ATOPIC DERMATITIS – ASSOCIATED IMMUNE DYSFUNCTION

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ABSTRACT

The immune system shows a complex role to defend the body in response to "non-self" antigens, respond abnormally to antigens allergens (hypersensitivity and autoimmunity) and shows immune tolerance by lack of reactivity to its own structures (self).

Aim. The aim of this study is to demonstrate that in atopic dermatitis immune deficiency influences the development of atopy, disease severity and comorbidities.

Material and methods. Following medical record review, 135 cases diagnosed with AD were included in the study. Statistical analysis was performed using SPSS v20 for determining the frequency and testing the hypotheses, for $p < 0.05$, by t tests and One-Way ANOVA.

Results. Of the 135 cases, 51.9% were male children and 48.1% female children aged 1 month to 127 months with a mean of 26.21. According to total serum IgE level, 64.4% of patients had elevated IgE levels, 35.6% normal levels. According to the SCORAD, children had mild AD in 20.7% of cases, moderate in 70.4%, and severe in 8.9%. IgA deficiency was found for 48.1% of cases, and for 51.9% normal. IgG deficiency was found in 38.5% of cases. The independent samples t tests showed statistical significant demonstrating correlations between IgE level and IgA immune deficiency, between SCORAD and IgG and IgA immune deficiency. Atopic march is influenced by elevated IgE, IgA and IgG immune deficiency, $p < 0.05$.

Conclusions. Atopy in AD can be influenced by complex factors, both internal and environmental, but this remains a controversial topic. External factors acting on a background genetically predisposed to atopy trigger the manifestation of AD.

Keywords: atopic dermatitis, immune dysfunction, IgA, IgG, IgE

INTRODUCTION

The immune system plays a complex role in defending the body by eliciting a response to specific "non-self" antigens, responds abnormally to allergenic antigens in hypersensitivity and autoimmunity and shows immune tolerance by non-reactivity to its own structures (self).

Since the prenatal period, particularly in the last trimester of pregnancy, the fetus is protected from external factors by the maternal immune system, antimicrobial peptides and proteins in the amniotic fluid, the fetus synthesizing the antimicrobial proteins in the epidermis (defensins and cathelicidins). The newborns are first colonized with bacteria from maternal flora during the birth process, and, by breastfeeding, in the early postnatal period the intestinal microbiota is formed, with antimicrobial and stimulating role in intestinal immune system development. Any disturbance in this microbiota may favor pathogen invasion at this level (1).

In the first year of life, maternal immunoglobulins acquired during the last trimester of pregnancy are gradually replaced, initially IgM (Immunoglobuline M), IgG (Immunoglobuline G), and only then the de novo production of IgA (Immunoglobuline A) takes place. Therefore, because of this deficit in the production of immunoglobulins characteristic to the neonatal period, infants are more susceptible and receptive to infections (1,2).

Susceptibility to develop atopy during life is determined by several factors, both internal and external, that are interconnected (3,4).

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The internal factors are the inherited genetic susceptibility with the sequential variation in DNA and formation of new genes, to which contribute changes in intrauterine environment influenced by such factors as: maternal asthmatic and allergic status, nutrition, socioeconomic status, activities, and stress. Thus, epigenetic modifications of DNA occur and determine neonatal phenotypes of leukocyte expression at the level of umbilical cord leukocytes, neonatal lung function, airway and lung parenchyma development, neonatal immune status with Th1/Th2 diversion, and neonatal sensitization. The contribution of external factors (air, animal exposure, repeated viral infections, damp and mould in the house, type of baby feeding, nutrition, daily care, stress) to inherited genetic susceptibility, favors again the epigenetic change of DNA by gene methylation and histone modifications generating intermediate phenotypes by a change in blood leukocyte gene expression. These factors acting on baby's immune status and innate immune response, results a deviation of Th1/Th2, specific allergen sensitization in early childhood, airway inflammation and remodeling, and occurrence of atopic status with cutaneous sensitization and elevated total IgE (Immunoglobuline E), and therefore of clinical phenotypes of atopy: eczema, bronchial asthma, allergic rhinitis, food allergies, wheezing, anaphylaxis (4-7).

MATERIAL AND METHODS

Retroprospective study, a total of 135 patients with atopic dermatitis diagnosed according to Haniffin and Rajka criteria being selected. The following data were analyzed: sex, age, area of residence, family history, personal medical history, SCORAD, total IgE, IgA, IgG and IgE specific levels, and further progression to allergic rhinitis or bronchial asthma. Statistical analysis was performed using SPSS v20.

RESULTS

Of the 135 patients included in the study 52% were male and 48% female, and 65% from urban areas. Most of the patients presented within the first two years of life, followed by age 30 months and between 50 and 80 months, mean age 26.21 months (Fig. 1).

