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## Allergic Fungal Sinusitis: CT Findings<sup>1</sup>

**PURPOSE:** To determine the computed tomographic (CT) findings in patients with allergic fungal sinusitis.

**MATERIALS AND METHODS:** The authors retrospectively reviewed CT scans and surgical and histopathologic reports in 45 patients (27 male, 18 female; age range, 8–68 years) with allergic fungal sinusitis from multiple institutions. The median age (25 years) and demographics of the patients were determined. Two head and neck radiologists together evaluated the CT scans for the presence of intrasinus high-attenuation areas, extent of sinus involvement, bone expansion and thinning, bone erosion, and extension of disease into the adjacent soft tissues.

**RESULTS:** Allergic fungal sinusitis was more common in male patients and in patients aged 20–30 years. All patients had increased intrasinus attenuation at non-contrast material-enhanced CT. Multiple sinus involvement occurred in 43 patients. Bilateral involvement was more common than unilateral disease. Forty-four patients had complete opacification of at least one of the involved sinuses; 43 of these patients had expansion of an involved sinus, 42 had remodeling and thinning of the bony sinus walls, and 41 had erosion of the sinus wall.

**CONCLUSION:** Allergic fungal sinusitis is a distinct clinical entity with nonspecific symptoms that may be initially suggested by the CT findings. These findings should alert the clinician to the possibility of allergic fungal sinusitis and prompt other diagnostic studies to establish the diagnosis and treatment plan.

Allergic fungal sinusitis is a clinical entity now thought to be the most common form of fungal sinusitis (1,2). Despite this, allergic fungal sinusitis is the least understood form of fungal sinusitis and may be underdiagnosed because it remains unfamiliar to otolaryngologists, pathologists, and radiologists (3). Accurate diagnosis is important because the treatment of allergic fungal sinusitis is substantially different from that of other types of fungal sinusitis (1,4).

In the most recent classification system (1), fungal sinusitis is divided into invasive and noninvasive forms. Patients with invasive fungal sinusitis typically have acute onset of fever, cough, nasal mucosal ulceration or eschars, epistaxis, and headache. Affected individuals are usually immunocompromised. Associated conditions include diabetes mellitus, severe malnutrition, and malignancy that results in severe neutropenia.

The most recent classification scheme lists the following categories of invasive fungal sinusitis.

Acute (fulminant) fungal sinusitis is characterized histologically by invasion of the mucosa, submucosa, or blood vessels by fungal hyphae. The most common organisms are of the order Mucorales and the genus and species *Aspergillus fumigatus*. Patients with acute fungal sinusitis require radical débridement, antifungal therapy, and treatment of the underlying condition (1).

Granulomatous invasive fungal sinusitis ("indolent fungal sinusitis") is a rare condition that has been reported primarily in Africa and Southeast Asia, with scattered reports in the United States. The disease is characterized by profuse fungal growth in the paranasal sinuses and regional tissue invasion. A *fumigatus* is the most commonly isolated organism. Affected individuals appear to be immunocompetent, unlike individuals with acute invasive fungal sinusitis. Histologic examination reveals noncaseating granulomas with giant cells and plasma cells. Treatment consists of surgical débridement and the administration of itraconazole (1).

Chronic invasive fungal sinusitis is characterized by a more prolonged course. The disease is typically associated with orbital apex syndrome owing to intra-orbital extension of disease from the ethmoid sinus. The most commonly isolated organism is *Aspergillus flavus*. These patients are usually immunocompromised and require treatment similar to that of patients with acute invasive sinusitis (1).

Patients with noninvasive fungal sinusitis present with chronic sinusitis that has failed to respond to prior medical or surgical treatment. The forms of noninvasive fungal sinusitis are categorized as the following.

Mycetoma is characterized histologically by a dense accumulation of fungal elements in a mucoid matrix. A *fumigatus* and the dematiaceous fungi are the most commonly isolated organisms. Mycetomas most frequently arise in the maxillary sinus and may occur in association with a chronically diseased sinus or polyps (1).

