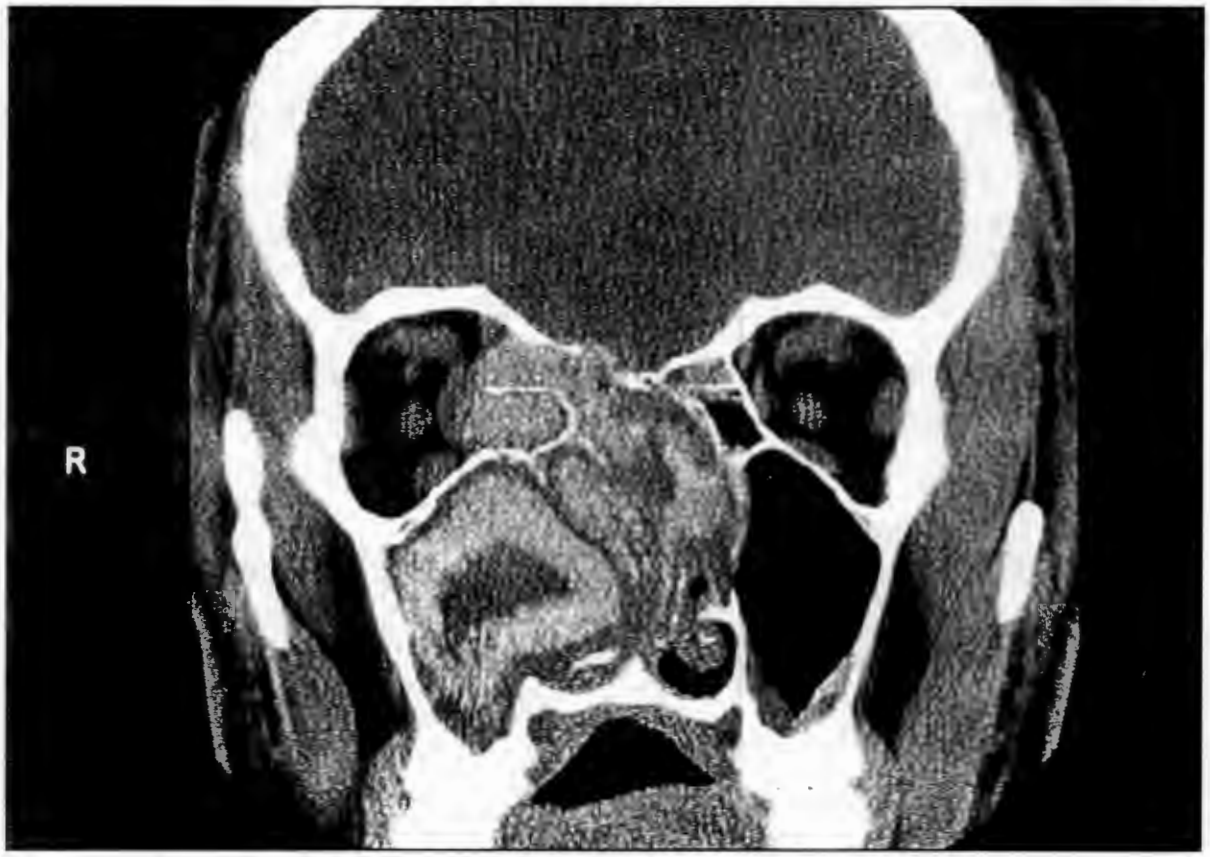
Ophthalmic Practice

February 2002 Vol. 20 No. 1



The Official Journal of the American Association of Ophthalmic Pathologists and the Canadian Society of Cataract and Refractive Surgery

Case Report: Allergic Fungal Sinusitis Secondary to Curvularia Lunata

Minutes of the AOA-AFIP Meeting

AAOP Abstracts

CSCRS Preliminary Meeting Program

Reprinted from:
Ophthalmic Practice
Volume 20, No 1, 2002

Allergic Fungal Sinusitis Secondary to Curvularia Lunata

Darryl J. Ainbinder, MD; Clifton S. Otto, MD; Gerald R. Christensen, MD; Anne L. Champeaux, MD; Robert A. Mazzoli, MD, FACS

