Abstract

Introduction: Recent findings about the pathogenesis of glaucoma have already demonstrated the presence of some specific autoimmune mechanisms. It has also been shown that autoimmune diseases often manifest in co-occurrence, such as celiac disease and type 1 diabetes mellitus or psoriasis. This association can be explained by sharing some of the risk variants of HLA molecules class II. Considering glaucoma an autoimmune disease, the question raises how the glaucoma genetic risk factors affect the phenotype of another autoimmune disease or *vice versa*, whether genetic risk variants associated for example with celiac disease can affect the glaucoma phenotype.

Aims: The aims of this study were to i) identify possible genetic risk markers associated with the development of glaucoma, based on the available literature, and to map their occurrence among members of a three-generation family suffering from glaucoma and multiple autoimmune diseases, ii) find carriers of HLA-DQ2/DQ8 among the members of the same family, iii) verify whether an individual's genotype correlates with his/her phenotype, and iv) determine the potential effect of specific HLA alleles on the glaucoma phenotype.

Material and methods: This study used DNA samples derived from 34 members of a three-generation family, in which coeliac disease, type 1 diabetes mellitus and psoriasis can be found. Eight genetic risk markers (single nucleotide polymorphisms (SNP)) that have so far been associated with glaucoma have been selected: rs74315329, rs74315329 (*MYOC*); rs28939688; rs11258194; rs75654767 (*OPTN*); rs1057517785 (*PAX6*); rs4986790 (*TLR4*); rs34595252 (*WDR36*). Genotyping was performed using the PCR-RFLP method and the HRM analysis, and the results were subsequently verified by sequencing. The DNA samples were also tested for the presence of HLA class II molecules DQ2 (DQA1*0501-DQB1*0201) and DQ8 (DQA1*0301-DQB1*0302), which are associated with coeliac disease.

Results: In all of the examined SNPs associated with glaucoma, all probands were found to be carriers of the major allele in homozygous form. HLA typing for proof of the presence of DQ2 and DQ8 antigens showed a strong correlation between the occurrence of coeliac disease and the presence of DQ2 antigen (P_k=0.001, OR=62.33, CI=2.91–1335). Same correlation with coeliac disease was found also for individual risk alleles DQA1*0501 (P_k=0,004, OR=49, CI=2.34–1024) and DQB1*0201 (P_k=0.004, OR=49, CI=2.34–1024). There was no correlation between the incidence of any autoimmune disease and glaucoma

(P_k=1.548) or between either of the coeliac disease risk antigens (DQ2 or DQ8) and glaucoma (P_k=1.630).

Conclusion: In a three-generation family with a multiple incidence of autoimmune diseases and glaucoma, a strong genetic predisposition to celiac disease was observed, specifically in relation to the HLA-DQ2 antigen. There was no correlation between glaucoma and the selected single nucleotide polymorphisms which have so far been associated with glaucoma, nor was there any correlation between glaucoma and autoimmune disease in family members.

Key words: glaucoma, autoimmunity, coeliac disease, T1D, HLA class II, polymorphism, association