

THE JOURNAL OF Allergy AND Clinical Immunology

September 2001 • Volume 108 • Number 3

Antileukotriene therapy for allergic fungal sinusitis

- [Previous article](#) in Issue
- [Next article](#) in Issue
- [Drug links](#) from Mosby's DrugConsult
- [Genetic information](#) from OMIM
- Citation of this Article
 - View on [PubMed](#)
 - Download in [citation manager format](#)
 - Download in [Medlars format](#)
- [Related articles](#) in PubMed

To the Editor:

Allergic fungal sinusitis (AFS) is a noninvasive form of fungal sinusitis. It is characterized as an allergic and immunologic response to fungi (usually dematiaceous) found within inspissated sinus allergic mucin. Patients with AFS are atopic, have hypertrophic rhinosinusitis-polyp formation, are immunocompetent, and often live in the southern or southwestern United States.^{1,2} Surgery is required to remove all fungal-containing allergic mucin and associated dysfunctional sinus mucosa. Postoperative medical management includes antihistamines, allergen immunotherapy, and topical and oral corticosteroids.³⁻⁵ Surgical recurrence rates remain high, especially without postoperative medical management. The pathophysiology of AFS has been proposed to lie within the biology of chronic hypertrophic rhinosinusitis and shares immunologic features with allergic bronchopulmonary aspergillosis.^{2,6} The first published treatment of AFS with the leukotriene receptor antagonist montelukast is described below.

The patient was a 41-year-old healthy woman who had allergic rhinitis since childhood and had previously been responsive to allergen immunotherapy. At age 28, 2 years after moving to Phoenix, Ariz, she required bilateral endoscopic sinus surgery for chronic hypertrophic

rhinosinusitis with nasal polyps. At age 29, she underwent a right-sided Caldwell-Luc procedure for persistent disease.

Rhinosinusitis with hyposmia and nasal cast production recurred again postoperatively. She was treated for over 9 years with topical corticosteroid nasal sprays, antihistamines, short courses of oral corticosteroids, and antibiotics. She then underwent endoscopic sinus surgery at age 38 for bilateral ethmoid, maxillary, and left sphenoid-right frontal hypertrophic sinusitis and nasal polyps. The results of surgical histopathology were positive for AFS according to diagnostic criteria previously published.^{1 2} The surgical fungal culture grew *Bipolaris spicifera*.

Within 7 months postoperatively, a repeat sinus computed tomography (CT) scan showed recurrent hypertrophic sinus disease completely opacifying the right ethmoid sinus and extending down into the right maxillary sinus with occlusion of the right nasal antral window. She then underwent her fourth sinus surgery. Inspissated extramucosal material characteristic for allergic mucin was described grossly in the operative report, but surgical laboratory test results were not obtained.

At age 41 (3 years after her fourth sinus surgery), another sinus CT was obtained for evaluation of persistent rhinosinusitis (Fig 1).

Fig. 1. Sinus CT scan obtained shortly before starting montelukast. Findings shown here include hypertrophic rhinosinusitis filling the right maxillary and ethmoid sinuses, hyperattenuation of right maxillary sinus contents, left inferior nasal turbinate hypertrophy, and nasal septal bowing to the left.



Click on Image to view full size

Repeat sinus surgery was scheduled by a third surgeon, and the patient was sent for allergy-

