

Allergic *Aspergillus* sinusitis with concurrent allergic bronchopulmonary *Aspergillus*: Report of a case

Theodore H. Sher, MD, and Howard J. Schwartz, MD Cleveland, Ohio

A 42-year-old female patient with previously diagnosed seasonal allergic rhinitis, anaphylactic food sensitivity, and exertional asthma is described who developed concomitant allergic bronchopulmonary aspergillosis and allergic aspergillus sinusitis. We believe that the present article is the first fully documented case in which these two syndromes coexist in the same patient. (J ALLERGY CLIN IMMUNOL 1988;81:844-6.)

Aspergillus is an ubiquitous mold found in many environments. Large numbers of spores are present in the air that may be inhaled and, under appropriate conditions, multiply in the host. The respiratory tract is involved in >90% of patients affected by *Aspergillus* that may cause a variety of diseases. ABPA, first reported in England almost 35 years ago, is characterized by asthma, recurrent lung infiltrates, eosinophilia, elevated IgE levels, and proximal bronchiectasis.¹⁻⁶ A new distinct clinical syndrome termed AAS has recently been described that shares similar histopathologic features with ABPA but affects the paranasal sinuses rather than the lung.^{7,8} The present study is, to our knowledge, the first fully documented case in which these two syndromes coexist.

CASE REPORT

A 42-year-old woman was evaluated originally in 1982 with a history of progressive seasonal allergic rhinitis, anaphylactic food allergy, episodic wheezing precipitated by exertion and allergen exposure, and recurrent sinusitis since childhood. At age 21 years, a left maxillary antrostomy was performed. At the time of initial allergy evaluation in 1982, the findings were consistent with allergic rhinitis. The nasal mucous membranes were edematous and boggy, the chest examination was normal, and allergy skin tests revealed positive prick test reactions to tree, grass, and weed pollens, several molds, including *Aspergillus*, *Alternaria*, *Cladosporium* (*Hormodendrum*), and *Penicillium*, house dust, dust mite, and several animal danders. Environmental con-

Abbreviations used

ABPA: Allergic bronchopulmonary aspergillosis
AAS: Allergic *Aspergillus* sinusitis
Af: *Aspergillus fumigatus*
CT: Computed tomography

trol measures and antihistamine/decongestant therapy were successful in controlling symptoms during the next 2 years.

In August 1984, the patient presented with a 1-month history of progressive dyspnea and wheeze associated with rhinitis symptoms. At that time, she started receiving a combination of antiasthma medications, including theophylline, metaproterenol, beclomethasone, and cromolyn. A serum IgE was 1002 IU/cc. Immunotherapy was declined.

During the next 2 years, the patient was observed on three separate occasions for symptoms of acute asthmatic bronchitis. In August 1986, a severe episode of sinusitis developed that was unresponsive to antibiotics. CT scan of the sinuses revealed a soft tissue density filling the left maxillary sinus without evidence of associated bone changes. A small amount of mucosal thickening was also present, involving the ethmoid sinuses bilaterally. After appropriate consultation, a left-sided Caldwell-Luc procedure was performed, and at the time of surgery, polypoid fragments of respiratory mucosa with marked edema, intense eosinophilic infiltration with some necrotic cells, Charcot-Leyden crystals, and mucin were observed. Branching septate hyphae were also found. Af was cultured from both the mucopurulent discharge and the pathologic tissue.

Laboratory evaluation revealed the following: The total serum IgE was 13084 ng/ml.* Af precipitating antibody was positive.* Index for IgE antibody to Af was 3.38, and the index for IgG antibody to Af was 4.14, both results

From the Department of Medicine and Pediatrics, Case Western Reserve University School of Medicine, and University Hospitals, Cleveland, Ohio.

Received for publication June 15, 1987.

Accepted for publication Oct. 25, 1987.

Reprint requests: Howard J. Schwartz, MD, 1611 So. Green Road, So. Euclid, OH 44121.

*Assays performed by Dr. Paul Greenberger, Northwestern University School of Medicine, Chicago, Ill.

elevated and consistent with ABPA.* Total eosinophil count was 1355/mm³. Serum protein electrophoresis and immunoglobulins were normal. The immediate type skin test with Af was positive. The skin test at 6 hours after placement was negative.

Chest roentgenograms revealed parenchymal scarring in the upper lobes. The hila were retracted upward. There was no evidence of active pulmonary disease present. A CT of the chest revealed bronchiectasis of the right upper lobe involving the apical and posterior segments, along with associated thickening of the bronchial walls in the area. Multiple areas of increased density were scattered throughout the lung fields consistent with interstitial scarring.

Treatment with prednisone was begun at a dose of 0.5 mg/kg/day with good response of both nasal and pulmonary symptoms. The total serum IgE has dropped to 4231 ng/ml within 1 month of therapy, and the patient continues to do well as the prednisone is tapered.

