

Brief communications

Childhood allergic bronchopulmonary aspergillosis

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Allergic bronchopulmonary aspergillosis (ABPA) is a clinical disease well defined in adult patients, and its diagnostic criteria are well established,¹ but its description in children is rare.²⁻⁶

We report two cases of childhood ABPA for which we carried out a close clinical follow-up and serial determinations of peripheral eosinophils, total IgE, IgE antibody to *Aspergillus fumigatus* (IgE-Af), and IgG antibody to *A. fumigatus* (IgG-Af) after corticosteroid treatment. A significant correlation between total IgE and IgE-Af was found in both cases.

METHODS

Total IgE was measured by microparticle enzyme immunoassay testing with the IMX system (Abbott Diagnostics, Chicago, Ill.).

Specific IgE was determined by fluoroenzymeimmunoassay (CAP System; Pharmacia Diagnostics, Uppsala, Sweden).

Specific IgG to *A. fumigatus* (Af) was assessed by CAP fluoroenzymeimmunoassay (Pharmacia Diagnostics) and the results expressed as a percentage of the mean fluorescence value of a control serum. Specific IgG to other fungi was assessed by ELISA and the results expressed in optical densities; a value at least twice that of the negative control (0.4) was considered positive.

Pearson's correlation coefficient between the levels of total IgE, and specific IgE and IgG, was calculated. Statistical significance was tested with Student's *t* test.

Abbreviations used

ABPA:	Allergic bronchopulmonary aspergillosis
Af:	<i>Aspergillus fumigatus</i>
Dpt:	<i>Dermatophagoides pteronyssinus</i>
Df:	<i>Dermatophagoides farinae</i>
GER:	Gastroesophageal reflux
IgE-Af:	IgE antibody to <i>Aspergillus fumigatus</i>
IgG-Af:	IgG antibody to <i>Aspergillus fumigatus</i>

CASE REPORTS

Case 1

A 6-year-old girl was seen in our outpatient clinic. During the previous 3 years she had had several afebrile episodes of cough, sputum production, dyspnea, and wheezing, and chest radiography had revealed an opacity in the right middle lobe on five occasions.

On physical examination disseminated ronchi were heard. Complementary studies yielded a blood eosinophil count of 2040 cells/mm³; blood chemical values, erythrocyte sedimentation rate, iontophoresis, and α_1 -antitrypsin and serum immunoglobulin levels were normal. Result of a Mantoux test was negative. Stool examinations for ova and parasites yielded negative findings. Skin prick test reactions were positive to *Dermatophagoides pteronyssinus* (Dpt) and *Aspergillus* sp., and intracutaneous tests were immediately positive (20 minutes) to several species of *Aspergillus* (Af, *A. niger*, *A. flavus*), *Penicillium notatum*, *Cladosporium herbarum*, and *Pullularia pullulans*. All late reactions (6 and 24 hours) were negative. The total IgE level was 2900 KU/L. Specific IgE was positive to Dpt (6.1 KU/L), *Dermatophagoides farinae* (Df) (1.6 KU/L), Af (28.0 KU/L), *Alternaria tenui* (7.9 KU/L), *C. herbarum* (4.1 KU/L), *P. notatum* (18.5 KU/L), and *P. pullulans* (>100 KU/L). Specific IgG was positive to Af (138%), *C. herbarum* (3.2), and *P. notatum* (3.4) and negative to *P. pullulans*. Precipitating antibodies by means of the Ouchterlony technique were positive to Af and negative to *P. notatum*, *A. tenui*, and *P. pullulans*. Paranasal sinus radiography revealed bilateral opacity of the maxillary sinuses. A bilateral interstitial infiltrate was shown on

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the chest x-ray film. Moderate eosinophilia was observed in sputum and nasal cell samples. Sputum culture for fungi was negative. In basal spirometry a mixed restrictive-obstructive pattern was observed, with a 16% improvement after inhaled bronchodilator administration. A computed tomographic scanning showed middle and central bronchiectasis in the right middle and left lower lobe and lingula.

An acute phase of ABPA (stage I), secondary alkaline gastroesophageal reflux (GER), and bilateral maxillary sinusitis were diagnosed. The patient continued antireflux treatment, and oral corticosteroid therapy was initiated with deflazacort (0.75 mg/kg/day), equivalent to 0.5 mg/kg/day of prednisone.¹ The patient was followed up monthly with serial measurements of blood eosinophilia, total IgE, and IgE-Af.

The patient has been in a remission phase (stage II) after she stopped oral corticosteroid therapy.

In January 1992 Af was isolated in sputum though the patient had no disease exacerbation.

Case 2

In May 1987 a 3-year-old girl had a diagnosis of immediate hypersensitivity to Dpt and Df, and of GER. Several periods of hospitalization were required both previously and subsequently because of atelectasis and chest condensation in the right lower lobe, and several mucous plug extractions by bronchoscopy were needed.