The analysis of immunoglobulin determinations showed elevated IgE levels in 64% of the cases, and IgA and IgG deficiency in 48% and 46%, respectively (8). To determine whether atopy is influenced by the presence of IgA or IgG immune deficiency we carried out the independent sample t-test

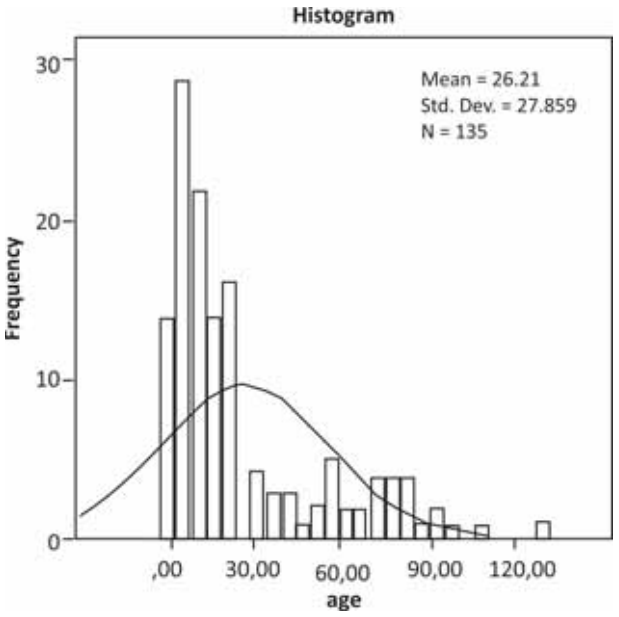

FIGURE 1. *Age distribution histogram*

where for a t(133) = 1.03 p value was > 0.05. The positive Levene's test (p <0.05) confirmed that only IgA deficiency had such an influence (Table 1).

It is well-known that in atopic dermatitis IgE level influences the SCORAD (scoring atopic dermatitis) index. The t-test used to examine the correlation between IgA and IgG deficiency and SCORAD was statistically significant (p <0.05) and Levene's test (p <0.01) for moderate and severe SCORAD (Table 2 and 3).

TABLE 1. *T-test for the comparison of the mean IgE and IgA levels*

Independent Samples Test				
			IgE	
			Equal variances assumed	Equal variances not assumed
Levene's Test for Equality of Variances	F		3.975	
	Sig.		.048	
t-test for Equality of Means	t		1.036	1.034
	df		133	130.828
	Sig. (2-tailed)		.302	.303
	Mean Difference		.08571	.08571
	Std. Error Difference		.08274	.08291
	95% Confidence Interval of the Difference	Lower	-.07794	-.07829
		Upper	.24937	.24972

Also analyzed was the occurrence of bronchial asthma, allergic rhinitis (AR), or a combination of both in atopic dermatitis patients, part of atopic march (9,10). Thus, in 73.30% of the cases the diagnosis of atopic dermatitis remained unchanged, 9.60% were diagnosed with allergic rhinitis,

TABLE 2. *T-test for the comparison of the mean IgA levels and SCORAD*

Independent Samples Test				
			IgA	
			Equal variances assumed	Equal variances not assumed
Levene's Test for Equality of Variances	F		74.278	
	Sig.		.000	
t-test for Equality of Means	t		2.177	2.654
	df		105	16.038
	Sig. (2-tailed)		.032	.017
	Mean Difference		.32807	.32807
	Std. Error Difference		.15072	.12363
	95% Confidence Interval of the Difference	Lower	.02921	.06603
		Upper	.62693	.59011

TABLE 3. *T-test for the comparison of the mean IgG levels and SCORAD*

Independent Samples Test				
			IgE	
			Equal variances assumed	Equal variances not assumed
Levene's Test for Equality of Variances	F		30.903	
	Sig.		.000	
t-test for Equality of Means	t		1.605	1.743
	df		105	14.658
	Sig. (2-tailed)		.111	.102
	Mean Difference		.24474	.24474
	Std. Error Difference		.15244	.14037
	95% Confidence Interval of the Difference	Lower	-.05753	-.05507
		Upper	.54700	.54454

14.10% with bronchial asthma, and 3% with allergic rhinitis associated with asthma (Fig. 2). As to the correlation between immune deficiency represented by elevated IgE and low IgA and IgG levels, t-test showed correlations between elevated total IgE and comorbidities (allergic rhinitis, bronchial asthma), and by performing a one-way ANOVA we have demonstrated that IgG deficiency is associated with subsequent development of allergic rhinitis, $p < 0.01$ (Tables 4 and 5). Figure 3 shows the gender distribution of comorbidities in our study group, most patients being female, and the combination of the two comorbidities (rhinitis and asthma).

