Atopic phenotype associations with rs7927894 inter gene polymorphism on chromosome 11q13.5 in Czech adult patients with atopic dermatitis

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Abstract

Aim: Aim of the study was phenotype-genotype association analysis of rs7927891 polymorphism in adult patients with Atopic Dermatitis (AD).

Material and methods: Finally, 90 patients were enrolled to the study, 31 men (30 ± 10 years) and 59 women (31 ± 11 years). Among them, 65% of men and 75% of women reported positive family history of atopic phenotype.

Results: We did not observe significant differences in genotype distribution and/or allelic frequencies between AD men and women in polymorphism rs792894. But, the CT genotype of polymorphism rs7927894 on chromosome 11q13.5 was more than 4 times more frequently observed in AD women with elevated levels of the total IgE above 158 IU/ml. In AD men, a significant association of polymorphism rs7927894 on chromosome 11q13.5 with atopic phenotype/predisposition was found: the genotypes CC and TT are 6 times more frequent in AD men with other atopic phenotype (asthma, atopic rhinitis) compared to AD men without it. The TT genotype of the polymorphism was 4 times more frequent in men with positive family history of atopic phenotypes.

Conclusion: We identified significant risky genotypes for some AD phenotypes in rs7927894 polymorphism in patients with AD, differently for adult AD men and women.

Introduction

Atopic Dermatitis (AD), or eczema, is one of the most common chronic inflammatory skin diseases with prevalence rates of up to 20% in children and 3% in adults. It commonly starts during infancy and frequently precedes or co-occurs with asthma and rhinitis. It is characterized by dry skin, intense pruritus, and a typical age-related distribution of inflammatory lesions with frequent bacterial and viral superinfections. Profound alterations in skin barrier function and immunologic abnormalities are considered key components affecting the development and severity of AD, but the exact cellular and molecular mechanisms remain incompletely understood [1].

In this study we performed genotype-phenotype study for rs7927894 single nucleotide polymorphism on chromosome 11q13.5 in a group of 90 adults with atopic dermatitis.

Material and methods

Patients

Total of 90 patients with AD, diagnosed and treated at the 1st Department of Dermatology of St Ann’s Faculty Hospital Brno were recruited to the study. The patients were diagnosed according to the generally accepted criteria Hanifin and Rajka [6].

Demographic data are presented in Table 1 and 2. None phenotypic differences between man and women (M/W) were significant.

All these patients were genotyped for rs7927894 by conventional PCR method with restriction analysis.

This study was approved by the Committee for Ethics of Medical Experiments on Human Subjects, Faculty of Medicine, Masaryk University.

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Key words: atopic dermatitis, gene polymorphism, genotype-phenotype study, rs7927891

Received: April 10, 2015; Accepted: May 20, 2015; Published: May 24, 2015
After division of the group of patients to men and women, some differences have been observed: in AD women, the CT genotype of polymorphism rs7927894 on chromosome 11q13.5 was more frequently detected in AD women with elevated levels of IgE (OR = 4.76, 95% CI 1.19-18.98, P = 0.02, Table 3). In AD women, we found a significant association of polymorphism rs7927894 on chromosome 11q13.5 with atopic phenotype: the genotypes CC and TT are 6 times more frequent in AD men with other atopic phenotype compared to AD men without it (OR = 6.22, 95% CI 1.212-31.938, P = 0.03). At the same time, the TT genotype was 4x more frequent in AD men with positive family history of atopic phenotypes (OR = 4.286, 95% CI 0.444-41.364, P = 0.05, Table 4).

Discussion

In addition to FLG, two European GWAS on atopic dermatitis established four susceptibility loci (C11orf30, OVOL1, ACTL9, and RAD50/IL13/KIF3A) [2-3]. Single nucleotide polymorphism rs7927894 appears to mark a genuine eczema susceptibility locus [7]. Recently, polymorphism C11orf30-rs2155219 was found to double the risk of poly-sensitization (specific IgE/4 allergens) [8].

According to our study, the TT genotype in rs7927894 of was 4 times more frequent in AD patients with positive family history of atopic phenotypes, but only in men. Austrian study refers a significant association of the rs7927894 variant on chromosome 11q13.5 with atopic dermatitis. But, genotype-phenotype study analysis revealed no significant association of rs7927894 with early age of onset of the disease, concomitant asthma and allergic rhinoconjunctivitis, total serum IgE levels and family history of atopy [9] which is not in agreement with our results. Different results could be caused by strictly separated statistical analysis of AD men and women data performed in our study.

Other polymorphic sites have been discovered in other QWAS studies [10-11], probably many of them in linkage disequilibrium and with some inter population differences.

We identified significant risky genotypes for some AD phenotypes in rs7927894 polymorphism in patients with AD, differently for adult AD men and women.

Acknowledgement

This publication was written at Masaryk university as part of the project “Experimentální molekulární patofyziologie vybraných

Table 3. rs7927894 (11q13.5) genotype and IgE levels in AD women.

| Genotype | No elevated IgE (≤158 IU/ml) | Elevated IgE (≥158 IU/ml) | Row Totals |
|----------|-------------------------------|---------------------------|------------|
| CC       | 11 (61%)                      | 17 (41%)                  | 28         |
| CT       | 3 (17%)                       | 20 (49%)                  | 23         |
| TT       | 4 (22%)                       | 4 (10%)                   | 8          |
| All Grps | 18                            | 41                        | 59         |

Table 4. rs7927894 (11q13.5) genotype and family history of atopy in AD men.

| Genotype | Family history of atopy | No family history of atopy | Row Totals |
|----------|-------------------------|----------------------------|------------|
| CC       | 7 (35%)                 | 4 (36%)                    | 11         |
| CT       | 7 (35%)                 | 7 (64%)                    | 14         |
| TT       | 6 (30%)                 | 0 (0%)                     | 6          |
| All Grps | 20                       | 11                         | 31         |
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