In November 1991 several bronchospasm crises, one of them associated with a consolidation in the left upper lobe, were reported. In the intervals between crises the patient had nocturnal dyspnea.

On physical examination disseminated pulmonary wheezing was heard. Laboratory studies showed a blood eosinophil count of 780 eosinophils/mm³; blood chemical values, erythrocyte sedimentation rate, serum immunoglobulin and α_1 -antitrypsin levels, and iontophoresis findings were normal. Prick test reactions were positive to Dpt, Df, and *A. tenui* and negative to other fungi (Af, *C. herbarum*, *Mucor racemosus*, *Rhizopus nigricans*, and *Neurospora sitophila*). Intracutaneous tests were immediately positive to *Aspergillus* (Af, *A. niger*, *A. clavatus*), *Alternaria tenui*, and *C. herbarum*. Late responses (24 hours) to *Alternaria tenui* and *Aspergillus clavatus* were noted. Result of a Mantoux test was negative. Stool examinations for ova and parasites were negative. The total IgE was 1596 KU/L. The specific IgE was positive to Dpt (45.1 KU/L), Df (43.5 KU/L), Af (3.25 KU/L), and *A. tenui* (15.9 KU/L) and negative to *C. herbarum*. Specific IgG was positive to Af (54.4%) and negative to *A. tenui*. Precipitating antibodies by means of the Ouchterlony technique were negative to Af and *A. tenui*. Chest radiography showed an infiltration in the right middle lobe and atelectasis. It was not possible to carry out a pulmonary function test, because of lack of patient collaboration. Bronchiectasis in the right middle lobe and left lower lobe were detected by computed tomographic scanning. Sputum samples showed intense eo-

sinophilia. Findings of a sputum fungi culture were negative.

Stage I of ABPA and GER were diagnosed, and therapy was started with 0.5 mg/kg/day prednisone. Subsequently, monthly measurements of eosinophils, total IgE, IgE-Af, and IgG-Af were carried out. Three months later she had only exercise dyspnea; total IgE, IgE-Af, and eosinophils had significantly fallen; and the chest x-ray film was normal. The treatment with oral corticosteroids was stopped. The patient is currently still in remission (stage II of ABPA).

We also calculated the index between the specific IgE to fungi in our patients and the geometric mean in a random sample of patients with childhood asthma with positive prick test reactions to fungi and without allergic bronchopulmonary mycosis.⁷ In case 1 the index was 4.1 for Af, 1.0 for *A. tenui*, 3.4 for *P. notatum*, and 3.4 for *C. herbarum*, and higher than 55 for *P. pullulans*. In case 2 the index was 0.5 for Af and 2.0 for *A. tenui*.

In both patients we determined whether there was a correlation between total IgE and IgE-Af on the one hand and total IgE and IgG-Af on the other at each control stage. We therefore analyzed 17 samples in case 1 and 10 samples in case 2. A significant linear correlation between total IgE and IgE-Af levels was observed (case 1, $r_s = 0.649$ [$p < 0.01$]; case 2, $r_2 = 0.866$ [$p < 0.01$]). Nevertheless, we found no significant correlation between total IgE and IgG-Af levels. The serial measurements of total IgE and IgE-Af can be seen in Figs. 1 and 2.

DISCUSSION

ABPA has seldom been described in children, although most published articles on adult ABPA report the onset of symptoms in childhood. This may be due to the correspondence of established diagnostic criteria to an advanced ABPA stage. To our knowledge case 1 is the only published case of childhood ABPA that fulfills all the diagnostic criteria.

It is interesting to note that both our patients had sensitization to other fungal allergens. In both cases other bronchopulmonary mycoses have been discarded, because those fungi were not isolated in sputum cultures. Nevertheless, in case 1 the high levels of IgE to *P. pullulans* suggest the presence of a mixed bronchopulmonary mycosis despite the absence of IgG to *P. pullulans* and the failure to isolate it in sputum.

In addition, both patients had GER that might have been caused by asthma and the antiasthmatic drugs used, and both had an associated sensitization to mites.

Total IgE and peripheral eosinophilia have been described as important and reliable aids in the management of ABPA. Thus ABPA exacerbations have been related to an increase in peripheral