Allergic fungal sinusitis is a disease of young adults that has a geographic predilection for warm and humid climates. The disease is characterized by the presence of allergic mucin within the involved sinus. At endoscopy, allergic mucin is a brown or greenish-black material that has the consistency of cottage cheese. Histologically, it is composed of laminated accumulations of intact and degenerating eosinophils, Charcot-Leyden crystals, cellular debris, and hyphae (1).

The diagnostic criteria for allergic fungal sinusitis have recently been updated: (a) the presence of allergic mucin at endoscopy; (b) the identification of fungal hyphae within allergic mucin; (c) the absence of fungal invasion of submucosa, blood vessels, or bone; (d) the absence of diabetes mellitus, immunodeficiency disease, or recent treatment with immunodeficiency drugs; and (e) radiologic confirmation (1). In the past, the imaging findings of allergic fungal sinusitis were grouped together with those of other forms of fungal sinusitis (5). Findings of several small series have suggested that imaging studies may help to identify patients with allergic fungal sinusitis and should be a part of the diagnostic criteria (2,3,6-8). The purpose of our study was to review the computed tomographic (CT) findings in patients with surgically proved allergic fungal sinusitis in an attempt to determine characteristics suggestive of the entity.

## MATERIALS AND METHODS

We retrospectively reviewed CT scans and surgical and histopathologic reports in 45

patients (27 male, 18 female; median age, 25 years; mean age, 27.8 years; age range, 8-68 years at initial CT evaluation) with allergic fungal sinusitis. Diagnosis of allergic fungal sinusitis in our series was based on criteria established by DeShazo et al (1). All patients had characteristic allergic mucin at endoscopy and fungal hyphae identified at light microscopy. Allergic mucin is a brown or greenish-black material that has the consistency of cottage cheese. It is composed of laminated accumulations of intact and degenerating eosinophils, Charcot-Leyden crystals, and cellular debris (1). Finding allergic mucin at endoscopy is thought to be the sine qua non for the diagnosis of allergic fungal sinusitis (2,9).

The presence of an allergic history of atopy and a Gell and Coombs type I allergic hypersensitivity has been associated with allergic fungal sinusitis (4). However, an in-depth allergic history was not available in our series because the majority of patients did not undergo comprehensive allergic testing before surgery. This was related to the fact that the majority of patients were treated by otolaryngologists who did not consider the diagnosis before treatment. The presence of allergic mucin at endoscopy was thought to be sufficient evidence for initiating treatment after surgery.

The CT studies were correlated with surgical and histopathologic reports in all patients. Because our study was a retrospective, multi-institutional review, the imaging techniques varied. All patients had coronal non-contrast material-enhanced CT studies reconstructed with bone and soft-tissue algorithms. Axial views were reviewed when available. The section thickness was 3-5 mm.

The CT findings in 35 of the patients were reviewed together by two head and neck radiologists. The CT findings in the remaining 10 patients were not available for review because of issues involving patient care but were reviewed by experienced radiologists (L.E.G., W.R.N., D.M.Y.) at the institution at which they were obtained. Studies were evaluated for (a) the presence of intrasinus high-attenuation areas, (b) the extent of sinus involvement, (c) bone expansion and thinning, (d) bone erosion, and (e) extension of disease into the adjacent soft tissues. Because of the difficulty in separating individual ethmoid sinuses on coronal images, no attempt was made to determine the specific ethmoid compartment involved by disease. Thus, the anterior, middle, and posterior ethmoid sinuses were grouped together as the ethmoid sinus complex.

## CT Findings of Allergic Fungal Sinusitis

CT Finding	No. of Patients
Mucosal thickening	45/45 (100)
Unilateral	22/45 (49)
Bilateral	23/45 (51)
Increased intrasinus attenuation	45/45 (100)
Involved sinus	
Ethmoid	43/45 (96)
Maxillary	42/45 (93)
Frontal	32/45 (71)
Sphenoid	30/45 (67)
Multiple sinus involvement	43/45 (96)
Complete opacification of at least one sinus	44/45 (98)
Expansion of opacified sinus	43/44 (98)
Remodeling of walls of opacified sinus	42/44 (95)
Thinning of sinus wall of opacified sinus	41/44 (93)
Involvement of adjacent soft-tissue structures	9/45 (20)

Note.—Number in parentheses is the percentage.

