Study of cytotoxic- T lymphocyte antigen 4 gene polymorphisms in immune thrombocytopenic purpura

Thesis

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Summary and conclusion

Idiopathic thrombocytopenic purpura is a bleeding disorder in which the immune system destroys platelets, which are necessary for normal blood clotting. ITP occurs when certain immune system cells produce antibodies against platelets. The antibodies attach to the platelets. The spleen destroys the platelets that carry the antibodies. In children, the disease sometimes follows a viral infection. ITP affects women more frequently than men, and is more common in children than adults. The disease affects boys and girls equally.

The cytotoxic T lymphocyte associated antigen- 4 (CTLA-4), also known as CD152, is expressed on T lymphocytes and inhibits the T-cell responses. Cytotoxic T-lymphocyte antigen-4 (CTLA-4), encoded by a gene on chromosome 2q33, is a receptor expressed by activated T lymphocytes. It interacts with the B-7 cell surface molecule on antigen-presenting cells and inhibits T cell activation and clonal expansion. CTLA-4 blockade leads to enhancement of the immune response. Many single nucleotide polymorphisms (SNPs) have been identified in the *CTLA*-4 gene that contains four exons and three introns.

The A49G polymorphism in exon 1 of the *CTLA-4* gene is especially important because it alters the structure of the CTLA-4 protein by causing Thr17Ala amino acid substitution. It has been suggested that this polymorphism reduces the inhibitory function of CTLA-4. The *CTLA-4* A49G polymorphism was found to be associated with autoimmune diseases.

The aim of the study is to examine the genetic association of the *CTLA 4* gene A49G polymorphism in children with idiopathic thrombocytopenic purpura using PCR-RFLP analysis

The present study was conducted on 30 children with acute idiopathic thrombocytopenia. Twenty age and sex matched healthy children with normal blood picture were also included as control group. Children included in the study were subjected to genomic DNA analysis for *CTLA-4* A49/G polymorphism using PCR- RFLP analysis.

Our study found that there was no association between the CTLA-4 A49G polymorphism and ITP. In the ITP group, eighteen patients had AA (60.0 %), twelve patients had AG (40 %) and none had GG genotype. A- allele frequency was 80% and G- allele frequency was 20% in this group while in the control group, eleven had AA (55%), nine had AG (45%) and none had GG genotype. A- allele frequency was 77.5% and G- allele frequencies was 22.5% in this group . There was no statistically significant difference between cases and controls as regards to genotype and allele frequencies as P-value > 0.05, odds ratio 0.815,and confidence interval 0.259-0.2.559.

In our study there was no statistically significant difference in genotype or allele frequency between males and females in the study group as p-value> 0.05.Also we did not find significance differences in platelet count, total leucocytic count, and absolute lymphocytic count between patient with AA genotype and patient with AG genotype.

In summary, the negative results of our study indicate that neither gene polymorphism nor allele frequency of CTLA-4 A49G might play a role as genetic risk factor in the pathophysiology of ITP. Further genetic and clinical studies including larger scale studies and studying different haplotypes of CTLA-4gene are required to understand the exact role of the CTLA-4 polymorphisms in the development of ITP .