Serum IgE and IgG Reactivity to Aspergillus Recombinant Antigens in Patients with Cystic Fibrosis with Aspergillus sensitisation, ABPA and Aspergillus bronchitis

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The diagnosis of aspergillosis in cystic fibrosis (CF) remains a challenge due to overlapping features of both diseases. This is further complicated by inconsistent antibody reactivity to the currently used crude antigen, which has led a more focused evaluation of the efficacy of IgE response to a number of pure *Aspergillus fumigatus* (Af) recombinant proteins in order to effect a diagnosis. In this study, we dissected the IgE and IgG responses to multiple Af recombinant antigens in CF patients with different *Aspergillus* diseases.

Methods: Serum IgE and IgG antibodies were measured in 12 CF patients with Allergic Bronchopulmonary Aspergillosis (ABPA), 12 with *Aspergillus* sensitization, and 12 with *Aspergillus* bronchitis against recombinant antigens Asp f1, f2, f3, f4, and f6.

ABPA criteria: elevated Af IgE levels (>0.35 kUA/l), raised total IgE levels (>1000 IU/ml), and at least two of the following: presence of Af IgG (>90 mgA/l), radiological findings compatible with ABPA, or eosinophilia (>0.5 x 10⁹/l).

Aspergillus Bronchitis (AB) criteria: elevated *Aspergillus* IgG (>90 mgA/l), and positive sputum culture for *Aspergillus* species.

Aspergillus sensitization (AS) criteria: elevated Af IgE levels (>0.35 kUA/l).

Results: IgE antibodies in the ABPA group significantly reacted to Asp f1, 2 and 4. There was generally low IgE response to these antigens in AS patients. *Aspergillus* bronchitis samples showed higher IgG positivity to Asp f1 and Asp f2 compared with ABPA. (See Figure)

Sera from ABPA patients with positive culture showed a higher median IgG level to Asp f1 compared with those with negative culture.

Conclusion: Whilst AS patient samples could be differentiated from ABPA samples based purely on total IgE levels, the use of multiple recombinant antigens may improve the diagnostic accuracy in CF complicated with ABPA or *Aspergillus* bronchitis. Specifically, IgG Asp f1 reactivity may relate to the presence of actively growing *Aspergillus spp.* which might be a useful marker for guiding antifungal therapy in both AB and subsets of ABPA patients.

Patient groups	Sex f/m	Age (median, range)	Asp IgG mg/l*	Asp IgE IU/l*	Total IgE IU/l*	Culture positive **
ABPA	4/8	16,3-23	132	26	2210	6/10
AB	7/5	25,5-36	130	<0.35	11	12/12
AS	3/9	26,13-52	48	5	130	3/12

Table: Characteristics of patients studied. (ABPA: Allergic Bronchopulmonary Aspergillosis, AS: Aspergillus Sensitization, AB: Aspergillus Bronchitis).
* Median results
** Positive culture for *Aspergillus fumigatus*.