FACTOR V AND VIII INHIBITOR IN PATIENTS WITH COMBINED FACTOR V AND VIII DEFICIENCY

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ABSTRACT

Patients with coagulation factor(s) deficiency who use coagulation therapy are susceptible to forming inhibitors against coagulation factor(s). In this survey we detected factor V and VIII inhibitor in ten patients with combined deficiency of factors V and VIII from north east of Iran (Khorassan province). It was revealed in our survey that eight patients had both factor V and factor VIII inhibitors and two patients had none. Because factor V and factor VIII share approximately 40% amino acid sequence homology in their A and C domains, it remains to be elucidated if it is one molecule that recognizes both factor V and VIII or whether there are two inhibitor molecules against common sites.


Keywords: Combined factor V&VIII deficiency, Factor V inhibitor, Factor VIII inhibitor.

INTRODUCTION

Already six types of combined hereditary deficiency of coagulation factors have been reported.1 Combined deficiency of factor V & VIII was reported in 1954 by Oeri et al.2 This inherited disorder is a rare bleeding diathesis that has been reported in 106 cases from 62 families throughout the world until 2000.3 Most patients are from the Mediterranean region, including Italy,4 Iran5 and Israel.6 Additional families have been reported from India,3,15 Japan,7 North America and Europe.4 In genetic defects of single coagulation factors, the relationship of the clinical severity with the plasma factor level is well established. However, the data available from published reports show wide variation with regard to clinical manifestations in cases of combined factor V & VIII deficiency.8 Many mechanisms have been proposed to explain this mysterious dual deficiency. In 1980 Marlar reported an apparent deficiency of protein C inhibitor as the underlying mechanism for this disorder.9 This intriguing model was based on the observation that 4 unrelated patients with combined deficiency of factor V &VIII had no protein C inhibitor in their blood.10 Despite this attractive hypothesis, subsequent studies failed to confirm it in these patients.11,12 Unfortunately, “the slaying of a beautiful hypothesis by an ugly fact” was played almost immediately.10 Genetic linkage studies in affected families mapped the gene for combined factor V & VIII deficiency to the long arm of chromosome 18q.13 Positional cloning studies led to the identification of Endoplasmic Reticulum Golgi Intermediate Compartment (ERGIC) as responsible mutations. It has been shown that 18 distinct ERGIC-53 mutations can cause complete loss of ERGIC-53 protein expression. Patients with combined deficiency factor of V and VIII use factor VIII preparation and Fresh Frozen Plasma (FFP) to compensate (the low level of coagulation factor V & VIII) in the circulation. Like other inherited deficiencies of coagula-
factor VIII inhibitors. Among 10 patients with combined factor V & VIII deficiency, 8 patients had factor V inhibitor. Minimum titer and maximum titer of factor V was 0.63 and 5 (B.U.) with mean of 1.77±1.44 (B.U.). All 8 patients had both factor V and VIII inhibitors.

RESULTS

As Table I show among 10 patients under survey, 8 patients had factor VIII inhibitor and 2 patients none. Minimum and maximum titer for factor VIII inhibitors were 0.57(B.U.) and 6 (B.U.) with mean of 2.06±1.75 (B.D.).

Table I. Status of factor V & VIII inhibitors in 10 patients with combined factor V & VIII deficiency from northeastern Iran.

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REFERENCES
