

IgE deficient patients have no IgE-encoding B cells in the periphery – a pilot study

Denisa Ferastraoru, MD¹, David Rosenstreich, MD¹, Scott Smith, MD²

¹Division of Allergy-Immunology, Montefiore Medical Center, Bronx NY, ² Department of Pathology, Microbiology and Immunology, Vanderbilt University Medical Center, Tennessee

BACKGROUND

- IgE deficiency is defined as IgE < 2.5 kU/L.
- While we learn more about different clinical presentations of IgE-deficient patients, the mechanism resulting in IgE deficiency is unknown.
- Through this small pilot study, we sought to investigate the frequency of IgE-encoding B cells in the peripheral blood of IgE-deficient individuals and allergic control patients

METHODS

- Peripheral blood mononuclear cells (PBMCs) were collected from 5 IgE-deficient and 5 non-IgE deficient patients with different allergy-like symptoms.
- Cells were counted and assessed for viability before culturing in the presence of murine anti-human kappa/lambda + irradiated murine fibroblasts expressing human CD40-ligand, B-cell activating factor and IL-21.
- The cells were screened for IgE secretion after 6 days of incubation

Table 1. IgE-encoding B cells frequency in patients with IgE deficiency versus allergic control patients with non-IgE deficiency

	No	Age	Sex	Allergic Diseases	Total IgE (kU/L)	Total PBMCs x 10 ⁶	IgE-B cell frequency (per 10 ⁷ PBMCs)
IgE deficiency	1	59	M	Allergic rhinitis (AR)	<2	8	0
	2	29	F	AR	<2	16	0
	3	52	F	Asthma, AR	<2	20	0
	4	45	M	AR	2	11	0
	5	57	F	Asthma, AR	<2	22	0
Allergic controls	6	12	M	Adverse food reaction (AF), Atopic dermatitis (AD), Asthma	812	24	3.3
	7	15	M	AF, Asthma	1,615	24	2.9
	8	8	F	AF, AD, Asthma	2,434	16	2.5
	9	4	F	AF, AD	4,340	8	2.5
	10	5	M	AF, AD, Asthma	260	24	4.8

Table 2. Immunological characteristics of patients with IgE deficiency

No	Mitogen/Antigen induced proliferation	Serum IL-4 (nl ≤5 pg/mL)	Serum IL-13 (nl ≤5 pg/mL)	MBL (nl ≥100 ng/mL)	Strep pneumoniae antibodies	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	IgG subclass	Lymphocytes subsets
1	normal	<5	<5	1,391	present	1,270	63.5	193	IgG4 deficiency	slightly low - CD3, CD4, CD8, CD19
2	normal	<5	<5	661	N/A	1,250	237	201	normal	low CD19
3	N/A	<5	<5	8	N/A	1,640	89.3	241	normal	slightly low CD3. Normal CD4, CD8, CD19. Slight increase in CD16
4	normal	<5	<5	661	present	1,030	84.4	298	IgG3 deficiency	normal
5	decreased tuberculin response	<5	<5	6	present	961	71.4	261	normal	normal

RESULTS

- All IgE-deficient patients presented for evaluation of allergic rhinoconjunctivitis-like and/ or asthma.
- The median PBMCs cultured was similar between IgE-deficient (16 cells x10⁶, range: 8-16 cells x10⁶) and non-IgE deficient individuals (24 cells x10⁶, range: 8-24 cells x10⁶, p=0.2). (**Table 1**)
- Median frequency of IgE-encoding B cells was 2.9 cells/10⁷ PBMCs (range: 2.5-4.8 cells/10⁷ PBMCs) in non-IgE deficient, allergic patients. In contrast, **IgE-deficient patients had zero IgE-encoding B cells.** (**Table 1**)
- Immunological tests in IgE deficient patients revealed IgG4 and IgG3 deficiency in 2 patients, MBL deficiency in 2 patients and a diminished response to tuberculin in 1 patient (**Table 2**)

CONCLUSION

- The absence of IgE-encoding B cells in the peripheral blood of IgE-deficient patients suggests a defect either in these cells' survival, or in the IgE class-switching process.
- Further research is needed to elucidate the exact mechanism resulting in absence of serum IgE in certain individuals.