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To Assess the Role of Genetic Factors in the Pathogenesis of Atopic Dermatitis

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ABSTRACT

This article attempts to reveal the main reasons for the role of genetic factors in the pathogenesis of atopic dermatitis (AD) in children and to determine the prognostic significance of the identified polymorphisms, depending on immunological parameters. To perform scientific work, the author conducted (PCR) polymorphic variants of the IL-4 gene: intron 3 in the VNTR region and snp variants of C/T-590 in children. The problem in question is still little studied, therefore, requires more thorough research.

Introduction: Atopic dermatitis (AtD, atopic eczema, atopic eczema/dermatitis syndrome) — chronic allergic dermatitis; a disease that develops in individuals with a genetic predisposition to catopia, has a relapsing course, age-related features of clinical manifestations. It is characterized by exudative and (or) lichenoid rashes, increased serum IgE levels and hypersensitivity to specific (allergenic) and nonspecific stimuli. It has a clear seasonal dependence: in winter - exacerbations or relapses, in summer - partial or complete remissions. The prevalence of AD among developed countries is 10-20%. The manifestation of AD symptoms in children is observed at the age of 6 months in 60% of cases, up to 1 year in 75%, up to 7 years in 80-90%. Over the past decades, there has been a significant increase in the incidence of AD, its course is becoming more complicated, and the outcome is aggravated. In the 20th century, the connection between AtD, pollinosis and bronchial asthma was confirmed, which was designated by the term "atopic triad" [2]. The combination of AD with bronchial asthma is observed in 34% of cases, with allergic rhinitis - in 25%, with hay fever - in 8%. AD may be the debut of an "allergic march", when further atopic diseases develop in such patients: food allergy, bronchial asthma, allergic rhinitis. AD associated with food allergy accelerates the progression of the "allergic march".

Aim: to evaluate the role of genetic factors in the pathogenesis of atopic dermatitis (AD) in children and to determine the prognostic significance of the identified polymorphisms, depending on immunological parameters.

Methods and materials: using polymerase chain reaction (PCR), polymorphic variants of the IL-4 gene were determined: intron 3 in the VNTR region and snp variants of C/T-590 in

children with AD and in the control group. In addition, for the listed groups, the IL-4 and IgE levels in the blood serum were determined using the "sandwich" variant of enzyme-linked immunosorbent assay (ELISA) using monoclonal antibodies.

Results: in 40 children with moderate and severe course of atopic dermatitis (> 40 points according to SCORAD), whose average age was 12 years at the time of hospitalization (girls - 13 years and boys 11 years), polymorphisms were determined by PCR diagnostics C590 T and VNTR intron 3 (where RP1 allele of 183 bp and RP2 of 253 bp). The C590 allele was detected only in 32.5% (13), while the mutant –590 T allele was found in 12.5% (5) and in the heterozygous C590 T variant in 55% (22). The RP1 allele was determined in 40% (16) of patients, while the mutant RP2 variant in 17.5% (7) and the heterozygous RP1/RP2 variant in 42.5% (17). These results were compared with those obtained in the comparison group (50 healthy girls, mean age 16 years). The mutant allele –590 T was found only in 2% (1) and in its heterozygous C590 T variant in 10% (5). The mutant RP2-in the control group was only in 6% (3) and its heterozygous variant RP1/RP2 was in 10% (5). According to ELISA data, in patients with atopic dermatitis, the IL-4 index (pg/ml) averaged 1.936±0.20 (Me= 2.028, R= 5.536), which differed from the control group: the average was 0.88±0.088 (Me= 0.961, R= 1.932), statistically significant differences with control $p<0.05$. The content of IgE (IU/ml) in the blood serum was significantly higher in patients (mean - 731.41±61.09, Me= 724.9, R= 1365.8, $p<0.05$) in comparison with the group of relatively healthy children (mean - 188.5±28.63, Me= 112.4, R=913.326, $p<0.05$). When comparing the average values of immunological parameters with the presence of a certain polymorphism, the following data were obtained: 1) in patients, the variant C590-IL-4 = 0.696, IgE =647.46, -590 T-IL-4 =2.575, IgE = 802, 86, C590 T-IL-4 = 2.523, IgE = 764.81; 2) in relatively healthy C590-IL-4 = 0.765, IgE = 161.88, -590 T-IL-4 = 1.931, IgE = 467.8, C590 T-IL-4 = 1.5348, IgE = 366, 89, and according to VNTR intron 3 polymorphism: 1) patients with RP1 variant-IL-4 = 0.88, IgE = 660.78, RP2 variant- IL-4 = 2.434, IgE = 686.62, RP1/RP2- IL-4 = 2.723, IgE = 695.49; 2) relatively healthy with RP1 variant - IL-4 = 0.781, IgE = 163.73, RP2 variant - IL-4 = 1.782, IgE = 435.86, RP1/RP2-IL-4 = 0.852, IgE = 249, 1.

Conclusions: the presented polymorphisms of the IL-4 gene can be prognostically significant, because mutant variants are more common in sick children in a homo- or heterozygous state, which is confirmed by immunological parameters of blood serum, because even in relatively healthy children in the presence of a mutated allele, the concentration of IL-4 and IgE increases. To assess the prognostic significance of the manifestation and course of atopic dermatitis and to introduce these diagnostic methods into routine practice, it is necessary to continue research on large samples.

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