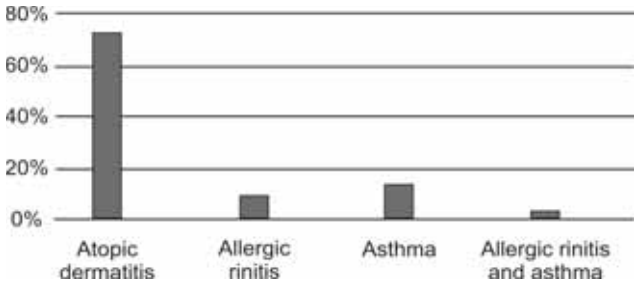

FIGURE 2. *Associated comorbidities in the study group (atopic march)*

TABLE 4. *T-test for comparing the mean IgE levels and atopic march*

Independent Samples Test				
			IgE	
			Equal variances assumed	Equal variances not assumed
Levene's Test for Equality of Variances	F		5.824	
	Sig.		.022	
t-test for Equality of Means	t		-1.511	-1.451
	df		30	22.150
	Sig. (2-tailed)		.141	.161
	Mean Difference		-.25101	-.25101
	Std. Error Difference		.16610	.17304
	95% Confidence Interval of the Difference	Lower	-.59023	-.60974
		Upper	.08821	.10771

TABLE 5. *One-way ANOVA for the comparison of mean IgG levels and atopic march (IgG deficiency favors the development of comorbidities)*

ANOVA					
IgG					
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	3.888	3	1.296	5.728	.001
Within Groups	29.638	131	.226		
Total	33.526	134			

In the study group the following comorbidities were recorded: 47% of cases were clinically diagnosed with cow milk protein allergy (CMPA), 5% had a positive test for CMP-*specific IgE,* and 48% IgE specific to other allergens.

Of the AR cases presenting comorbidities 23% had a history of CMPA and 15.38% of allergy to dust mites, dog or cat epithelium, peanuts, egg white. 21.05% of the asthma cases initially presented CMPA, and 26.31% allergy to dust, cat and dog epithelium, egg white, chocolate, mold, pollen, nuts, peanuts. In the group with both AR and asthma rye allergy, dust allergy and CMPA were present in 1 case each.

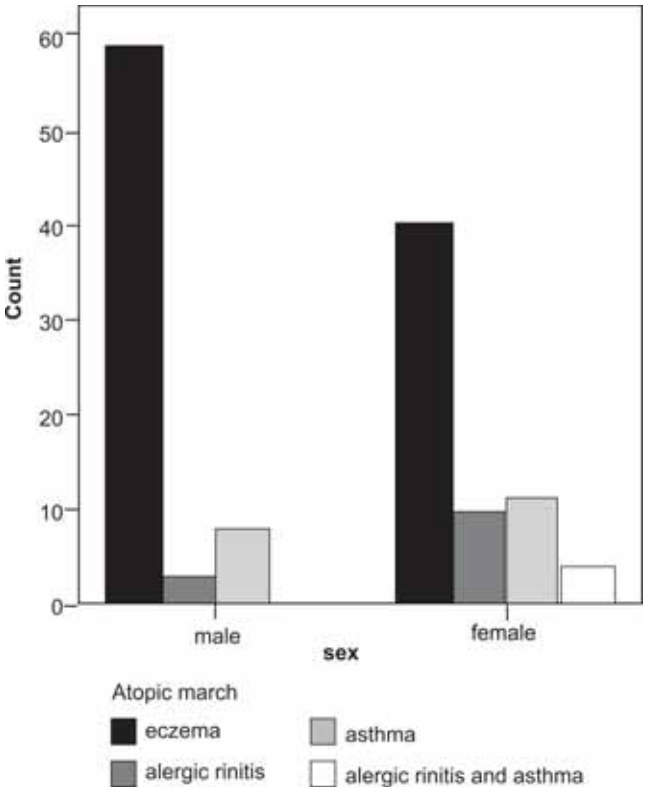

FIGURE 3. *Sex distribution of comorbidities*

DISCUSSIONS

Immune tolerance is the ability of the host to recognize the inoffensive inhaled or ingested antigens in order to prevent activation of an immune response to these antigens (11,12).

Infants are particularly less immunologically prepared to face all antigens, as proved by the IgA and IgG immune deficiency both in the first year of life and at older ages.

Early sensitization and respiratory infections increase the risk of asthma and allergic rhinitis.

Sensitization to food allergens is important given the progression to asthma and allergic rhinitis in the patients clinically diagnosed with allergy to cow milk protein.

CONCLUSIONS

Immunity plays an important role during childhood and sometimes dictates the course of development of allergic diseases in children, therefore the IgA and IgG immune deficiency influences the development of atopy since the early ages.

In this case immune deficiency favors a clinically more severe atopic dermatitis and early sensitization favors evolution to asthma and allergic rhinitis manifested away from the first episode of atopic dermatitis.

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