CASE REPORT

Ophthalmic Practice is pleased to offer the American Association of Ophthalmic Pathologists (AAOP) Case Report under the direction of Dr. Seymour Brownstein, University of Ottawa Eye Institute, Ottawa, Ontario. This section presents clinical pathologic case reports of interest to ophthalmologists. In this issue, Drs. Darryl J. Ainbinder, Clifton S. Otto, Gerald R. Christensen, Anne L. Champeaux, and Robert A. Mazzoli talk about allergic fungal sinusitis secondary to Curvularia lunata.

Allergic Fungal Sinusitis Secondary to Curvularia Lunata

Darryl J. Ainbinder, MD; Clifton S. Otto, MD; Gerald R. Christensen, MD; Anne L. Champeaux, MD; Robert A. Mazzoli, MD, FACS

ABSTRACT

***Objective*: To report the characteristic clinical, radiologic, and histopathologic findings in two cases of allergic fungal sinusitis secondary to Curvularia lunata infection. *Methods*: Two case reports. *Results*: Two patients with allergic fungal sinusitis, both presented with proptosis, motility and visual disturbance. The first patient was treated with endoscopic surgical debridement and sinus aeration along with inhaled steroid therapy, which provided complete return of visual function. The second patient was treated with repeated surgical debridement and aeration alone, which resulted in a chronic smoldering disease process. *Conclusions*: Allergic fungal sinusitis is a well-defined, common disorder that typically occurs in young, healthy adults who have a long history of allergic rhinitis. Patients often present with nasal congestion and sinus opacification that is unresponsive to antibiotic therapy. Proptosis and motility disturbance are the most common ophthalmic manifestations. CT imaging demonstrates a heterogeneous mass with compressive bone erosion. Treatment of the fungal hypersensitivity response is paramount.**

D.J. Ainbinder, C.S. Otto, R.A. Mazzoli — Madigan Army Medical Center, Department of Ophthalmology, Tacoma, WA; G.R. Christensen — University of Nebraska Medical Center, Department of Ophthalmology, Omaha, NE; A.L. Champeaux — Madigan Army Medical Center, Department of Pathology, Tacoma, WA 98431

Correspondence to: Dr. Darryl J. Ainbinder, LTC, MC, USA, Madigan Army Medical Center, MCHJ-SOU, Tacoma, WA 98431, Email: «darryl.ainbinder@nw.amedd.army.mil»

Grants: (Christensen) Research to Prevent Blindness Challenge Grant;

Department of Defense Disclaimer: The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the view of the Department of the Army or the Department of Defense.

INTRODUCTION

Allergic fungal sinusitis (AFS) is an indolent disease process when it occurs in healthy, young, immunocompetent patients. The disease is the result of a patient's hypersensitivity reaction to non-invasive fungal elements residing in the sinuses. Many patients have a history of allergic rhinitis or atopic disease. A mild form of AFS is common and widely recognized in the primary care literature.[1,2] Dematiaceous molds, including Curvularia, *Bipolaris*, and other species are the most common antigens for allergic fungal sinusitis.[3,4] Characteristically, these fungi do not invade surrounding tissues. The patients' sinuses are filled with allergic mucin that is, laminated pools of thick mucin with numerous foci of eosinophils, Charcot-Leyden crystals and fungal elements.[5] Compressive bone erosion is common, and not due to fungal tissue invasion. The treatment of choice for AFS is endoscopic debulking surgery of the sinuses, debridement of impacted mucin, and aeration of diseased sinuses. Treatment of the hypersensitivity component of the disease, including long-term use of potent, inhaled nasal steroids is the therapeutic cornerstone of AFS. Systemic anti-fungal drugs have little indication in this disease process.

