

CORRESPONDENCE

The switch from non-IgE-associated to IgE-associated atopic dermatitis occurs early in life

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Dear Sir,

We have read with high interest the article by Bieber et al. (1) in which they suggest possible biomarkers associated to the three characteristic phenotypes of atopic dermatitis (AD) already proposed in 2008 (2): non-IgE-associated AD, IgE-associated AD, and autoimmune AD.

As part of a protocol study aimed at correlating AD genotype and phenotype (AllerGene2), we obtained the clinical and allergological characteristics of 184 children with AD referred to the Pediatric Dermatology and Pediatric Allergology Outpatient Clinics of our Hospital. Allergometric tests (skin prick test and/or total and specific (s)IgE for the main food and inhalant allergens) were performed at the first observation (time 0), others at intermittent times according to the clinical needs, and at follow-up (time 1; mean age of follow-up 10 years).

Concerning the non-IgE-associated form of AD, we decided to consider it as intrinsic AD, adopting the classification proposed by Wutrich (3) which defines it by (i) clinical phenotype of AD, according to the criteria of Hanifin and Rajka; (ii) absence of other atopic diseases such as allergic asthma and rhinoconjunctivitis; (iii) negative skin prick tests for common inhalant and food allergens and normal total serum IgE levels (according to age). Moreover, we chose to consider (i) normal level of total IgE as a value between 2 SD for age; (ii) negative sIgE as a value <0.7 kU/l for food and <0.35 kU/l for inhalant allergens without clinical symptoms.

If we consider the characterization at time 0, that is, the first clinical and laboratory evaluation, performed before the age of 2 years (99 patients) or before the age of 5 (85 patients), 30/184 had been classified as having non-IgE-associated AD (16%). Later, at a median age of 36 months, 15 children became allergic, so that at time 1, after at least 10 years of follow-up, of the total 184 patients, 169 (92%) were classified as having IgE-associated and 15 (8%) non-IgE-associated AD (Table 1).

All the 15 patients who switched from non-IgE- to IgE-associated form had an early onset of AD and had been first referred to our Clinics before the age of 2; moreover, in 14/15 cases, the switch happened in the first 5 years of life. On the contrary, the 15 patients with persistent non-IgE-associated AD had a later age of onset (mean, 30 months; $P < 0.00$), while the other clinical characteristics were similar. Furthermore, we found that AD remission is more frequent among patients with the IgE-associated form (Fig. 1).

There are a limited number of studies (4) reporting the results of allergometric tests performed during the first years of life in patients with AD and allowing classifying these cases according to Wutrich's parameters; other authors have already observed a switch from a non-IgE-associated to an IgE-associated form (5). It is important to define the AD phenotype in childhood because it has been shown that early atopic sensitization in these patients is associated with a worse prognosis in terms of subsequent wheezing and asthma (6).

Table 1. Main clinical features among 184 children affected by atopic dermatitis after a 10-year follow-up

	IgE-AD		Non-IgE-AD	
	All IgE-AD	Switch non-IgE- to IgE-AD	All non-IgE-AD	Total
Number (%)	169 (92%)	15	15 (8%)	184
M/F (M%)	95/74 (56%)	9/6 (60%)	7/8 (M 47%)	102/82 (M 55%)
Positive family history for atopy	120 (71%)	8 (53%)	10 (67%)	130 (71%)
Positive family history for AD	23 (14%)	1 (7%)	1 (7%)	24 (13%)
Mean age at AD onset (months)	8*	4	30*	10 months
Persistent AD at follow-up	91/162 (56%)	9/15 (60%)	6/11 (54%)	97/173 (56%)
Mean age of AD remission (months)	61**	45	125**	65 months
Median age of switch from non-IgE- to IgE-AD (months)	–	36	–	–

* P value = 0.0001.

** P value = 0.0006.

AD, atopic dermatitis; IgE-AD, IgE-associated AD.

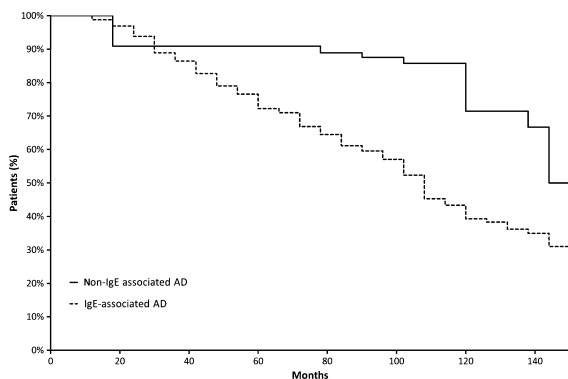


Figure 1 Remission of atopic dermatitis among 184 children affected by non-IgE-associated ($N = 15$) and IgE-associated ($N = 169$) form.

We agree with Bieber's hypothesis (1, 2) and stress the fact that, in the natural history of AD, the first clinical phase without IgE sensitization switches rapidly to the IgE-associated form, and this should more frequently happen during the first months of life as in most of our cases (84/99 were already IgE-sensitized before the age of 2).

According to this concept, among patients with an early onset of AD, it might be useful to perform a precocious evaluation of the biomarker tests to clarify the mechanisms which underlie the switch from non-IgE-associated to

IgE-associated AD and the allergic sensitization through the skin and for a subclassification of the patients who might take advantage from individualized treatment approaches (7).

Authors contributions

AD took part in the study design drafting, data collection, paper drafting and revision, and approval of the final version; LR took part in data collection, paper drafting and revision, and approval of the final version; IN took part in the study design drafting, paper revision, and approval of the final version; GR took part in the study design drafting, data collection, paper revision, approval of the final version; AP took part in the study design drafting, paper revision, and approval of the final version.

Conflicts of interest

No conflicts of interest to declare.

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