DISCUSSION

Since ABPA was first described in 1952 by Hinson et al.,¹ increasing numbers of cases have been identified. Improved diagnostic criteria for identifying this disease have been developed.²⁻⁹ The clinical diagnostic features of ABPA include the following: (1) asthma, (2) peripheral blood eosinophilia, (3) immediate skin test reactivity to Af antigen, (4) precipitating antibodies to Af antigen, (5) history of pulmonary infiltrates, (6) proximal (central) bronchiectasis, (7) markedly elevated total serum IgE, and (8) elevated serum IgE-Af and IgG-Af.^{3, 10} Other characteristics may include a positive sputum culture for Af, a history of expectoration of brown mucus plugs, and Arthus-type skin reactivity to intracutaneous testing with Af antigen.

In addition to causing several types of pulmonary disease, *Aspergillus* species can affect the paranasal sinuses in both an invasive and noninvasive fashion.¹¹ Invasive aspergillosis usually occurs in immunocompromised persons and may be a life-threatening disease. Aspergilloma or mycetoma is a noninvasive form that is analogous to pulmonary mycetomas and appears as a localized mass within a thin walled cavity. AAS is the most recently described category of *Aspergillus* sinus disease. It usually presents as pansinusitis and progresses from a unilateral to a bilateral condition. Patients may be atopic, have a history of bronchial asthma, and may have a past history of paranasal sinus surgery.

Katzenstein et al.⁷ described seven patients with

TABLE I. Diagnostic criteria for ABPA in patient J.G.

Obstructive airway disease	Reversible
Total IgE	13084 ng/mL
Total eosinophil count	1355/mm ³
Precipitating antibody to Af	Positive
Specific antibody to Af	
Index for IgE antibody	3.38
Index for IgG antibody	4.14
Immediate skin test reactivity to Af	Positive
Chest CT scan	
Bronchiectasis	Right upper lobe
Changes	Interstitial fibrotic

AAS who had histologic findings in their sinuses indistinguishable from the findings observed in mucoid impaction of bronchi in tissue from patients with ABPA. The mucoid material was termed allergic mucin and contained eosinophils, scattered fungal hyphae, cellular debris, and Charcot-Leyden crystals. Chest roentgenograms were normal, and almost all patients had asthma. All patients had opacification of sinuses observed on x-ray films and nasal polyps. There was no evidence of tissue invasion by hyphae forms. Serum precipitin reactions with Af were demonstrated in six patients, total serum IgE levels were elevated in three patients, specific IgE and IgE-Af were elevated in one patient, and none of their patients had elevated levels of both IgE and IgG antibodies to Af. There was no suggestion of concurrent ABPA in any of the patients reported.

Our patient has evidence of AAS and concurrent ABPA. She initially presented with a prior history of bronchial asthma, sinusitis, a left maxillary antrostomy at age 21 years, and upper respiratory tract allergy. Progressive asthma symptoms during the preceding 2 years required intense bronchodilator therapy. Multiple courses of antibiotics were necessary to control acute flares of rhinosinusitis complicating the asthma. An otolaryngologic consultation was obtained because of the development of recalcitrant sinusitis unresponsive to medical therapy.¹¹

At surgery, findings consistent with AAS were found, which included intense inflammatory eosinophilia, polypoid mucosa completely filling the left maxillary sinus, and septate fungal hyphae resembling *Aspergillus* species. The culture was positive for Af. There was no evidence of tissue invasion. Unlike patients reported by Katzenstein et al.,⁷ our patients also had evidence of ABPA that is summarized in Table I.

*Assays performed by Dr. Paul Greenberger, Northwestern University School of Medicine, Chicago, Ill.

The IgG and IgE anti-Af antibody indices are both elevated. These are classic findings in patients with ABPA and are distinguishing characteristics as compared to mold-sensitive patients with asthma and without ABPA.^{3, 12} After 1 month of large doses of prednisone therapy, the total IgE declined from 13084 ng/ml to 4231 ng/ml, which is also observed with prednisone treatment of ABPA. The patient is receiving a tapering course of prednisone with no recurrences of either AAS or ABPA.

We are aware of one prior case report of possible concomitant ABPA and AAS.¹³ A 24-year-old woman developed recurrent nasal obstruction, rhinorrhea, blood-tinged nasal casts, and nasal polyps. Radiographic opacification of her sinuses was present. A Caldwell-Luc drainage procedure and polypectomy was performed after unsuccessful medical treatment. Cultures obtained at surgery grew Af. Three months after surgery, she was noted to have a right upper lobe infiltrate, and a diagnosis of ABPA was made based only on positive immediate and late skin tests, serum precipitins to Af, and a pulmonary infiltrate with eosinophilia. Dramatic response of both lung and nasal lesions were obtained on corticosteroid therapy at that time, and symptoms recurred when the corticosteroids were stopped. Our patient differs from this case report because of the additional diagnostic criteria applied to make the diagnosis of concomitant ABPA and AAS, which were not available at that time. These diagnostic criteria include elevated IgE-Af, IgG-Af, elevated total IgE, and the presence of allergic mucin in the diseased sinuses.

