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Reporting a novel mutation causing elongated protein in Hemophilia A in Iran

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Introduction

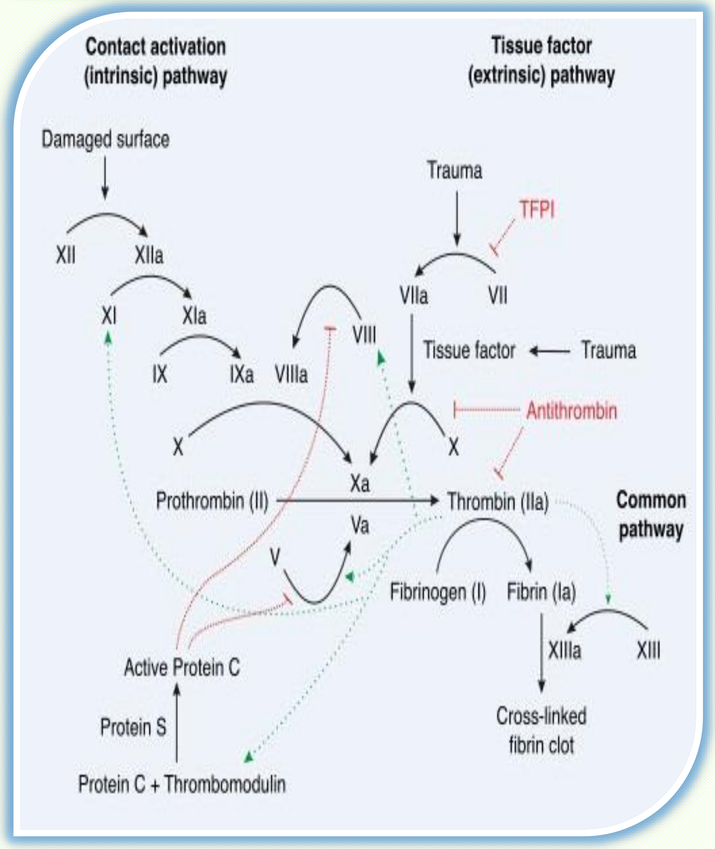
Hemophilia A is one of the most common X-linked recessive bleeding disorders caused by F8 gene deficiency. The disease incidence is 1 in 5000 males. Although different types of mutations in F8 gene have been reported, novel mutations have a high proportion of the disease causing mutations. Herein we report a novel mutation in F8 gene which confirmed with linkage analysis.

Material & Methods

Two brothers affected with severe form of hemophilia (F8<1%) and positive family history of the disease referred us for mutation detection. Fallowing genetic counseling and taking blood from all family members, DNA extraction was performed. The possibility of the inversion 1& 22 was tested. Exons and intron-exon boundaries of the F8 were directly sequenced. Linkage analysis was performed with the help of STR (Short tandem repeat) markers linked to the gene to track the mutated allele. Then the haplotypes were drawn.

Results

The index cases showed no abnormality in inversion studies. Sanger sequencing revealed a novel single nucleotide insertion in c.6799-6780. Heterozygosity of the mutation was also confirmed in mother.



Discussion:

The insertion caused a frame shift leads to an impaired protein production with an extra 32 amino acids residues which couldn't be active properly.

Finding novel mutations will expand the databases reporting disease causing variants and helps understanding the pathologic knowledge of the disease.

Molecular screening of patients can make epidemiological data for implantation of community-based carrier testing in populations. It also facilitates prenatal diagnosis (PND) and pre-implantation genetic diagnosis (PGD) for at- risk families.

Key word: Hemophilia A, Novel mutation, Iran