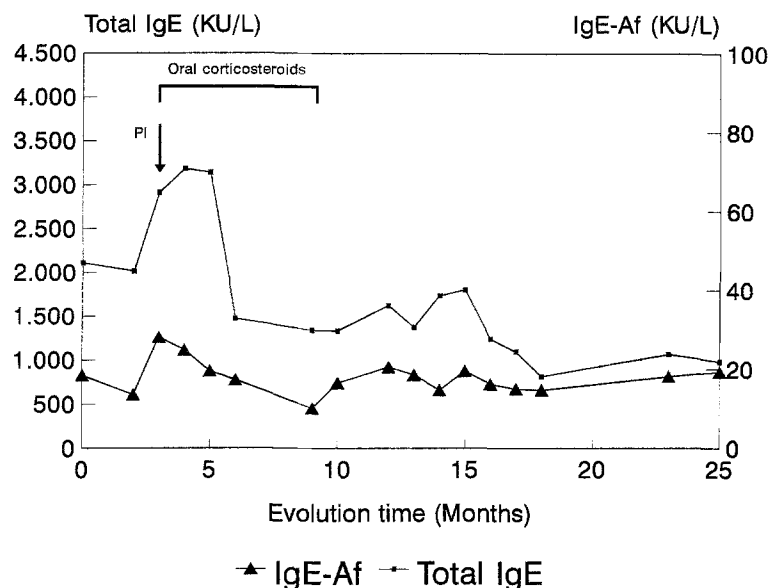


FIG. 1. Case 1. Evolution of total IgE and IgE-Af levels. *PI*, Pulmonary infiltrate (marked by arrow).

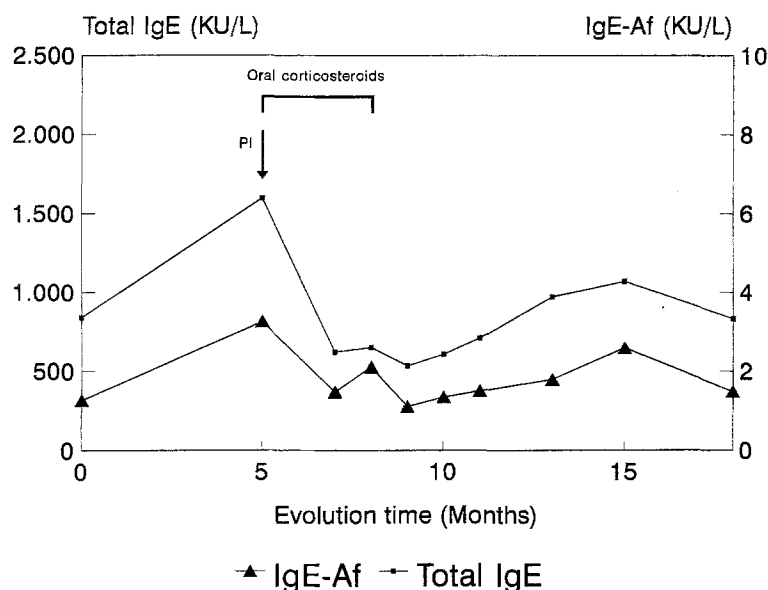


FIG. 2. Case 2. Evolution of total IgE and IgE-Af levels. *PI*, Pulmonary infiltrate (marked by arrow).

eosinophilia and to at least a twofold increase in total serum IgE.¹ Nevertheless, there have been only a few evaluations of other parameters such as IgE-Af and IgG-Af. Rosenberg et al.⁸ studied the IgE-Af and IgG-Af levels before and after the treatment of ABPA with systemic corticosteroids and showed a pronounced decrease of both parameters after treatment. Moreover, the IgE-Af and IgG-Af values were studied in patients with differ-

ent ABPA stages, and the highest values were found in patients with active phases of ABPA (stages I and III).⁷ Leser et al.⁹ classified ABPA in three phases (active, intermediate, and remission) according to asthmatic symptoms, peripheral eosinophilia, and total IgE; studied IgE-Af and IgG-Af levels in these three phases; and found the highest levels in the active phases of ABPA. In our two cases we made serial measurements of IgE-Af

and IgG-Af and observed in both parameters a progressive decrease related to the clinical improvement of the two patients. We also found a high and significant correlation between IgE-Af and total IgE. Nevertheless, we found no correlation between IgG-Af and total IgE. Thus IgE-Af could be a good indicator of ABPA activity and so could be used as an important aid in the management of ABPA.

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A case of lymphocytic pneumonitis, myositis, and arthritis associated with exposure to *Aspergillus niger*

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CD8 lymphocytic alveolitis has been reported in various disorders.¹ One of the leading causes is hypersensitivity pneumonitis (HP). We describe here a case of CD8 lymphocytic pneumonitis with myositis and arthritis, associated with exposure to *Aspergillus niger*. Up to now, *A. niger* has been described as an agent of chronic necrotizing pneumonia,² bronchial asthma,³ invasive aspergillosis,⁴ and mycetoma.

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Abbreviations used

CPK: Creatine phosphokinase
HP: Hypersensitivity pneumonitis

CASE REPORT

A 50-year-old nonsmoking man was admitted to the hospital in October 1991 because of a 6-week history of exertional dyspnea, weakness, myalgias, dysphagia, and arthralgias. He owned a fishing article store where he prepared bait with several compounds including corn flour, bread crumbs, oat, salt, barley, malt, coconut, polenta, and nitrates; all were mixed with a scoop and then manually packaged.

Physical examination revealed inspiratory dry crackles in both lungs. Painful fingers and stiffness were noted. No rash or adenopathy was found, and results of neurologic examination were normal. No clear amyotrophy