
Case report

Contemporaneous occurrence of allergic bronchopulmonary aspergillosis, allergic *Aspergillus* sinusitis, and aspergilloma

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Background: The clinical categories of *Aspergillus*-related respiratory disorders usually remain mutually exclusive. The coexistence of allergic bronchopulmonary aspergillosis (ABPA) with aspergilloma is uncommon, whereas concurrent ABPA and allergic *Aspergillus* sinusitis (AAS) is rare. The association of these 3 clinical entities has previously been documented only once in a patient who had earlier been operated on for an aspergilloma before the diagnoses of ABPA and AAS were established.

Objective: To describe an adult in whom ABPA, AAS, and aspergilloma were diagnosed simultaneously.

Methods: Spirometry, radiography, computed tomography, skin allergy testing with *Aspergillus* antigens, serum precipitins against *Aspergillus*, total and specific IgE, functional endoscopic sinus surgery, and fungal culture were performed.

Results: A 26-year-old man who had asthma and rhinitis since childhood presented with hemoptysis. Serial chest radiographs revealed transient pulmonary infiltrates and an aspergilloma. Computed tomography of the thorax confirmed the aspergilloma and showed bilateral central bronchiectasis along with patchy infiltrates. Strong bands of precipitins were detected against *Aspergillus fumigatus*, and intradermal testing with *Aspergillus* antigens elicited strong type I and III hypersensitivity reactions. Specific IgE and IgG antibodies against *A fumigatus* were positive, and total IgE levels were significantly elevated. Peripheral blood eosinophilia was also detected. Sinus involvement was confirmed on computed tomography, and pathologic material obtained by functional endoscopic sinus surgery demonstrated allergic mucin that contained fungal elements. In addition, *A fumigatus* was cultured.

Conclusions: ABPA, AAS, and aspergilloma can occur simultaneously in the same patient.

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INTRODUCTION

The spectrum of *Aspergillus*-associated respiratory disorders ranges from saprophytic colonization of the respiratory tract to rapidly invasive disseminated disease and can be categorized as allergic aspergillosis, aspergilloma, and invasive aspergillosis.¹ Allergic bronchopulmonary aspergillosis (ABPA) remains the most frequently recognized manifestation of allergic aspergillosis. In allergic *Aspergillus* sinusitis (AAS), a more recently defined clinical entity,^{2,3} mucoid impaction akin to that in ABPA occurs in the paranasal sinuses. Saprobic colonization of the airways ensues in aspergilloma formation in cavities and sinuses.

The 3 clinical categories of *Aspergillus*-related respiratory disorders usually remain mutually exclusive.⁴ Although cavitation is known to occur in ABPA, the coexistence of ABPA and aspergilloma is uncommon,^{5,6} whereas concurrent ABPA and AAS is a rarity.⁷ The association of ABPA, AAS, and aspergilloma in a single patient has been previously docu-

mented only once,⁸ more than a decade ago. The patient had earlier been operated on for an aspergilloma before the diagnoses of ABPA and AAS were established. To our knowledge, we describe for the first time a patient in whom ABPA, AAS, and aspergilloma were diagnosed simultaneously.

CASE REPORT

A 26-year-old, human immunodeficiency virus–negative, nonsmoking man was referred to our institution for evaluation of progressive pulmonary disease since childhood. His clinical course was characterized by progressive wheezing dyspnea and cough dating back to early childhood accompanied by repeated bouts of sneezing, rhinorrhea, nasal blockage, and postnasal discharge. For these complaints, he had received frequent short courses of oral prednisolone along with oral bronchodilators. He was never prescribed inhaled medications. During the past year, the patient had experienced productive cough and multiple episodes of hemoptysis, 2 of which necessitated blood transfusions. Nine months before referral, based on his symptomatic and radiologic profile, he began antituberculous therapy despite sputum smears and cultures being negative for *Mycobacterium tuberculosis*. The patient did not experience any relief but was still undergoing antituberculous therapy when he reported to us.

