the fungus is grown in laboratory culture and characteristic conidiophores are seen that an accurate identification can be made (Fig. 3). It may be possible that previous case reports describing allergic *Aspergillus* sinusitis, but without culture confirmation, may have other fungal organisms as the causative agents. Therefore, we recommend that fungal cultures be obtained in order to identify more accurately the pathogenic organism. The addition of the Masson Fontana stain for melanin also will help distinguish the phaeohyphomycetes or dematiaceous molds from nonpigmented fungus species.

Treatment

The optimal treatment of AFS is not yet known. Restoration of sinus aeration and drainage is of obvious importance. This can be accomplished in many cases by either conventional sinus surgery or functional endoscopic sinus surgery. In our experience the ethmoid disease can be well addressed by the latter, but when the maxillary sinuses are filled with inspissated mucus, conventional surgery such as a Caldwell-Luc approach may be needed to debulk the allergic mucin and potential antigen load.

A significant number of patients have recurrences despite what is felt to be adequate sinus surgery. Understanding that AFS is a hypersensitivity reaction and not an invasive process lends support to the use of systemic corticosteroids. The treatment of choice for ABPA is systemic corticosteroids over a prolonged period of time and complete response rates of 80% are reported.²⁹ The current suggested therapy for ABPA is prednisone (0.5 mg/kg/day) for 2 weeks, then alternate day therapy for 3 to 6 months followed by a tapering dose. To date controlled prospective trials that document the long-term efficacy and safety of systemic steroids in AFS have not been done. Waxman and Spector²² have treated 15–20 patients with steroids without any progression of the disease to invasion. Our experience with steroids is limited to two patients who were treated for recurrent disease. Their conditions have responded well to a 3-month tapering dose.

Another controversial point is the role of systemic antifungal agents such as amphotericin B in noninvasive fungal sinusitis. In several cases in the literature, which we suspect were AFS, recurrences were reported despite treatment with intravenous amphotericin B.¹² It would seem prudent to avoid the significant side effects of these drugs except in patients in whom inva-

sion of tissue or significant extension beyond the confines of the paranasal sinuses is documented. The role of topical antifungal agents is intriguing but not well studied.

SUMMARY

Fungal sinusitis can present in one of four distinct forms: 1) fulminant, 2) indolent, 3) mycetoma, and 4) allergic. Allergic fungal sinusitis was originally described as being caused by *Aspergillus* but has since been found to be associated with at least five dematiaceous molds. Several studies, including our own, suggest that the incidence of AFS among patients with chronic sinusitis is as high as 7%. Diagnosis requires a high index of suspicion and requires special fungal stains. We also recommend fungal cultures in all cases of suspected fungal involvement to document the specific organism. The ideal treatment is not known but may well include adequate surgical drainage as well as systemic corticosteroids. Systemic antifungal agents are not indicated in the absence of invasive disease.

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