CHAPTER 5

MUTATION ANALYSIS IN INFANY WITH FXI DEFIENCY

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Factor XI deficiency was first described in 1953.it is often observed in the Jewish race. Increased prekalikrein crecreine and high molecular kininogen (HK) is observed with FX activation activation occurs with negative charge.FXI operates on the intrisictive pathway.FXI is synthesized in megakaryocytes and liver. FXI is a 160-kDa glycoprotein, which separates into two 80-kDa sub- units linked by disulfide bonds. It comprises heavy chains with four repeats that have binding sites for high-molecular-weight kininogen (HK), thrombin, platelets, FIX, and FXII. There is a protease on the light chain.Serine protease is activated by the interaction of calcium, platelet and thrombin. Thrombin's role in the activation of FXI is the result of a "feed-forward loop" to promote stable clot formation and protection against fibrinolysis by throm- bin activatable fibrinolytic inhibitor (TAFI). FXI was be activated by FXII or HK, due to contact activation and the so-called intrinsic pathway. Contact activation is not thought to be as important in the physio- logic activation of FXI, and instead the activation of FXI is predominately mediated by thrombin. Relationship between FXI and fibrinolysis might explain reason, in contrast to other coagulation factor deficiencies, FXI deficiency tendency to excessive mucosal bleeding. (2) Factor XI deficiency and functional defects :Homozygotes or compound heterozygotes have an FXI level of <15 U dL and heterozygotes display levels of 25– 70 U dL or normal values [6,7]. Vertical transmission of severe Factor XI deficiency has got a poor correlation between factor XI level and bleeding tendency. It has be may be caused by different molecular variants of factor XI.but studies comparing antigenic measurements of factor XI have shown no diversity suggesting that the deficiency is due to reduced amounts of clotting factor (6,7).

There are different bleeding risks in different surgical interventions in mild factor XI deficiency. No bleeding was observed after dental extraction and tonsillectomy.

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p.W519* and c.325+1G>A) identified in this study had been previously described in other Turkish patients with FXI deficiency.

Seyma C et all reported in Turkey the patients' F11 genes were direct DNA sequencing of 11 amplicons containing the 5 untranslated region, all exons, and exon/ intron boundaries by PCR-amplified and analysed .14 patients had F11 gene mutations were observed in this analysed. Eight different mutations were reported.. Six of the mutations were recurrent mutations (p.Thr51Pro, p.Glu135X, p.Cys416Tyr, p.Gly418Val, p.Trp519X, and c.325+1G>A), two were novel mutations were ; (p.Val522Gly, and p.Cys581Arg)All the mutations were specific to the families in which they were detected, except p.Thr51Pro and p.Trp519X which were detected in two families.(34)

Heterozygous c.623C> A (p. Thr208Lys) Heterozygous c.1556G> A (p.Trp519 *) mutations in infant with factor IX defiency This mutation was not detected mutations before the turkey. FXI: C level was 1u / dL. Clinically heavy progress. In order to contribute to the determination of gene mutations in FXI deficiency in our country, the case was considered appropriate.

Disclosures

The authors state that they have no interests that might be perceived as causing a conflict or bias.

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