## RESULTS

### Clinical Findings

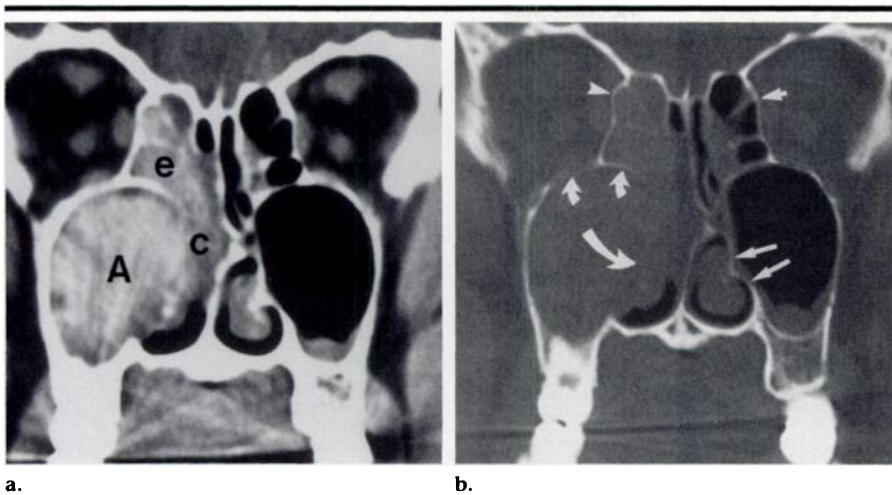
Clinical findings in our series showed that allergic fungal sinusitis was more common in male patients.

Our results are consistent with prior reports that have suggested a geographic distribution of allergic fungal sinusitis (2,10,11). This series consisted of cases obtained from seven academic institutions: four in the southeastern and southwestern and three in the northeastern and western United States. The number of patients from the southern institutions in warm and humid climates ( $n = 31$ ) was greater than the number from institutions in dryer climates ( $n = 14$ ).

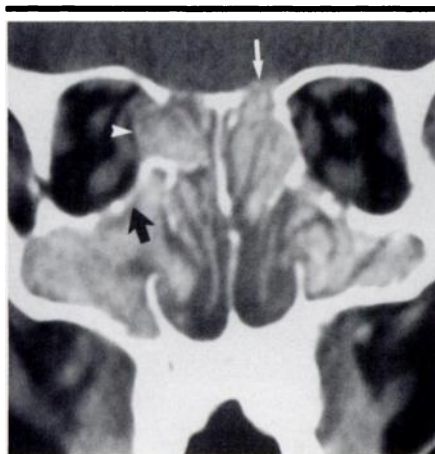
The presenting clinical complaints were nonspecific and consisted mainly of symptoms of chronic sinusitis. Six patients with advanced disease also presented with proptosis in addition to chronic sinusitis owing to extension of allergic fungal sinusitis into the retrobulbar region. No patients had meningitis or neurologic symptoms due to intracranial extension of disease.

### CT Findings

All of our patients had increased intrasinus attenuation within the mucosal opacification on unenhanced studies (Table). The mucosal thickening in allergic fungal sinusitis involved any of the sinuses. The ethmoid sinus complex was most commonly involved, with at least one eth-



**Figure 1.** Allergic fungal sinusitis with unilateral involvement in a 25-year-old man. (a) Coronal unenhanced CT scan shows the typical appearance of unilateral allergic fungal sinusitis. There is an expansile lesion centered in the right maxillary sinus antrum (A) that also involves the ipsilateral ethmoid sinus complex (e) and nasal cavity (c). The increased intrasinus attenuation suggests that this mass is a benign inflammatory process rather than a malignant sinonasal neoplasm. (b) Bone-algorithm image of a demonstrates expansion and thinning of the lamina papyracea (arrowhead), the roof of the maxillary sinus (small curved arrows), and the medial wall of the maxillary sinus (large curved arrow). Compare this with the normal appearance of the bony structures on the left (small straight arrow = contralateral lamina papyracea, large straight arrows = medial wall of left maxillary sinus).



