Protein Z (rs3024735; G79A) and (rs3024719; G-103A) gene polymorphisms in Egyptian patients with Behçet's disease

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Summary

Behçet disease (BD) is a multisystemic inflammatory disorder, which can affect all types of blood vessels. The pathogenesis of BD is not completely clear, but genetic background has been reported to play a decisive role in BD development. Thrombosis related complications of the disease can be serious and even life threatening. A large amount of data supports the hypercoagulable /prothrombotic state in BD. Many studies supported the role of the genetic polymorphisms of PZ in pathogenesis of a variety of thrombotic diseases but not sufficient in Behçet disease. Protein Z (PZ) is a vitamin K-dependent plasma protein that plays an important role in the regulation of the coagulation cascade. It is a cofactor that causes rapid inhibition of factor Xa by PZ dependent protease inhibitor.

Our study was aimed to investigate the prevalence of intronic protein Z G79A (rs3024735) and promoter protein Z G-103A (rs3024719) polymorphisms in Egyptian patients with Behçet disease and

and possibility of using these variants in risk stratification of occurrence of vascular affections and other clinical findings

The present study conducted on a total of 200 participants that were divided into two groups. The first group consisted of 100 Behçet disease cases with clinical and laboratory signs consistent with Behçet disease. The second group consisted of 100 age and sex matched normal controls. They were subjected to full clinical evaluation, laboratory investigations and allelic discrimination of these two PZ SNPs by using real-time PCR TaqMan probes.

In the present study, the PZ G79A (rs3024735) genotyping revealed the prevalence GA and AA genotypes among BD cases, also there was higher percentage of A alleles among cases than controls, so it may be considered as one of the factors that increase the susceptibility of Behcet's disease in the Egyptian population. On the other hand, there was no statistically significant difference between cases and controls as regards PZ G-103A (rs3024719) genotypes.

In our study, an attempt was further made to evaluate whether PZ G79A (rs3024735) and PZ G-103A (rs3024719) genotypes and allele frequencies were associated with specific clinical characteristics through comparing patients with and without certain manifestations, laboratory data and activity of the disease. There was a highly significant association between PZ G79A (rs3024735) GA and AA genotypes and vascular lesions specially with deep vein thrombosis. Also, there was association between PZ G79A GA and AA genotypes and eye lesions, mainly with retinal vascular occlusion in our BD patients. On the other hand, there was no a statistically significant difference between different PZ G79A genotypes as regards the activity of the disease which evaluated by BDCAF score.

Furthermore, our data revealed that there was a highly significant association between PZ G79A (rs3024735) AG and AA genotypes and high neutrophils count, increased neutrophil to lymphocyte ratio (NLR), elevated ESR and positive CRP. Considering this, there may be a possible direct regulatory role of this polymorphism on disease development.

On the other hand, there were no statistically significant difference between different PZ G-103A (rs3024719) genotypes as regards the existing clinical manifestations, laboratory data or activity of the disease.

In conclusion, protein Z G79A(rs3024735) polymorphism A allele might be associated with increased susceptibility of Behçet's Disease and its vascular lesions. However, Protein Z G-103A (rs3024719) polymorphism was not associated with parallel increase in Behçet's disease susceptibility in studied population.

More explorations in more diverse geographical regions with large sample size are expected to further verify the findings in the future. There is also a need for larger studies involving more protein Z gene polymorphisms as PZ promoter (rs3024718 and rs3024731) and exon (rs3024778 and rs3024772) to investigate their role in Behçet disease susceptibility by using more advanced techniques like DNA sequencing.