CASE REPORTS

Case 1

In 1998, a 31-year-old, previously healthy male presented with a six-month history of nasal congestion, and chronic sinusitis that was unresponsive to antibiotic therapy and with a progressive proptosis of the right eye. His past medical history was significant for allergic rhinitis. On

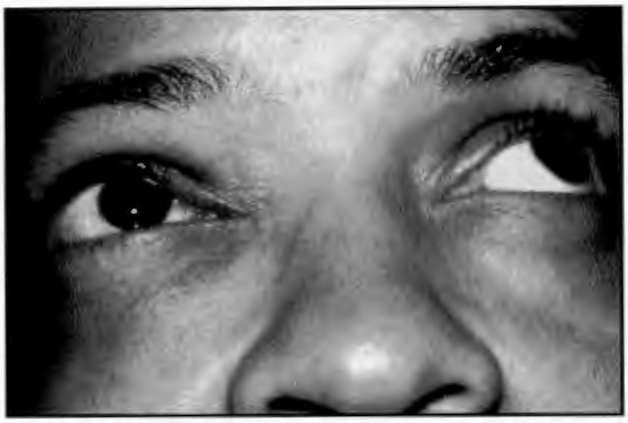


Fig. 1 (Case 1) The patient has significant proptosis and reduced motility of the right eye.

examination, the patient had proptosis of the right eye, but did not appear ill or septic. His visual acuity was 6/7.5 in the right eye and 6/6 in the left. Pupils were normally reactive. There was 7 mm of proptosis of the right globe, with reduced motility in all fields of gaze, that was more pronounced with adduction and elevation (Fig. 1). Hypoesthesia was present bilaterally along the cutaneous distributions of the infraorbital and anterior ethmoidal nerves. Olfactory function was also reduced. Nasal endoscopic examination revealed friable, laminated, dark-brown tissue filling most of both nasal cavities. There was no regional adenopathy or evidence of meningismus. The patient was HIV negative.

CT examination revealed a heterogeneous mass with pan-sinus involvement, affecting the right side more than the left (Fig. 2). The mass demonstrated extensive expansile remodeling of surrounding bone, including erosion of the infero-medial wall of the right orbit and the base of the anterior cranial fossa. Gadolinium-enhanced MRI confirmed a lack of dura or orbital soft tissue involvement. The MR signal characteristics of the mass were characteristic of inspissated mucin, which supported the diagnosis of allergic fungal sinusitis (Fig. 3).

Curvularia lunata was cultured from the numerous surgical specimens. Its identification was based on colony visual and microscopic evaluation (Fig. 4). The patient was evaluated by the otolaryngology service and taken to the operating room for endoscopic sinus debridement. The surgical material consisted of multiple fragments of soft, friable, dark-tan tissue with the consistency of thick peanut butter (Fig. 5). Microscopic examination showed large amounts of laminated, mucinous material with numerous degenerated eosinophils, chronic inflammatory cells, and fungal elements. The microscopic appearance of allergic mucin was consistent with a clinical diagnosis of AFS (Fig. 6). The dematiaceous fungus Curvularia lunata was isolated from the surgical material. There was no evidence of fungal invasion into orbital soft tissue or bone (Fig. 7), no purulent exudate, no granulomatous inflammation, and no evidence of vasculitis.

The patient received pulse doses of IV dexamethasone, followed by one month of oral prednisone and consolidation with long-term nasal steroid therapy.

He has returned to a normal status including resolution of all ophthalmic, nasal-respiratory, and sensory functions. He continues therapy with nasal saline and nasal steroids and remains symptom free at three years.

Case 2

In 1992, a 23-year-old male presented with a three-month history of progressive painless visual loss in the left eye. The patient noted mild, frontal headaches for the past month that were controlled with aspirin. He reported difficulty with nasal respiration over the past nine months. His past medical history was significant for severe seasonal allergy that began in childhood. He suffered a traumatic hyphema from a baseball injury to the left eye at the age of 16 years, with complete visual recovery. His comprehensive ophthalmic exams were completely normal following this injury, until he presented at age 23 with proptosis, visual loss, and nasal congestion.