**Figure 2.** Allergic fungal sinusitis with bilateral involvement in a 39-year-old man. Coronal unenhanced CT scan shows opacification of the maxillary and ethmoid sinuses. Erosion of the lamina papyracea (arrowhead), planum sphenoidale (white arrow), and orbital floor (black arrow) could also be seen in a slowly growing neoplasm. However, the diffuse intrasinus areas of increased attenuation suggest allergic fungal sinusitis.

moid sinus complex involved in 43 (96%) of 45 patients. This was followed in frequency of involvement by the maxillary sinus (42 patients [93%]), the frontal sinus (32 patients [71%]), and the sphenoid sinus (30 patients [67%]). Multiple sinus involvement was the rule: Only two of the 45 patients had disease limited to

one sinus (one with disease in the ethmoid sinus complex, one with disease in the maxillary sinus).

Twenty-two (49%) of 45 patients had unilateral involvement, with the right side ( $n = 15$ ) involved more commonly than the left ( $n = 7$ ) (Fig 1). Twenty-three (51%) of 45 patients had bilateral disease (Figs 2, 3). Of these 23 patients, 10 had symmetric involvement and 13 had asymmetric involvement. Of the 13 patients with asymmetric involvement, eight had disease predominantly on the left side and five had disease predominantly on the right.

Forty-four (98%) of 45 patients had complete opacification of at least one sinus. Of these 44 patients, 43 (98%) had expansion of the opacified sinus, 42 (95%) had remodeling of the bony sinus walls, and 41 (93%) demonstrated erosion of a sinus wall.

Nine (20%) of the 45 patients had evidence of disease extending into adjacent structures. All nine patients had bone erosion: Three had intracranial disease extension, three had intraorbital disease extension, and three had both intraorbital and intracranial disease extension. Of these nine patients, six had bilateral disease and three had unilateral disease.

## DISCUSSION

In the span of only 2 decades, interest in allergic fungal sinusitis has grown. This

diagnosis should be suspected in atopic patients with chronic, often intractable sinusitis and polyposis (1). The similarities allergic fungal sinusitis shares with allergic bronchopulmonary aspergillosis led to the first case report by Safirstein (12). Millar et al (13) and later Katzenstein et al (14) noted characteristic mucoid sinus impactions and nasal polyposis in small groups of patients with chronic sinusitis. Histologic evaluation of that mucoid material revealed acute branching fungal hyphae thought to be a species of the genus *Aspergillus*. Terms such as "allergic aspergillosis of the paranasal sinuses" and "allergic aspergillus sinusitis" were initially used to describe the disease. Later studies that relied on actual cultures of fungi revealed the role of dematiaceous fungi in the pathogenesis of this disease, prompting Robson et al (15) to coin the term "allergic fungal sinusitis" in 1989. The most common fungi are *Curvularia*, *Bipolaris*, *Pseudallescheria*, *Aspergillus*, and *Fusarium*.

Allergic fungal sinusitis continues to be underdiagnosed because it is often not recognized as a distinct clinical entity (3,7). In the past, allergic fungal sinusitis has been grouped under the broad classification of "fungal sinusitis" rather than recognized as a separate disease (5,16,17). Recent advances have led to a better understanding of fungal sinus infections (1). Several different entities are now thought to compose what was once known collectively as "fungal sinusitis" (5). Fungal sinus disease is now classified as (a) allergic fungal sinusitis, (b) sinus mycetoma, (c) acute (fulminant) invasive sinusitis, (d) chronic invasive fungal sinusitis, and (e) granulomatous invasive fungal sinusitis (1).

Allergic fungal sinusitis may constitute, in part, what radiologists have referred to in the past as "superimposed fungal colonization" of the sinuses. Our investigation demonstrates that the CT findings that may suggest a diagnosis of allergic fungal sinusitis consist of complete unilateral or bilateral opacification of multiple paranasal sinuses, sinus expansion and erosion of a wall of the involved sinus, and scattered intrasinus high-attenuation areas amid mucosal thickening on unenhanced CT scans.

Our CT findings are similar to those previously described by Manning et al (2). Because our study is a retrospective one in which we evaluated known cases of allergic fungal sinusitis, we cannot conclude that the imaging findings are "highly specific," as previously suggested (2). However, our findings suggest that

the presence of a unilaterally opacified sinus associated with sinus expansion, bone remodeling, and increased internal attenuation on unenhanced CT scans should raise the possibility of allergic fungal sinusitis.

