

Allergic bronchopulmonary aspergillosis with low serum IgE levels in a child with cystic fibrosis

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A five-year-old girl was diagnosed with cystic fibrosis (CF) at age 8 months on the basis of failure to thrive, steatorrhea, and a positive sweat chloride determination of 95 mEq/L. She was seen in our outpatient clinic four times per year. During the last 4 years she remained well with mild pulmonary symptoms and no evidence of asthma. She had experienced a few episodes of infectious bronchitis without wheezing, which improved with oral antibiotic therapy. There was no history of production of brown sputum plugs, and she had never been treated with bronchodilators or oral or inhaled corticosteroids. At age 1 year, *Staphylococcus aureus* was cultured from her sputum. At age 2 years, *Pseudomonas aeruginosa* grew on her sputum culture without pulmonary involvement, and a 3-week course of intravenous antibiotic was given. Over the next three years, *S. aureus*, and sometimes *P. aeruginosa*, were cultured from her sputum. *Aspergillus fumigatus* (*Af*) only grew twice at age 2 and 3 years. Her routine chest roentgenogram showed minor changes, such as increased lung markings and mild hyperinflation, without acute changes. On routine clinical examination, clear lung fields were heard. Routine laboratory evaluation always showed a peripheral eosinophil count less than 300 cells/mm³. Since June 1995, as part of the Allergic Bronchopulmonary Aspergillosis (ABPA) screening study, the patient was evaluated every 4 months with total serum IgE and IgE against *Af* (IgE-*Af*) by CAP fluoroenzymeimmunoassay (Pharmacia, Uppsala, Sweden); precipitins against *Af* by means of the Ouchterlony technique; IgG, IgA, and IgM antibodies against *Af* (IgG-*Af*, IgA-*Af*, IgM-*Af*) assessed by ELISA; peripheral eosinophil count; and immediate skin testing with *Af*.

In February 1996, when the patient was free of symptoms laboratory data showed a blood eosinophil count of 300 cells/mm³, a total serum IgE of 41 kU/L (normal value <84 kU/L) and a negative IgE-*Af* (<0.35 kU/L). In August 1996 a left upper lobe infiltrate was seen on a routine chest roentgenogram. She had no symptoms, and clinical examination was normal. Sputum

Abbreviations used

ABPA:	Allergic bronchopulmonary aspergillosis
<i>Af</i> :	<i>Aspergillus fumigatus</i>
CF:	Cystic fibrosis

culture grew *S. aureus* and *Candida albicans*. Her total serum IgE increased to 140 kU/L, and she had positive assay results for IgE-*Af* (4.3 kU/L). All specific immunoglobulin classes to *Af* were increased (Table I). Three weeks later she had mild pulmonary wheezing on physical examination. Chest roentgenogram showed a persistence of pulmonary infiltrate. Precipitins to *Af* and skin prick test responses to *Af* were positive. Total serum IgE was 158 kU/L and a white blood cell count revealed 11,160 cells/mm³ with 750 eosinophils/mm³. The patient was treated with oral trimethoprim/sulfamethoxazole for 3 weeks, inhaled bronchodilators, and vigorous chest physical therapy. In October 1996 the left upper lobe infiltrate improved, but on physical examination increased disseminated wheezing was heard. Her eosinophil count increased to 1100 cells/mm³, total serum IgE was 122 kU/L, IgE-*Af* was 5.6 kU/L, and all specific immunoglobulin classes to *Af* remained elevated. Sputum samples contained 80% eosinophils. Despite the total low IgE levels, the clinical, radiologic, and immunologic data suggested the diagnosis of ABPA, and oral therapy with prednisone (1 mg/kg/day) was started.¹ Although her physical findings and the pulmonary infiltrate resolved by the end of 7 weeks of therapy, prednisone was tapered and discontinued 4 months later.

DISCUSSION

ABPA is characterized by stages of exacerbation demonstrating reversible airflow obstruction, pulmonary infiltrates, peripheral eosinophilia, immediate skin reactivity to *Af* extract, total serum IgE more than 1000 ng/ml, and the presence of precipitins against *Af*.² Additional criteria are proximal bronchiectasis and significant elevated levels of IgE-*Af* and IgG-*Af*.³ During exacerbations of ABPA, the high antigen load resulting from fungal growth causes a vigorous polyclonal antibody response, resulting in high IgG, IgA, and IgM titers against *Af*.⁴ When complete clinical symptoms and radiographic and laboratory findings are present, diagnosis of ABPA does not represent a problem. Although

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J Allergy Clin Immunol 1997;100:431-2.

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0091-6749/97 \$5.00 + 0 1/54/83357

TABLE I. Immunologic and roentgenographic findings

Date	Immediate ST to <i>Af</i>	Precipitins to <i>Af</i>	IgE (kU/L)	Eosinophils† (cells/mm ³)	IgE- <i>Af</i> (kU/L)	IgG- <i>Af</i> †	IgA- <i>Af</i> †	IgM- <i>Af</i> †	PI
6/27/95	—	—	36	290	<0.35	0.100	0.160	0.500	—
10/18/95	—	—	96	200	<0.35	0.300	0.200	0.800	ND
2/5/96	—	—	41	300	<0.35	0.200	0.170	0.600	ND
5/21/96	ND	—	39	600	1.95	ND	ND	ND	ND
8/14/96	ND	+	140	ND	4.3	0.800	0.400	1.150	+
9/11/96	+	+	158	750	2.45	0.750	0.450	1.300	+
10/1/96*	ND	+	119	1100	5.6	0.700	0.300	1.100	+
11/14/96	ND	ND	122	300	8.9	0.600	0.300	1.000	—

ST, Skin test; PI, pulmonary infiltrate; ND, not done.

*After therapy with prednisone for 7 weeks, starting 10/1/96.

†Eosinophil count in peripheral blood.

‡Results are expressed in optical densities.

elevated total serum IgE has been considered essential for diagnosis of ABPA,⁵ an acute clinical ABPA without an elevated total serum IgE level has been reported in a 20-year-old woman with CF with clinical asthma and pulmonary infiltrates.¹

In our patient, at the time of pulmonary infiltration, although total serum IgE levels were below values reported in ABPA,² there was an increase greater than 100% over the baseline IgE levels,² and she also had an increase in all serum immunoglobulin classes against *Af*, eosinophilia in blood and sputum, immediate skin prick test response to *Af*, and presence of precipitins to *Af*. The low total serum IgE levels in this child might be due to early diagnosis and treatment. Elevated levels might only occur if the process becomes chronic or recurrent, and perhaps some episodes of ABPA with low IgE levels are not diagnosed. In this case total serum IgE titers might not be useful in follow-up, and additional clinical, radiologic, and laboratory (IgE-*Af*, IgG-*Af*, and IgA-*Af*)

criteria should be used and periodically monitored. To the best of our knowledge, this is the first well-documented case of acute symptomatic ABPA with low serum IgE levels in a child with CF.

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