The significance of concurrent ABPA and AAS is unclear. It has been speculated that ABPA begins with inhalation and trapping of Af spores in the viscid secretions of the respiratory tract of the subject with asthma. Af germinates and forms mycelia at body temperature, continually shedding antigens into the tissues, which subsequently provokes an immunologic and concomitant inflammatory response. Bronchial wall damage and a surrounding pulmonary eosinophilic consolidation ultimately develop. It appears that both IgE- and IgG-precipitating antibody are required for tissue damage to occur.^{3, 4} The possibility of an analogous pathogenic mechanism involved in the development of AAS must be considered. Our patient is atopic with a long history of prior allergic respiratory disease similar to a patient with AAS reported by Goldstein et al.¹¹ Atopic disease was also present in three of seven patients with AAS reported by Katzenstein et al.⁷ However, none of their patients developed the immunologic findings characteristic of patients with ABPA that must cast some doubt as to whether a common pathogenic mechanism causes the

tissue injury in both parts of the respiratory tract. Sinusitis occurs with some frequency in asthma, especially in recalcitrant disease.^{12, 14, 15} Nonspecific sinusitis has been reported in one series of patients with ABPA.¹⁶

We believe our patient has coexisting AAS and ABPA. It is unclear whether or not this is a random concurrence of diseases. The relationship between these two disorders is, at present, speculative. The possibility exists that fungal antigens from the sinuses may seed the lungs and play a role in the development of ABPA in predisposed subject with asthma. Appropriate therapy for AAS may alter the natural history of the disease and prevent the future development of ABPA in these patients.

REFERENCES

1. Hinson KFW, Moon AJ, Plummer WS. Bronchopulmonary aspergillosis. *Thorax* 1952;7:317.
2. Rosenberg M, Patterson R, Mintzer R, Cooper BJ, Roberts M, Harris KE. Clinical and immunologic criteria for the diagnosis of allergic bronchopulmonary aspergillosis. *Ann Intern Med* 1977;86:405.
3. Greenberger PA. Allergic bronchopulmonary aspergillosis. *J ALLERGY CLIN IMMUNOL* 1984;74:645.
4. Slavin RG. Allergic bronchopulmonary aspergillosis. In: Middleton EJ Jr, Reed CR, Ellis E, eds. *Allergy: principles and practice*. St. Louis: The CV Mosby Co, 1983:1067-84.
5. Imbeau SA, Nichols D, Flaherty D, Valdivia E, et al. Allergic bronchopulmonary aspergillosis. *J ALLERGY CLIN IMMUNOL* 1978;62:243.
6. Ricketti AJ, Greenberger PA, Mintzer RA, Patterson R. Allergic bronchopulmonary aspergillosis. *Arch Intern Med* 1983;143:1553.
7. Katzenstein A, Sale SR, Greenberger PA. Allergic *Aspergillus* sinusitis: A newly recognized form of sinusitis. *J ALLERGY CLIN IMMUNOL* 1983;72:89.
8. Katzenstein A, Sale SR, Greenberger PA. Pathologic finding in allergic *Aspergillus* sinusitis. *Am J Surg Pathol* 1983;7:439.
9. Wang JLF, Patterson R, Rosenberg M, Roberts M, Cooper BJ. Serum IgE and IgG antibody activity against *Aspergillus fumigatus* as a diagnostic aid in allergic bronchopulmonary aspergillosis. *Am Rev Respir Dis* 1978;117:917.
10. Patterson R, Greenberger PA, Ricketti AJ, Roberts M. A radioimmunoassay index for allergic bronchopulmonary aspergillosis. *Ann Intern Med* 1983;99:18.
11. Goldstein MF, Atkins PC, Cogen FC, Romstein MJ, Levine RS, Zweiman B. Allergic *Aspergillus* sinusitis. *J ALLERGY CLIN IMMUNOL* 1985;76:515.
12. Slavin R, Cannon R, Friedman W, et al. Sinusitis and bronchial asthma. *J ALLERGY CLIN IMMUNOL* 1980;66:250.
13. Safirstein B. Allergic bronchopulmonary aspergillosis with obstruction of the upper respiratory tract. *Chest* 1976;70:788.
14. Friedman R, Ackerman M, Wald E, et al. Asthma and bacterial sinusitis in children. *J ALLERGY CLIN IMMUNOL* 1984;74:185.
15. Berman S, Mathison D, Stevenson D, et al. Maxillary sinusitis and bronchial asthma: correlation of roentgenograms, cultures, and thermograms. *J ALLERGY CLIN IMMUNOL* 1974;53:311.
16. McCarthy D, Pepys J. Allergic bronchopulmonary aspergillosis: chemical features. *Clin Allergy* 1971;1:261.