On physical examination, the patient's best-corrected vision was 6/6 in the right eye and 6/120 in the left. Visual loss in the left eye was due to compressive optic neuropathy caused by AFS. There was a 1+ afferent pupillary defect in the left eye. Hertel measurements were 22 mm on the right and 25 mm on the left, with both globes displaced directly forward. There was notable bilateral resistance to retropulsion, but ocular motility was full. There was significant pallor of the left optic disc. There was also marked swelling and congestion of the nasal mucosa in both nostrils, and numerous nasal polyps. The patient's breath had a foul odor.

CT of the sinuses and orbits revealed complete obliteration of all paranasal sinuses with a heterogeneous soft tissue opacification consistent with hemorrhage or inspissated secretions. There was expansile erosion of the mass through the left posterior ethmoid sinus wall with lateral displacement of the left medial rectus muscle against the optic nerve (Fig. 8). The mass had also eroded through the sphenoid sinus, the planum sphenoidale, tuberculum sella, floor of the sella turcica, and the margins of the optic foramen.

Biopsies from the left ethmoid sinus revealed fragments of respiratory mucosa that were edematous and infiltrated with lymphocytes, plasma cells, and eosinophils. There was prominent endothelial cell proliferation with numerous capillary channels, as well as many large reactive fibrocytes. There were numerous

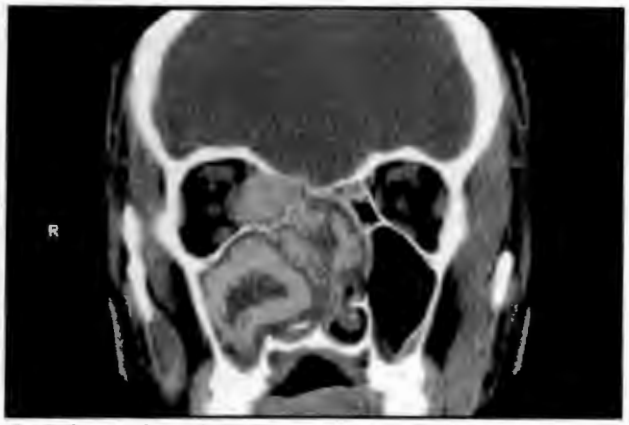


Fig. 2 (Case 1) Coronal CT with contrast demonstrates a heterogeneous mass with pansinus involvement. There is extensive expansile remodeling of bone including erosion of the infero-medial wall of the right orbit, and base of the anterior cranial fossa.

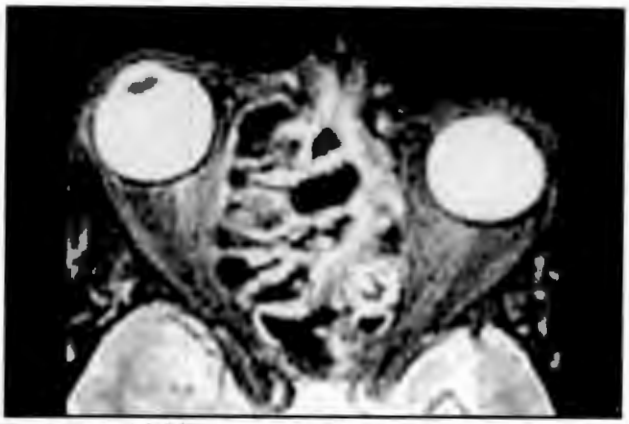


Fig. 3 (Case 1) Axial T-2 weighted MRI with gadolinium enhancement. The dense native proteins of the crystalline lens share the same hypo-intense signal characteristics as the inspissated pools of mucin within the sinus mass. The distorted sinus mucosa demonstrates gadolinium enhancement, surrounding the lakes of mucin.

Fig. 4 (Case 1) Photomicrograph of Curvularia mold shows its septate hyphae and curved cylindrical spores that contain transverse septa.

