

Protein tyrosine phosphatase-22 (PTPN-22) polymorphism in the pathogenesis of chronic urticaria

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Pathophysiology of chronic urticaria (CU) includes inflammatory, hormonal as well as autoimmune abnormalities.

Autologous serum skin test (ASST) is a valuable marker of circulating functional autoantibodies. From the clinical point of view, the coexistence of CU and autoimmunity has been well documented. The genetic basis of autoimmune disorders is gradually uncovered.

Protein tyrosine phosphatase-22 (PTPN-22) is located at 1p13.3-p13.1 and is considered to be the strongest genetic factor for human autoimmunity besides MHC (1). Polymorphism in the PTPN-22 (1858C > T) is associated with the risk of development of multiple autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis and type 1 diabetes (2). Additionally, it was proved to be associated with Graves' Disease and Hashimoto's thyroiditis (3, 4). 1858C > T causes a

functional change in lymphoid tyrosine phosphatase protein (Lyp). Disease-associated T allele encodes a protein not binding to the protein tyrosine kinase Csk, which results in hyperresponsiveness of T cells. Generally, 1858C > T variant is associated with these autoimmune disorders that present contribution to autoantibodies. Because several forms of autoimmunity have been associated with CU, we decided to evaluate whether PTPN-22 T allele is associated with CU in the Polish population.

We enrolled in the study 90 unrelated, ASST-positive CU patients (63 women and 27 men, mean age 37.8, age range 21–58). For the control, 106 unrelated healthy volunteers (72 women and 34 men, mean age 46.4, age range 19–59) were studied.

In all examined subjects, we analysed the 1858C > T polymorphism (rs2476601) in exon 14. Genotyping was performed by allelic discrimination using Custom TaqMan® SNP Genotyping Assays and 7300 Real-time PCR System (Applied Biosystems, CA, USA). To analyse disease intensity, Urticaria Activity Score (UAS) was used. Moreover, in all CU subjects, disease-onset age was analysed.

The statistical significance of the differences in the allele and genotype frequencies between patients and controls was analysed with Chi-square test. Unpaired Student's *t*-test was applied for UAS and disease onset age comparisons among different genotype distribution subgroups.

We analysed our study sample for Hardy–Weinberg equilibrium and found no deviation in CU group or in the control group. No statistically significant differences in the allele and genotype distribution between patients with CU

and controls were found (Table 1). The estimated statistical power of the analysis was 22%. We did not observe any dependency between PTPN-22 genotype and the severity of urticaria or disease onset age. It was assumed after the analysis of those parameters in patients with different genotype distribution (data not presented).

We speculated genetic background of CU as the occurrence of CU is frequently associated with autoimmune thyroid diseases (AITD) and genetic susceptibility for AITD is well proved. As PTPN-22 is generally connected with autoantibodies production, we selected ASST-positive patients. Although we studied a relatively small group of patients, our results initially indicate no contribution of PTPN-22 1858C > T polymorphism to susceptibility to CU with positive ASST in the Polish population. 1858C > T variant represents the main disease-related variant in PTPN-22 locus, although the effect of PTPN-22 polymorphisms is limited to some diseases and populations, i.e. this polymorphism has not been found in Japan and therefore does not contribute to autoimmunity in the Japanese population (5). These differences can be explained by Kaufman et al. (6) who assumed the association between PTPN22 1858C > T and familial SLE, but not sporadic SLE. In our opinion, additional genetic studies on other polymorphisms in PTPN-22 and other loci in patients with CU are necessary in order to analyse in detail a possible role of the genetic background in its pathogenesis.

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Table 1 PTPN22 (1858C>T) genotype and allele distribution in patients with chronic urticaria (CU) and healthy controls (OR, odds ratio; CI, confidence interval; *P*, statistical significance; the odds ratio was calculated for patients homozygous or heterozygous carrying risk allele vs. homozygous)

Group	Genotype distribution			Allele		OR (95% CI)	<i>P</i>
	Total number (%)			Total number (%)			
CU	CC	CT	TT	C	T	1.46 (0.77–2.78)	0.24
	63 (70)	26 (29)	1 (1)	152 (85)	27 (15)		
Controls	CC	CT	TT	C	T		
	82 (77)	24 (23)	0 (0)	188 (89)	24 (11)		

Conflict of interest

Authors declare no conflict of interest.

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