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On interrogation, he admitted to a history of passage of brownish plugs in the sputum and from the nostrils. His father had asthma. Physical examination revealed a young man in no acute distress but with mild pallor. Diaphragmatic excursions were within normal limits. On auscultation, vesicular breath sounds along with bilateral polyphonic expiratory rhonchi and coarse crepitations were audible. The nasal mucosa on the left side was erythematous with thick mucopurulent secretions. Left maxillary sinus tenderness was also elicited.

Laboratory evaluation showed a hemoglobin level of 9.6 g/dL, and the total leukocyte count was 10,700/ μ L with 24% eosinophils. Pulmonary function testing showed a forced vital capacity (FVC) of 2.82 L (56% of predicted), forced expiratory volume in 1 second (FEV₁) of 1.55 L (37% of predicted), and an FEV₁/FVC ratio of 55%. There was a 220-mL increase in the FEV₁ after inhalation of 200 μ g of salbutamol, which was suggestive of moderately severe airflow limitation with reversibility.

A review of 8 serial chest radiographs performed during a period of 1 year before referral revealed transient pulmonary infiltrates with multiple cavitating lesions. An intracavitary round density with an "air crescent" sign, better defined on an apicogram (Fig 1), was visible in the right upper lobe. This opacity showed positional change. Computed tomography (CT) of the thorax confirmed the presence of a fungal ball in one of the bronchiectatic cavities (Fig 2). Bilateral saccular bronchiectasis was also visualized proximally, a feature pathognomonic of ABPA. Left maxillary sinus haziness was seen on a radiograph of the paranasal sinuses, and the CT (Fig 3) showed soft tissue masses in the left maxillary sinus, bilateral sphenoid sinuses, left middle meatus, and part of the left nasal cavity. Hyperdense lesions, suggestive of inspissated secretions, were visualized within the soft tissue masses. However, there was no evidence of bony destruction or intracranial extension.



Figure 1. Chest radiograph (apicogram) showing a rounded opacity with "air crescent" sign in the right upper lobe, suggestive of an aspergilloma. A V-shaped opacity is also visible adjacent to the fungal ball.

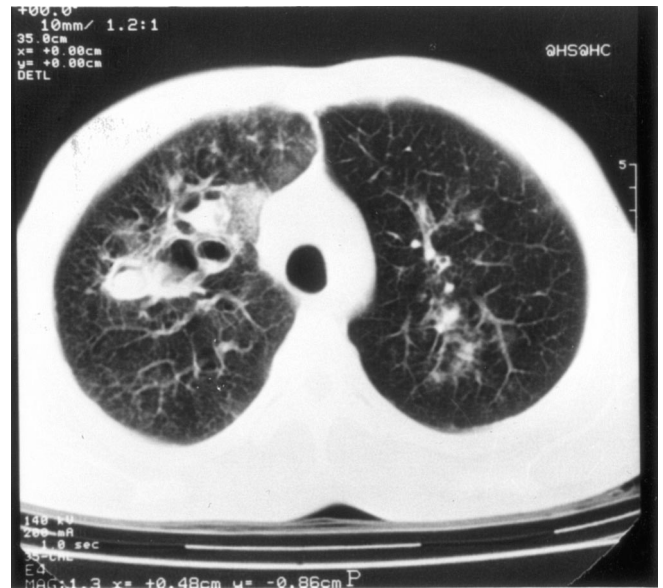


Figure 2. Computed tomography of the thorax at the level of the upper lobes confirming the aspergilloma in the right upper lobe. Central bronchiectasis is present bilaterally. Infiltrations are also seen in the left upper lobe.



Figure 3. Computed tomography of the paranasal sinuses showing complete opacification of the left maxillary sinus and partial opacification of the left ethmoid sinus. Hyperdense lesions, suggestive of inspissated secretions, are also visible within the soft tissue masses.

Intradermal challenge with *Aspergillus* antigens elicited both type I and type III hypersensitivity reactions to *Aspergillus fumigatus*, *Aspergillus flavus*, *Aspergillus niger*, and *Aspergillus tamarii*. Gel diffusion studies detected precipitin bands against *A. fumigatus*. The total IgE count was 34,132 IU/mL, and *A. fumigatus* specific IgE and IgG were positive. Histopathologic examination of the material obtained by functional endoscopic sinus surgery from the left maxillary sinus showed inspissated inflammatory exudates with mucin that was infiltrated by eosinophils. Fungal hyphae of *As-*

pergillus were also seen interspersed in the allergic mucin (Fig 4). Culture of this material yielded *A fumigatus*.