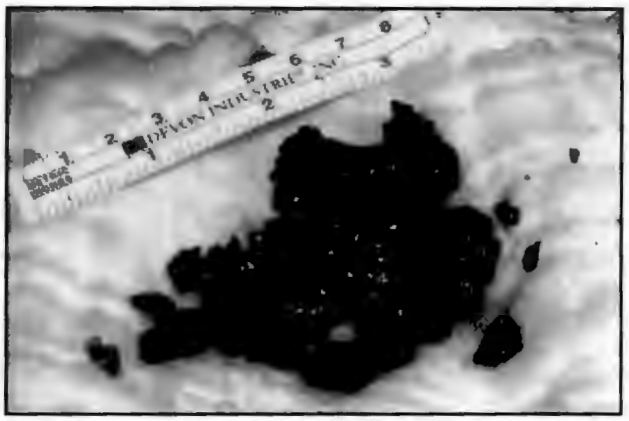


Fig. 5 (Case 1) Gross pathology of the debulked intra-sinus mass has the consistency of dark, thick peanut butter.

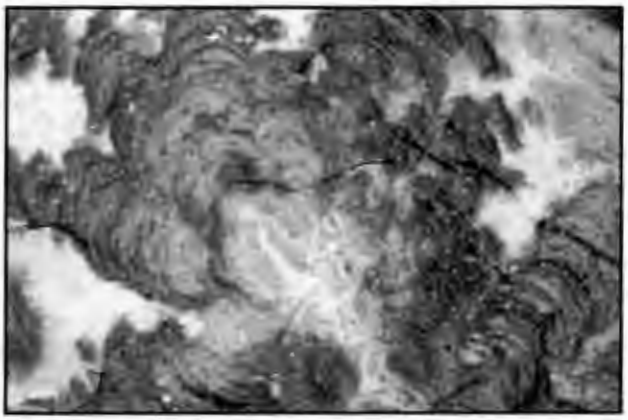


Fig. 6 (Case 1) Photomicrograph of laminated pools of allergic mucin. (10X H&E)

Fig. 7 (Case 1) Photomicrograph of a fragment of bone obtained from the margin of the specimen. There is no evidence of fungal invasion into bone. (40X H&E)

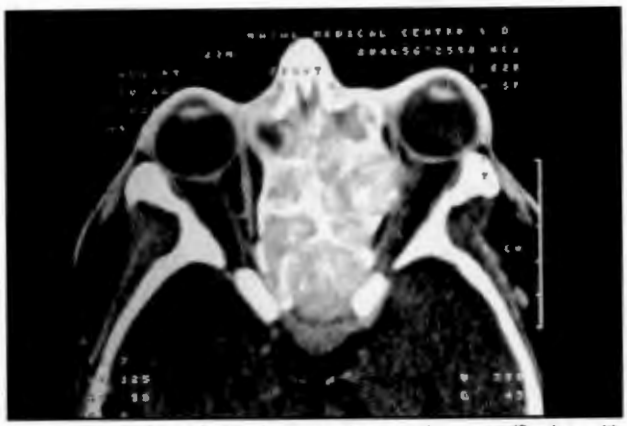


Fig. 8 (Case 2) Axial CT demonstrating pansinus opacification with expansile erosion through the left posterior ethmoid sinus wall with lateral displacement of the left medial rectus muscle against the optic nerve.

areas of large concentric mucus pools, marginated with thick, laminated layers of eosinophils in various stages of degeneration and necrosis. Confined within these mucus concretions were scattered fragments of individual fungal hyphae, which were well demonstrated with both Gomori methenamine silver (GMS) and Fontana stains. Fungal cultures isolated the dematiaceous fungus Curvularia lunata that was morphologically consistent with the isolated surgical fragments.

A diagnosis of allergic fungal sinus disease was established based on the patient's history, imaging and pathology. In 1992, the role of nasal or systemic steroid therapy in AFS was controversial, and infrequently used. The patient underwent endoscopic debridement and aeration of the para-nasal sinuses. No therapy was directed against the allergic component of his disease. He did not receive corticosteroids. The patient did not recover visual function in the left eye. The left optic nerve demonstrated progressive pallor and atrophy. The patient was able to breathe somewhat better, yet he complained of persistent nasal stuffiness. Additional endoscopic procedures were required to prevent impaction of recurrent allergic mucin.