Bilateral sinus involvement also is common and present in patients with advanced disease. Patients with advanced bilateral involvement are more likely to have intracranial or intraorbital extension of disease at the initial imaging evaluation than are patients with unilateral disease (Fig 3). The degree of bone erosion and extension beyond a sinus may mimic aggressive sinonasal neoplasms. The presence of increased internal attenuation on unenhanced CT scans may help to distinguish allergic fungal sinusitis from the more common sinonasal tumor (Fig 3) (5,17). It is conceivable that rare sinonasal meningiomas or sarcomas that produce a chondroid or osteoid matrix could contain high-attenuation areas and may mimic allergic fungal sinusitis on unenhanced CT scans. It also is possible that CT may not be able to help distinguish allergic fungal sinusitis from desiccated secretions within mucocoeles or polyps. However, the presence of expansion and thinning of the sinus walls may help separate allergic fungal sinusitis from chronic disease with desiccated secretions, which often results in thickening and sclerosis of the adjacent sinus walls (Fig 4).

Our results suggest that CT may help identify patients with allergic fungal sinusitis and may differentiate this from other forms of fungal sinusitis. The CT finding of mycetoma is a focal round area of increased attenuation that is usually centered within a diseased maxillary sinus (1,16,17). Conversely, allergic fungal sinusitis typically involves multiple sinuses, expands the involved sinus, and is associated with diffuse scattered intrasinus areas of increased attenuation. Acute invasive fungal sinusitis is characterized by aggressive bone erosion with extension of disease into the adjacent soft tissues (16–18). Infection arising in the maxillary sinus may spread anteriorly into the canine fossa or posteriorly into the pterygopalatine fossa (19). It is uncommon for acute invasive fungal sinusitis to expand a sinus or remodel a sinus wall. Intrasinus high-attenuation areas at CT are unusual in acute invasive fungal sinusitis (17,18). The imaging findings of granulomatous and chronic invasive fungal sinusitis have not been clearly defined. Thus, it is unclear whether CT can be used to differentiate allergic fungal

sinusitis from these latter two disease entities.

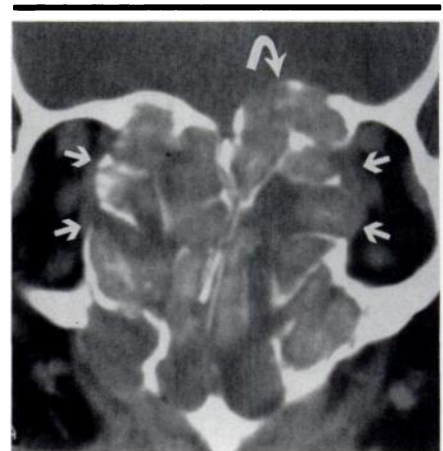
Our findings reinforce the need to look at soft-tissue–algorithm images when performing CT in patients with chronic sinusitis, because the internal intrasinus areas of increased attenuation are best identified at these settings. The high attenuation in allergic fungal sinusitis is likely due to a combination of heavy metals (iron and manganese), calcium, and inspissated secretions that are often found in fungal elements (5,16,17,20).

Our study is a retrospective analysis in which we evaluated the CT findings of documented cases of allergic fungal sinusitis. Because we did not compare the imaging of allergic fungal sinusitis with that of sinonasal polyposis or with that of mucocoeles, we are unable to comment on the predictive value of our findings (2,3,4,11,21,22). Thus, even though allergic fungal sinusitis may be suggested, it may not be possible to differentiate allergic fungal sinusitis from advanced sinonasal polyposis or mucocoeles that also contain multiple mycetomas or desiccated secretions (Figs 2, 4). It is probable that early cases of allergic fungal sinusitis with only partial opacification of the sinuses may be indistinguishable from cases of other nonfungal types of mucosal thickening seen in patients presenting with similar nonspecific symptoms.

Common spread patterns in advanced allergic fungal sinusitis included intraorbital extension through the lamina papyracea and intracranial extension by means of erosion of the sphenoid sinus, planum sphenoidale, and posterior wall of the frontal sinus (Figs 1, 3). The bone expansion and thinning typically associated with allergic fungal sinusitis is likely due to pressure from a combination of the underlying sinonasal polyposis and the allergic mucin (2,6,22).