A diagnosis of concomitant ABPA, AAS, and aspergilloma was established (Table 1) as per previously described criteria.^{7,9-11} The fungal ball was presumed to be an aspergilloma. This was based on the strong evidence for the presence of *Aspergillus*. The patient was given a 30-mg/d dose of oral prednisolone (0.5 mg/kg daily). Within 2 weeks, there was a noteworthy improvement in the respiratory and nasal symptoms. Prednisolone was reduced to 30 mg biweekly for 3 months and then tapered off by 5 mg every month. The total IgE level dropped to 20,998 IU/mL after 2 months, whereas serum precipitins were no longer detectable. Although the aspergilloma persisted, there was a remarkable improvement in the chest radiographs. The patient was maintained with inhaled bronchodilators and inhaled and intranasal corticosteroids. One and a half years later, he experienced a relapse symptomatically, radiologically, and serologically. The symptoms were abolished when prednisolone therapy was restarted in a biweekly regimen as was prescribed earlier. The patient is now symptom free while undergoing maintenance therapy with 1 to 2 short courses (7-10 days) of oral prednisolone per year. The aspergilloma was no longer visible in a subsequent thorax CT performed 3.5 years later.

DISCUSSION

The concurrent occurrence of ABPA, AAS, and aspergilloma in a patient is indeed a rarity. It is perhaps surprising that despite similar immunopathologic responses, the coexistence of ABPA and AAS is infrequent.¹² In our earlier analysis⁷ of 95 patients with ABPA, 22 had radiologic evidence of sinusitis and AAS was diagnosed in 7 of the 9 patients who consented to undergo the surgical procedure required to establish the diagnosis. Recently, the term *sinobronchial allergic mycosis* (SAM syndrome) was coined to highlight the expression of fungal hypersensitivity in both upper and lower

Table 1. Diagnostic Criteria Fulfilled by Our Patient

Allergic bronchopulmonary aspergillosis	
1.	Presence of asthma, confirmed on spirometry
2.	Expectoration of golden brownish plugs in sputum
3.	Transient pulmonary infiltrates (fleeting shadows) on serial chest roentgenograms
4.	Peripheral blood eosinophilia
5.	Type I and type III skin hypersensitivity to <i>Aspergillus</i> antigens
6.	Elevated total serum IgE
7.	Precipitating antibodies against <i>A fumigatus</i>
8.	Specific IgE and IgG against <i>A fumigatus</i>
9.	Central bronchiectasis with normal tapering of distal bronchi on CT
Allergic <i>Aspergillus</i> sinusitis	
1.	Passage of golden brownish plugs from nostrils
2.	Roentgenologic evidence of sinusitis: hyperdense lesions within soft tissue masses on CT
3.	Presence of inspissated inflammatory exudates with allergic mucin infiltrated by eosinophils on evaluation of pathologic material from the left maxillary sinus
4.	Demonstration of fungal elements in sinus material
5.	Growth of <i>A fumigatus</i> from sinus material

Abbreviation: CT, computed tomogram.

airways.¹³ This description was on the basis of 5 patients, 3 of whom were earlier described by us^{8,14,15} for their unusual presentations. The authors also stated in the addendum that 4 other patients in our analysis⁷ also fulfilled the criteria for SAM syndrome enunciated by them.