Discussion

These two, healthy, young adults, ages 23 and 31 at the time of presentation, had slowly progressive proptosis, diplopia, nasal stuffiness, pan-sinus opacification and compressive bone erosion. Both patients had a history of seasonal nasal allergy. AFS secondary to Curvularia lunata was confirmed based upon clinical, radiographic, histopathologic and culture data.

The disease process of the patient seen in 1992 had progressed to the point of compressive optic neuropathy. He was treated with endoscopic debridement and aeration of the paranasal sinuses. His visual function did not improve and his nasal allergic symptoms continued to smolder.

Our more recent patient was treated with endoscopic sinus debridement, and aeration of the paranasal sinuses. In addition, he was treated with pulse systemic steroids followed by long-term nasal inhaled steroids. He continues therapy with nasal saline and nasal steroids and has remained symptom-free three years following surgery. He has experienced a resolution of all ophthalmic, nasal-respiratory, olfactory, and trigeminal sensory symptoms.

These two cases were separated by 6 years (1992 to 1998). During that time, patients with AFS have been effectively treated with inhaled nasal steroids. These agents have gained widespread effective use by primary care providers, otolaryngologists and ophthalmologists familiar with this disease. The ophthalmic community has gained significant insight into AFS and the approach to therapy has evolved. Patients with severe AFS can easily present to your office with indolent proptosis, motility and visual disturbance.

These two patients, with ophthalmic manifestations of severe AFS, highlight three important points: (1) It is important to differentiate AFS from invasive fungal sinus disease; (2) compressive bone erosion does not indicate invasive disease; and (3) control of the allergic response is the therapeutic cornerstone for AFS. In the interim between our two cases, potent inhaled nasal steroids have attained an increasingly vital therapeutic role.

There are four distinct types of fungal sinus disease, two are invasive and two are non-invasive processes. All are well described in the otolaryngology and pathology literature.[6] Treatment options for one form of fungal sinus disease may be unnecessary or even dangerous for another form of the disease. Recognition of each type is vital to ensure appropriate treatment.

Invasive Fungal Sinus Disease

Acute invasive fungal sinusitis is a fulminating, often-fatal disease of metabolically compromised or immuno-compromised patients. The offending fungal pathogens are notorious, including Mucormycosis (Phycomycosis) and Aspergillosis, which are organisms commonly present in soil and respiratory environments. The term "phycomycosis" encompasses a group of organisms including Rhizopus, Absidia, and Mucor. Mucor fungal hyphae have a distinct ability to invade intact vascular endothelium creating septic thrombosis. The hyphae of mucormycosis are large, non-septate, and frequently identified along the internal elastic lamina of the vascular wall. Microscopically, there is vascular fungal invasion with secondary vasculitis, septic thrombi, and widespread tissue necrosis.

Chronic invasive fungal sinusitis is frequently a result of infection with Aspergillus species in an otherwise healthy patient. The disease process has an insidious onset followed by an unrelenting course. Histopathology demonstrates tissue-invasive fungal elements surrounded by a sclerosing granulomatous response. In cases of Aspergillus, GMS stain highlights the wall of the invasive pathogen demonstrating the slender, septate, branching hyphae. This organism can invade vessels leading to septic thrombosis and extension to the brain. Aspergillus species are capable of producing both invasive and non-invasive fungal sinus disease. Identification of this organism does not determine classification of the sinus disease process. Invasive and non-invasive disease are defined based upon clinical, radiographic, and histopathologic criteria.

Non-Invasive Fungal Sinus Disease

Mycetoma is a "fungus ball" of saprophytic organisms growing within a sinus cavity, much like a tissue culture. It is most frequently seen in healthy patients with alteration in sinus drainage following trauma. The organism does not invade surrounding tissues and produces little inflammatory response. *Aspergillus* species are a common etiology.