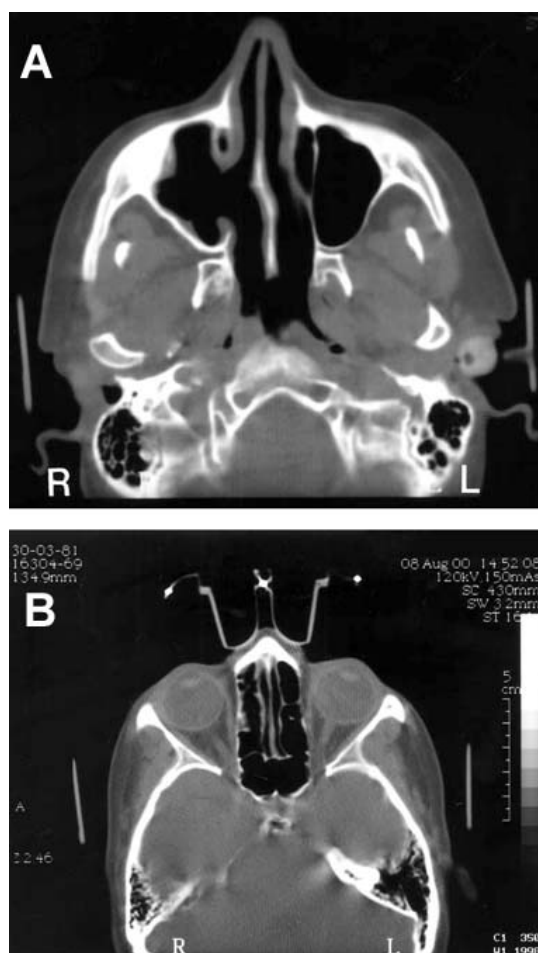
immunology evaluation.

With the exception of mild iron deficiency anemia, she was otherwise healthy. She did not have a history for asthma and was a lifelong nonsmoker. She was not allergic to aspirin, nonsteroidal anti-inflammatory drugs, or other medications. She had an indoor dog, but there were no cats, other animals, or smokers at home. Her mother had a history of chronic rhinosinusitis. The only medication used was budesonide nasal aerosol (4 sprays each nostril once daily). Physical examination showed a large right-sided nasal polyp and a left hypertrophic inferior nasal turbinate.

The laboratory evaluation disclosed positive type I immediate hypersensitivity skin test results to multiple pollens, cat dander, and *Aspergillus fumigatus* and *Helminthosporium* species mold spores by using the prick and intradermal methods, as previously described.² *B spicifera* was not available for skin testing. A complete blood count with differential showed mild anemia. Other screening laboratory test results were within normal ranges, including liver function; renal function; serum glucose; cholesterol; calcium; electrolytes; erythrocyte sedimentation rate; total serum IgG, IgA, IgM, and IgE (29 IU/mL); urinalysis; and delayed hypersensitivity skin tests for T-cell anergy, as previously described.² Results of chest radiography were unremarkable.

The patient was given 10 mg of oral montelukast daily, and the topical budesonide was continued as before. She related rapid improvement in symptoms of rhinosinusitis on her follow-up visit 1 month later. Nasal examination showed resolution of the previous hypertrophic mucosal findings. A repeat sinus CT scan demonstrated clearing of the previous hypertrophic sinus mucosal disease and associated radiographic hyperattenuation (Fig 2).

Fig. 2. Sinus CT scan shows clearing of disease after 1 month of montelukast treatment. Residual nasal septal bowing to the left persists. **A**, Image taken through the maxillary sinuses. **B**, Image taken through the ethmoid and sphenoid sinuses.



Click on Image to view full size

Plans for the fifth sinus surgery were canceled.

The sinus mucosal histopathology in patients with AFS and in other patients with chronic hypertrophic rhinosinusitis recapitulates asthma.^{2,7} Leukotrienes are involved in the pathophysiology of asthma. Analogously, leukotriene levels are elevated in sinus mucosa and nasal polyp tissue,⁸ as well as in sinus lavage fluid,⁹ from patients with chronic hypertrophic rhinosinusitis. A recent report of 36 patients with chronic hypertrophic rhinosinusitis treated with either zileuton or zafirlukast reported that 72% had subjective improvement, and 50% had objective improvement or stabilization of sinus disease.¹⁰ Zileuton has also been reported to reduce the symptoms of hyposmia and rhinorrhea in patients with the triad of hypertrophic rhinosinusitis, asthma, and aspirin sensitivity.¹¹