Magnetic resonance (MR) imaging does not appear to play a substantial role in the initial diagnosis of allergic fungal sinusitis. The signal intensity loss in sinus contents reported in allergic fungal sinusitis is likely due to a combination of an absence of freely mobile protons and the presence of heavy metals within dense fungal concretions. The concomitant susceptibility effects that lower signal intensity on T2-weighted MR images are not specific to allergic fungal sinusitis and could result in the underestimation of the extent of sinus involvement at MR imaging (16,17) (Fig 5).

As additional information has accumulated, it has become increasingly apparent that allergic fungal sinusitis repre-

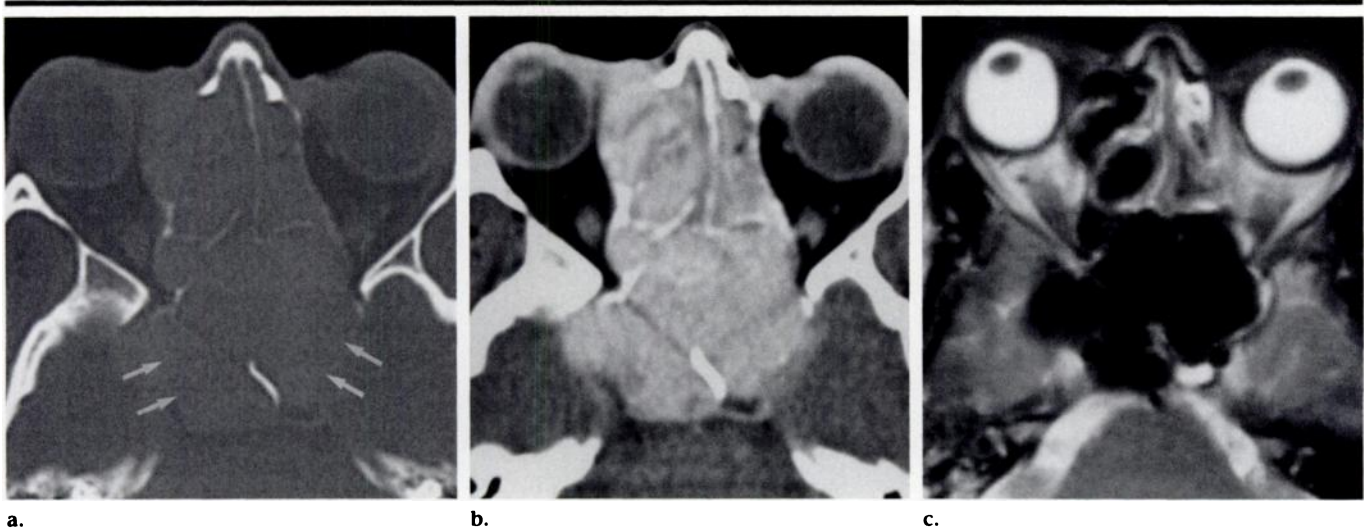


**Figure 3.** Advanced allergic fungal sinusitis mimicking an aggressive sinonasal neoplasm in a 45-year-old man. Unenhanced coronal CT scan demonstrates an aggressive sinonasal mass that erodes the lamina papyracea and invades the orbits (straight arrows). The mass also erodes the skull base and extends intracranially (curved arrow). The presence of the intrasinus area of increased attenuation suggests a benign inflammatory process.



**Figure 4.** Diffuse sinonasal polyposis mimicking allergic fungal sinusitis in a 28-year-old man. Coronal unenhanced CT scan shows complete opacification of the maxillary and ethmoid sinuses. There are intrasinus areas of high attenuation similar to those in Figure 2. Note the thickening of the walls of the maxillary sinus (arrows). This thickening was confirmed on bone–algorithm scans. Endoscopy showed diffuse sinonasal polyposis without evidence of allergic mucin. No fungal hyphae were identified at histologic evaluation.

sents an immunologic, rather than an infectious, disorder. Although the exact pathophysiology remains a matter of conjecture, it is postulated that the pathophysiology of allergic fungal sinusitis is similar to that of allergic bronchopulmonary aspergillosis, involving both immediate and delayed hypersensitivity (3).