Allergic Fungal Sinusitis

It is remarkable that allergic fungal sinusitis was not fully elucidated until recently. In 1981, Millar described the histologic similarities common to expelled pulmonary plugs from allergic bronchopulmonary *Aspergillus* and sinus samples from allergic Aspergillus paranasal sinusitis.[7] In 1983, Katzenstein collected a series of seven patients with what he called "allergic *Aspergillus* sinusitis," emphasizing the characteristic histologic findings of inspissated mucin, degenerating eosinophils, Charcot-Leyden crystals and fungal hyphae, along with an associated history of nasal polyps and allergies.[8] De Juan, Green and Iliff concurrently reported the histopathologic findings in two children with a very similar allergic periorbital process.[9] De Juan et al stressed the significance of a history of hypersensitivity, and the importance of treating the allergic component of this disease process. These observations were critical and ahead of their time.

Robson, in 1989, introduced the term "allergic fungal sinusitis," when it was recognized that other fungal organisms besides *Aspergillus* were common culprits.[10] It now appears that the most prevalent inciting organisms are the dematiaceous fungi including *Bipolaris* and Curvularia.[4,11] Dematiaceous fungi are ubiquitous soil contaminants. They are darkly colored due to the presence of melanin in their cell walls, and, as such, may stain with the Fontana stain.

Until recently, many reports of AFS unfortunately equated compressive bone erosion with the concept of "invasive" disease. This resulted in therapeutic confusion, with some patients who did not have invasive disease receiving potentially toxic Amphotericin B therapy. AFS is characteristic in its absence of fungal tissue invasion.[12]

Histopathologic examination confirms that the opacification of the paranasal sinuses in AFS is due to allergic mucin. This material consists of necrotic or partially necrotic eosinophils suspended in lakes of laminated mucinous material. Charcot-Leyden crystals (hexagonal crystal proteins associated with degraded eosinophils), and fungal elements are suspended in this inspissated mucin. There is a characteristic absence of fungal invasion of bone or soft tissue, purulent exudates, tissue necrosis, or granulomatous inflammation. This disease process is an allergic response to these saprophytic fungi suspended within the paranasal sinuses. The patient history, imaging features, and histopathology of allergic fungal sinusitis provide a characteristic pattern for appropriate diagnosis and management. Confident diagnosis and control of the allergic response are therapeutic cornerstones. ❑

References

1. Maltinski G. Nasal disorders and sinusitis. Primary Care 1998; 25(3): 663-683.
2. Nash DR, Fireman P. Allergic fungal sinusitis. Immunol Allergy Clin North Am 1998; 18(3): 695-710.
3. Carter KD, Graham SM, Carpenter KM. Ophthalmic manifestations of allergic fungal sinusitis. Am J Ophthalmol 1999; 127(2): 189-195.
4. Torres C, Ro JY, El-Naggar AK, et al. Allergic fungal sinusitis: a clinicopathologic study of 16 cases. Hum Pathol 1996; 27(8): 793-799.
5. Ponikau JU, Sherris DA, Kern EB, et al. The diagnosis and incidence of allergic fungal sinusitis. Mayo Clin Proc 1999; 74: 877-884.
6. Ence BK, Gourley DS, Jorgensen NL, et al. Allergic fungal sinusitis. Am J Rhinology 1990; 4(5): 169-178.
7. Millar JW, Johnston A, Lamb D. Allergic aspergillosis of the maxillary sinuses (Abstract). Thorax 1981; 36: 710.
8. Katzenstein AA, Sale SR, Greenberger PA. Pathologic findings in allergic aspergillus sinusitis: a newly recognized form of sinusitis. Am J Surg Pathol 1983; 7: 439-443.
9. De Juan E Jr, Green WR, Iliff NT. Allergic periorbital mucopyocele in children. Am J Ophthalmol 1983; 96: 299-303.
10. Robson JM, Hogan PG, Benn RA, Gatenby PA. Allergic fungal sinusitis presenting as a paranasal sinus tumor. Aust N Z J Med 1989; 19(4): 351-353.
11. Friedman GC, Hartwick RWJ, Ro JY, et al. Allergic fungal sinusitis: report of three cases associated with dematiaceous fungi. Am J Clin Pathol 1991; 96(3): 368-372.
12. Allphin AL, Strauss M, Abdul-Karim FW. Allergic fungal sinusitis: problems in diagnosis and treatment. Laryngoscope 1991; 101: 815-820.