Endothelial cell protein C receptor (EPCR) gene exon III, 23 BP insertion mutation in Turkish Cypriots

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To the Editor,

The protein C anticoagulant pathway is critical to the negative regulation of the blood clotting cascade. EPCR plays an important role in this pathway [1]. Mutations in the genes of protein C (PC), protein S and thrombomodulin have been identified in patients with venous and/or arterial thrombosis. Recently, an additional endothelial cell-specific transmembrane protein has been identified that binds protein C and activated protein C (APC) on the cell surface, which is named as endothelial cell protein C/APC receptor (EPCR). Although the EPCR itself does not have any direct anticoagulant effect in the absence of APC, it influences the rate of PC activation by the thrombin/thrombomodulin complex. If the binding of protein C to EPCR is blocked, then the rate of PC activation is reduced.

The cloned human EPCR gene consists of four exons [2]. It was reported that a 23 bp insertion (ins) in exon III (nt4031) of the EPCR gene predicts the introduction of abnormal residues followed by a stop codon which deletes the whole of the alpha 2 domain of the gene. This mutation may contribute to thrombosis in myocardial infarction and deep vein thrombosis [3].

One hundred and sixty-one healthy unrelated Turkish Cypriot individuals with no familial history of thrombosis or stroke were included in the study [4]. DNA was extracted by conventional methods and polymerase chain reaction of exon III of the EPCR gene was performed according to a previously described method using primers 5'-ACACCTGGCACCCTCTCT- 3' and 5' -CATCCTTCAGGT CCATCC- 3' [4]. Amplification was performed for 35 cycles with an annealing temperature of 58°C. Amplified DNA was subjected onto 2.5% agarose gel electrophoresis.

Of the 161 healthy Turkish Cypriots, 5 (3.1%) carried the EPCR ins mutation.

The distribution of the 23 bp insertion of exon III of the EPCR gene revealed that 1 (0.8%) of the 116 healthy Anatolian Turkish individuals carried the 23 bp insertion mutation. 23 bp insertion carriers did not have familial thromboembolism.

Previous reports revealed a frequency of 0-3.6% in different healthy and patient populations. The frequency of the insertion is high in the Turkish Cypriot population. However, it is difficult to assess its role and importance in the pathogenesis of thrombosis in this population.

As it is an island population, a higher frequency is expected, as our previous data revealed in factor V Leiden (FVL) and prothrombin (PT) mutations [5,6].

Further studies including other possible mutations at the gene are needed for the evaluation of its possible effect on pediatric thrombosis.
References