**Figure 5.** (a, b) CT scans and (c) MR image of allergic fungal sinusitis in a 38-year-old man. (a) Axial unenhanced bone-algorithm CT scan shows an expansile mass that involves the ethmoid and sphenoid sinuses. The diffuse erosion of the walls of the sphenoid sinus (arrows) suggests a neoplasm. (b) Soft-tissue-algorithm unenhanced CT scan shows diffuse intrasinus areas of increased attenuation. This finding favors a diagnosis of allergic fungal sinusitis over a diagnosis of sinonasal neoplasm. (c) Axial T2-weighted MR image (3,000/90 [repetition time msec/echo time msec]) demonstrates diffuse areas of signal intensity loss within the sphenoid and right ethmoid sinuses. Note how the extent of disease is substantially underestimated in c as opposed to that in a or b. The signal intensity loss is likely due to a combination of an absence of freely mobile protons and the presence of heavy metals within fungal concretions.

Patients with allergic fungal sinusitis often have allergic rhinitis, asthma, eosinophilia, and elevated total and fungus-specific immunoglobulin E concentrations (1). These associated findings are best diagnosed by means of allergic testing, which includes skin and radioallergosorbent testing (1). However, these findings may not always be identified in patients with allergic fungal sinusitis (6). This may be related to the fact that a majority of patients are treated by otolaryngologists who do not consider the diagnosis before treatment. Thus, in-depth presurgical allergy testing is often not performed during the examination of these patients.

Manning et al (23) suggest that several related factors are necessary for the development of allergic fungal sinusitis. Initially, an atopic individual inhales fungi, which come to rest within a paranasal sinus. The presence of this fungal antigenic stimulus incites a Gel and Coombs type I (immunoglobulin E-mediated) and type III (immune-complex-mediated) inflammatory response, resulting in obstruction of a sinus ostium and mucostasis within that paranasal sinus. Within this environment, the inciting fungus continues to proliferate, further exacerbating immunologically mediated inflammation. Eventually, eosinophilic allergic mucin, in combination with proliferating fungal hyphae and polyposis, give rise to an expanding sinus, yielding the characteristic clinical picture of allergic fungal

sinusitis. Thus, the treatment of allergic fungal sinusitis differs from other types of fungal sinusitis and consists of the oral or topical administration of prednisone after surgical débridement. The suggested therapy is a 4-week course of oral prednisone followed by a long-term course of short-acting intranasal corticosteroids (1,7). Recent study findings suggest that allergen immunotherapy to downregulate the production of fungus-specific immunoglobulin E and decrease the inflammatory reaction may also be beneficial (1,4).

Preoperative CT findings that suggest allergic fungal sinusitis may facilitate obtaining the necessary laboratory studies required to establish the diagnosis. Every attempt should be made to fulfill the diagnostic criteria of allergic fungal sinusitis before the initiation of steroid therapy because of its inherent side effects (21). This is especially important given the preponderance of allergic fungal sinusitis in the pediatric population, as reported by others (21). The presence of Charcot-Leyden crystals within the tenacious mucin will help corroborate the diagnosis of allergic fungal sinusitis (7,22). Suspicion of allergic fungal sinusitis alerts the pathologist to evaluate the histopathologic specimen specifically for this histologic marker. Special fungal stains may be necessary to identify fungal hyphae that may not be seen with standard hematoxylin-eosin staining (3,9,24). Because of the

variety and fastidiousness of the organisms that may be present in allergic fungal sinusitis, special culture media may be required for growing the specific fungal species (3,6).

In summary, allergic fungal sinusitis, a distinct clinical entity with nonspecific symptoms, may be initially suggested by the CT findings. Our results are consistent with those of smaller series and suggest that the diagnosis of allergic fungal sinusitis may be indicated by certain findings at CT (2,7,8,25,26). When present, these findings should alert the clinician to the possibility of allergic fungal sinusitis and prompt the referring physician to perform the other studies necessary to establish the diagnosis and plan treatment (2,4,7,11,22).

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