The presence of nasal symptoms in a patient with ABPA should alert the physician to the possibility of coexisting AAS. This possibility is heightened if a history of passage of nasal and sputum plugs is elicited, as was seen in our patient and 4 of our 7 patients described earlier.⁷ We had earlier reported that one fourth of patients with perennial rhinitis had positive skin reactivity to *Aspergillus* antigens.¹⁶ We also recently determined the sensitization to *Aspergillus* antigens in 105 patients with bronchial asthma and found that 30 patients (29%) were sensitized to *Aspergillus* antigens.¹⁷ Eight patients (8%) fulfilled all 8 major criteria for the diagnosis of ABPA. Based on clinical and serologic parameters, our patients with *Aspergillus*-sensitive asthma had a significantly more severe form of the disease compared with those with a skin test positive to antigens other than *Aspergillus*.¹⁷ This was evidenced by longer duration of illness ($P < .001$), higher mean absolute eosinophil count ($P < .001$), and higher total serum IgE level ($P < .001$).¹⁷ It is thus imperative to identify all cases of asthma and/or rhinitis with positive skin reactivity to *Aspergillus* and exclude ABPA and/or AAS in them.

We reported cavitation in 11% patients with ABPA.¹⁸ Although cavitation and chronic lung damage appear to provide a favorable milieu for aspergilloma formation, aspergillomas are rather infrequent in patients with ABPA.^{5,6} Our patient had asthma and rhinitis since childhood, but hemoptysis had occurred only in the past year, which resulted in him



Figure 4. Photomicrograph of pathologic material from left maxillary sinus (methenamine silver staining, original magnification $\times 100$) showing hypha of *Aspergillus*.

receiving antituberculous therapy. Aspergilloma was most probably the cause of hemoptysis. This symptom is reported to be the most common presentation and is seen in up to 85% of the patients.¹⁹ It was postulated that aspergilloma formation could be accelerated by corticosteroid therapy in ABPA with cavitary lung disease.^{5,20} In our patient, intermittent prednisolone therapy in addition to inadequate treatment, before referral, for asthma could possibly have aided aspergilloma formation.

Radiologic techniques have always been crucial to the diagnosis of ABPA, AAS, and aspergilloma.^{21–23} Imaging techniques help to not only establish the diagnosis but also monitor the progress of the disease. Currently, CT of the thorax has emerged as the modality of choice for the demonstration of central bronchiectasis^{24,25} and aspergilloma. On a plain chest radiograph, aspergilloma is characterized by a well-defined ovoid dense lesion inside a cavity along with a crescent of air. This is the classic air crescent sign described by Pesle and Monod.²⁶ Radiologic techniques can demonstrate positional change when the fungal mass remains free within the cavity, as seen in our patient. Computed tomography of the paranasal sinuses too is essential to the diagnosis of AAS and is characterized by the presence of heterogeneous densities, signifying opacification of the sinuses, along with seriginous areas of increased attenuation.^{22,27}

The only patient⁸ in whom ABPA, AAS, and aspergilloma were present had earlier undergone left lower lobectomy for severe hemoptysis as a result of an aspergilloma in a bronchiectatic cavity. The diagnosis of ABPA and AAS was made later when the patient presented with collapse of the left lung and associated pleural effusion. In contrast, in this patient, all the 3 clinical entities, ABPA, AAS, and aspergilloma, were diagnosed concurrently. On follow-up, a CT performed 3.5 years later did not show any evidence of the aspergilloma. The British Thoracic and Tuberculosis Association²⁸ in a 3-year follow-up survey recorded spontaneous disappearance of aspergilloma in 3 of the 58 patients with aspergilloma in persistent lung cavities.

Our patient showed a remarkable response to a biweekly regimen of oral prednisolone, which we recently demonstrated to be as effective as an alternate day regimen generally used for the management of ABPA and AAS.²⁹ Since oral prednisolone is often given repeatedly for long periods in these patients, a biweekly regimen would help reduce the well-known adverse effects of long-term corticosteroid therapy.

Our case highlights the fact that ABPA, AAS, and aspergilloma can occur simultaneously in the same patient. In high tuberculosis-prevalent areas, upper lobe fibrocavitary disease along with fungal ball, as seen in our case, is often associated with inactive pulmonary tuberculosis.³⁰ Failure to recognize ABPA as the cause of this clinical condition could possibly result in diagnostic delay and increased morbidity. Furthermore, since asthma and sinusitis are 2 diseases often treated by physicians in 2 different specialties, the occurrence of AAS in ABPA and ABPA in AAS may easily be overlooked.

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