Treatment of Allergic Aspergillosis with Triamcinolone Acetonide Aerosol*


The successful management of a patient with allergic aspergillosis with triamcinolone acetonide for one year is reported. This patient had been maintained previously on systemic corticosteroids continuously for eight years. An initial attempt to withdraw systemic steroids after initiation of aerosol therapy was unsuccessful; however, following bronchoscopic removal of mucus plugs, the transfer to maintenance therapy with triamcinolone aerosol alone was uneventful.

Allergic bronchopulmonary aspergillosis is an entity which ordinarily occurs as a complication of atopic asthma. In addition to the history of asthma, other clinical features of the syndrome include episodes of fever, recurrent bouts of pneumonia, cough productive of thick plugs of mucous material, blood and sputum eosinophilia,1-7 as well as very high levels of IgE.8 Intradermal skin testing with aspergillus protein extract produces a dual type I and type III reaction. Serum precipitins against Aspergillus antigen are often present.1 There are recurrent bouts of pneumonia which are usually located in the upper lobes of lung. In addition, there is a specific pattern of bronchiectasis,8-10 which is characterized by irregular dilatation of the medium-sized bronchi with normal bronchiolar anatomy distally. Occasionally, mucus plugs lying within the bronchiectatic areas are visible on routine chest roentgenograms.10 Late in the course of the disease, upper lobe fibrosis and retraction may occur.10,11

In the past, the principal therapy advocated for allergic aspergillosis has been systemic corticosteroids.2-7 These agents appear to be very effective in controlling the asthmatic attacks, fever, mucus plugging and pulmonary infiltrates. Antifungal agents have been advocated by some;5,11 however, in most instances they appear unnecessary.7 Sodium cromolyn may be effective prophylaxis against the asthmatic attacks of aspergillosis once the patient has improved on corticosteroid therapy.8 A recent report dealing with the use of beclomethasone dipropionate in a small group of patients with allergic aspergillosis suggested improvement in the majority.11 Triamcinolone acetonide, another nonpolar, water insoluble, aerosolized corticosteroid shown to be effective in the treatment of asthma,12 would seem to be another agent offering promise in the treatment of this disease entity. This report details the one year of management with triamcinolone acetonide of a patient with well-documented allergic aspergillosis. We also emphasize the necessity of assuring that the aerosolized dose of medication reaches the diseased portions of the lung in order to be effective.

Case Report

This 24-year-old white woman, with a history of asthma dating to 1961, was first hospitalized for complications of asthma in 1967. At that time, she had lethargy, malaise, fever, productive cough, and bilateral upper lobe infiltrates. Repeated sputum examinations grew Aspergillus fumigatus on culture. She had eosinophilia of 17 to 25 percent of peripheral leukocyte counts. The complement fixation titer for fungi revealed a titer of 1:16 for Aspergillus fumigatus. Her clinical picture was not recognized as allergic aspergillosis and she was submitted to a diagnostic lung biopsy of lingula which demonstrated bronchiolitis with striking eosinophilic infiltration. There were no demonstrable fungi. She was treated with amphotericin B parenterally, but also received hydrocortisone to minimize the side-effects of amphotericin B and improved symptomatically. Following discharge from the hospital and discontinuation of corticosteroids, she developed clinical deterioration. At readmission in 1968, she had a right upper lobectomy because of increasing right upper lobe infiltrate with cavitation. Histologically, the upper lobe demonstrated bronchiectasis with masses of Aspergillus within necrotic debris in the bronchial lumen.

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FIGURE 1. Roentgenogram illustrates mucus plugging in the left upper lobe bronchus (arrow).
She was treated again with amphotericin B.

The patient was followed-up in the chest outpatient department. Her clinical features conformed to the syndrome of allergic bronchopulmonary aspergillosis described by Henderson. She was subsequently demonstrated to have dual positive skin test reaction to Aspergillus protein antigen and elevated levels of IgE. From 1968 until 1975, she was maintained on oral prednisone. Multiple attempts to lower the dose of prednisone below a maintenance level of 20 to 25 mg on alternate days resulted in symptomatic and clinical deterioration. In September, 1974, she was noted to have mucus plugging in the left upper lobe bronchus (Fig 1); however, she was asymptomatic and the lung parenchyma surrounding the bronchus appeared normal. In March, 1975, it was elected to begin a trial of aerosolized triamcinolone acetonide. The patient was started on 800 µg a day, and a withdrawal schedule from systemic corticosteroids was begun. After six weeks of aerosol therapy and when the prednisone maintenance had been reduced to 10 mg on alternate days, she developed a pulmonary infiltrate around the left upper lobe mucus plug (Fig 2) and symptomatically deteriorated. At that time it was elected to increase the dosage of oral steroids to 40 mg of prednisone a day. This regimen improved her symptoms and infiltrate, but she was left with persistent mucus plugging in the upper lobe.