The favorable response to montelukast in AFS suggests a fundamental role for cysteinyl leukotrienes in its pathophysiology, which is not surprising given the strong presence of eosinophils in the disorder.^{2,6,12} The resolution of both the mucosal and extramucosal components of AFS in this patient demonstrated that reversible leukotriene-dependent inflammation and sinus mucosal hypertrophy, rather than true mucosal hyperplasia, characterized the mucosal abnormalities and anatomic findings assessed clinically and by means of sinus CT. Whether this improvement with an antileukotriene can be generalized,

at least to some extent, to most patients with AFS has not been published. Our experience has generally been favorable.⁶ Because of the significant response in this patient, antileukotriene therapy should be further studied and considered for future treatment of patients with AFS as well as other patients with chronic hypertrophic rhinosinusitis.

1/8/117592

doi:10.1067/mai.2001.117592

Mark S. Schubert, MD, PhD

Clinical Associate Professor of Medicine, Department of Medicine, University of Arizona College of Medicine, Phoenix and Tucson, Ariz and Allergy Asthma Clinic, Ltd, 31 W Camelback Rd, Phoenix, AZ 85013

References

TOP

1. deShazo RD, Swain RE. Diagnostic criteria for allergic fungal sinusitis. *J Allergy Clin Immunol* 1995;96:24-35.

MEDLINE

ABSTRACT

FULL TEXT

2. Schubert MS, Goetz DW. Evaluation and treatment of allergic fungal sinusitis. I. Demographics and diagnosis. *J Allergy Clin Immunol* 1998;102:387-94.

MEDLINE

ABSTRACT

FULL TEXT

3. Kupferberg SB, Bent JP. Allergic fungal sinusitis in the pediatric population. *Arch Otolaryngol Head Neck Surg* 1996;122:1381-4.

MEDLINE

4. Mabry RL, Marple BF, Folker RJ, Mabry CS. Immunotherapy in the treatment of allergic fungal sinusitis: three years' experience. *Otolaryngol Head Neck Surg* 1998;119:648-51.

MEDLINE

ABSTRACT

FULL TEXT

5. Schubert MS, Goetz DW. Evaluation and treatment of allergic fungal sinusitis. II. Treatment and follow-up. *J Allergy Clin Immunol* 1998;102:395-402.

MEDLINE

ABSTRACT

FULL TEXT

6. Schubert MS. Medical treatment of allergic fungal sinusitis. *Ann Allergy Asthma Immunol* 2000;85:90-101.

MEDLINE

7. Hamilos DL. Chronic sinusitis. *J Allergy Clin Immunol* 2000;106:213-27.

[MEDLINE](#)

[ABSTRACT](#)

[FULL TEXT](#)

8. Ogino S, Irifune M, Harada T, Kikumori H, Matsunaga T. Arachidonic acid metabolites in human nasal polyps. *Acta Otolaryngol Suppl* 1993;501:85-7.

[MEDLINE](#)

9. Georgitis JW, Matthews BL, Stone B. Chronic sinusitis: characterization of cellular influx and inflammatory mediators in sinus lavage fluid. *Int Arch Allergy Immunol* 1995;106:416-21.

[MEDLINE](#)

10. Parnes SM, Chuma AV. Acute effects of antileukotrienes on sinonasal polyposis and sinusitis. *ENT J* 2000;79:18-25.

11. Dahlen B, Nizankowska E, Szczeklik A, Zetterstrom O, Bochenek G, Kumlin M, et al. Benefits from adding the 5-lipoxygenase inhibitor zileuton to conventional therapy in aspirin-intolerant asthmatics. *Am J Respir Crit Care Med* 1998;157:1187-94.

[MEDLINE](#)

12. Khan DA, Cody TC III, George TJ, Gleich GJ, Leiferman KM. Allergic fungal sinusitis: an immunohistologic analysis. *J Allergy Clin Immunol* 2000;106:1096-101.

[MEDLINE](#)

[ABSTRACT](#)

[FULL TEXT](#)