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Combined factor V and factor VIII deficiency: A rare case report and literature review

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ABSTRACT

Background: Combined factor V and factor VIII deficiency (F5F8D) is a rare autosomal recessive inherited coagulopathy. It has a higher prevalence in the Mediterranean region (1:100,000) compare to its prevalence in the general population which is estimated to be (1:1000,000). **Case report:** We report a 59 years old Lebanese lady who was referred from the general surgery clinic with an asymptomatic prolongation of prothrombin time (PT), international normalized ratio (INR) and activated partial thromboplastin time (aPTT) detected during pre-operative work up for an elective umbilical hernia repair. The patient had history of bleeding following dental procedures since childhood as well as easy bruising with minimal trauma. Physical examination was unremarkable. haematological investigations were normal apart from the prolonged PT, INR and aPTT which were corrected following mixing studies. Factor assay revealed factor V level of 5.5% and factor VIII level of 11.9% with other factors within normal ranges confirming the diagnosis of combined F5F8D. **Conclusion:** Combined factor V and factor VIII deficiency should be suspected in patients with prolonged PT, INR and aPTT especially if they are of Mediterranean, Middle east or Arabic origin with a history of consanguineous marriages. Treatment is generally not indicated unless the patient has recurrent serious bleeding manifestations.

Keywords: Factor V, Factor VIII, combined, Lebanese, Mediterranean

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Background:

Combined deficiency of factor V and factor VIII was first described in 1954 [1]. Since then more than 200 cases have been reported, a significant number of these cases belong to the Mediterranean area and Asia particularly the middle east countries. Considering that the mode of inheritance for this condition is autosomal recessive, parents of affected individuals are obligatory heterozygote carriers of the affected genes, thus the condition seems to be more prevalent in areas with higher rates of consanguineous marriages [2-4], the prevalence of this disease in middle eastern Jewish and Iranian population is estimated at 1 case per 100,000 individuals [5]. The resultant low levels of factor V and factor VIII can present with mild, moderate or serious bleeding symptoms including epistaxis, menorrhagia, muscular hematomas, hemarthrosis and post-operative bleeding [6,7].

Combined factor V and factor VIII deficiency is characterized by normal platelet count and bleeding time but with prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT). Mixing studies result in correction of PT and aPTT. Subsequent factor assays should be done to reach the diagnosis. Further genetic analysis can be done to identify the exact gene mutation responsible for the condition.

Case Report:

We report a 59 years old Lebanese lady who was referred from the general surgery clinic with asymptomatic prolongation of prothrombin time (PT), international normalized ratio (INR) and activated partial thromboplastin time (aPTT) detected during pre-operative work up for an elective umbilical hernia repair. The patient had history of bleeding following dental procedures since childhood as well as easy bruising with minimal trauma. Past surgical history was significant for post appendicectomy bleeding at the age of ten years which was managed with administration of fresh frozen plasma. She had no history of spontaneous bleeding, joint or muscle bleeding. family history was significant for a paternal female cousin with similar symptoms.

Physical examination was unremarkable. Haematological investigations showed normal platelet count and peripheral smear, PT of 20 seconds, INR of 1.8 of and aPTT of 90 seconds. mixing study resulted in correction of PT, INR and aPTT. Factor analysis revealed factor V level of 5.5% and factor VIII level of 11.9% with other factors within normal ranges confirming the diagnosis of combined F5F8D.

Due to the history of post-surgical bleeding our patient received prophylaxis with fresh frozen plasma and recombinant factor VIII concentrate 24 hours prior to her surgery, on the day of surgery and post-surgery. Her post-operative course was unremarkable with no bleeding complications.

Discussion

Combined factor V and factor VIII deficiency is a rare autosomal recessive inherited coagulation disorder with increased prevalence observed in areas with higher rates of consanguineous marriages [2-4] however this was not the case for our patient. A mong combined coagulation factor deficiency, combined FV and FVIII deficiency is the most prevalent.

Bleeding symptoms vary but in general are similar to those with single factor V or VIII deficiency. The most common presentations include epistaxis, menorrhagia, easy bruising, bleeding post trauma or surgery and to a lesser extent haemarthrosis and muscular bleeding [5-7].

The Disease is caused by mutations in one of two genes (LMAN1 and MCFD2) located in chromosomes 18 and 2 respectively [8], the products of which help transporting glycosylated FV and FVIII during the secretion process, unfortunately genetic testing for these mutations was not done for our patient due to financial constraints.

In combined F5F8D regular prophylaxis is not required and the patients are generally not

treated unless treatment is required, however in cases of recurrent haemarthrosis or muscular hematoma prophylaxis should be considered [9]. The treatment is to replace the factors. While factor V can be replaced with fresh frozen plasma, factor VIII replacements is better achieved with special factor concentrates whether plasma derived or recombinant. Desmopressin can be used in some cases of mild bleeding [10]

Conclusion:

Combined factor V and factor VIII deficiency is more prevalent in individuals from the middle east and Mediterranean region where more consanguineous marriages are seen. The diagnosis should be suspected in any patient who fits the epidemiological characteristics and presents with prolongation of PT and aPTT with or without bleeding symptoms. Regular replacement with fresh frozen plasma and factor VIII concentrates are generally not indicated unless the patient has recurrent serious bleeding manifestations.

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