On April 25, 1975, she underwent fiberoptic bronchoscopic lavage to loosen the mucus plugs from the left upper lobe, since increase in oral prednisone dosage and vigorous chest physiotherapy had been unsuccessful in clearing this area. Following bronchoscopy, the roentgenogram revealed clearing of the area (Fig 3). At this time, the patient was again begun on aerosolized triamcinolone, 800 µg a day, followed by an attempt to diminish systemic steroids. On this occasion, the prednisone withdrawal went smoothly and by June 1, 1975, she was completely off oral steroids. She has been successfully maintained on triamcinolone aerosol alone for the past year except for one period when she suffered an exacerbation of asthma requiring a two-week course of oral prednisone from which rapid withdrawal was uneventful. She continues at this time (June, 1976) on a maintenance dosage of 800 µg of aerosolized triamcinolone a day.

**DISCUSSION**

While the exact pathogenesis of allergic aspergillosis remains unknown, it appears to represent a combination of type I, type III, and perhaps type IV reactions to Aspergillus antigens. The type I reaction is responsible for the immediate component of the positive skin test and the immediate asthmatic attack following Aspergillus inhalation challenge. Type III response causes the delayed six- to eight-hour skin test reaction and perhaps some component of the pulmonary infiltrates. A type IV response has been implicated on the basis of the histology of pulmonary infiltrates. While the exact pathogenesis has remained obscure, systemic corticosteroids have been effective therapy for this allergic disorder.

Our patient demonstrates many features typical of allergic aspergillosis. While taking systemic corticosteroids, she remained relatively free from asthmatic attacks despite chronic mucus plugging in the left upper lobe bronchus. She had, however, developed mild cushingoid features and, therefore, a trial of triamcinolone acetonide seemed warranted. We believe that the initial failure to respond to triamcinolone acetonide was related to inadequate deposition of the drug in the upper lobe bronchi because of obstruction from mucus plugging. Following bronchoscopic lavage for removal of the mucus plugs, it was possible to maintain the patient...
on triamcinolone aerosol without systemic corticosteroids except for one short period during the year. It is important to note that the patient had not been successfully maintained without administration of systemic corticosteroids for eight years despite multiple attempts to taper the dosage of steroids. We conclude that triamcinolone acetonide was effective in replacing systemic corticosteroids in the management of this patient’s asthmatic symptoms. Whether or not the drug will be equally effective in preventing her recurrent pulmonary infiltrates can only be assessed with further follow-up. In this case, triamcinolone aerosol was ineffective in clearing an existing pulmonary infiltrate and we believe that fiberoptic bronchoscopy was useful in removing existing mucus plugs, permitting more appropriate distribution of the aerosol. With triamcinolone acetonide aerosol, the side-effects of long-term systemic corticosteroids can be avoided. Therefore, further study of this agent in a larger number of patients with allergic bronchopulmonary aspergillosis seems justified.

REFERENCES


Aortic Regurgitation Associated with Ventricular Septal Defect*

Echocardiographic and Hemodynamic Observations

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Ventricular septal defect is sometimes associated with aortic regurgitation. In this report, an echocardiogram demonstrating dramatic prolapse of the noncoronary cusp into the left ventricular outflow tract and ventricular septal defect in a patient with Down's syndrome and ventricular septal defect, confirmed by angiographic studies, is presented. The echocardiogram supports the concept of anatomic lack of support of the aortic ring due to a deficient septum and hemodynamically significant flow of blood to the right ventricle through the ventricular septal defect, resulting in trauma to aortic cusps and prolapse.

Echocardiography has been useful in the diagnosis of various valvular and nonvalvular cardiac diseases; however, aortic cusp prolapse has not been well defined. This report describes the echocardiographic manifestations of marked aortic cusp prolapse associated with an infrafacial ventricular septal defect confirmed angiographically. The anatomic and hemodynamic features in the pathogenesis of aortic cusp prolapse are reviewed.

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Figure 1. Supra-aortic angiogram in left anterior oblique projection, showing prolapse of noncoronary cusp (arrow) into left ventricular outflow tract.