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Case Report

Inherited Factor X (Stuart–Prower Factor) deficiency and its management

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Introduction

Morawitz in 1905 may have been the first to isolate Factor X when he identified a factor named ‘thromboplastin’ that interacted with thrombogen to form thrombin.¹ In 1955, Duckert reported a factor deficiency distinct from FVII and FIX in patients receiving coumarins and named the new factor as

Factor X.² Inherited Factor X deficiency was first reported in 1956 by Telfer et al³ in a 22-year-old woman patient, Miss Audrey Prower with a bleeding diathesis and in 1957 by Hougie et al⁴ in a 36-year-old male patient, Mr Stuart (hence, Factor X is also known as Stuart–Prower Factor).

Factor X is a vitamin K dependent, liver produced serine protease that serves as a pivotal role in coagulation as the first enzyme in the common pathways to thrombus formation. It is located on chromosome 13 (13q34) and its deficiency can be inherited or acquired. Factor X deficiency is an extremely rare autosomal recessive inherited coagulation disorder in children. It occurs with a frequency of one in 2 million in general population and so far only fifty cases have been reported worldwide.⁵ Symptomatically, homozygous patient with severe hemorrhagic symptoms present early in life whereas symptomatic heterozygotes may bleed only after severe challenges to haemostatic system, like in trauma or major surgery.

Case report

We present a case of one year old male child patient (product of a non-consanguineous marriage), who manifested with

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spontaneous bleeding diathesis. He presented with complaints of easy bruisability since 4–5 months and haemarthrosis of right knee joint of one week duration. No family history of minor trauma related excessive bleeding or any other bleeding diathesis. No history of liver failure. Complete haemogram, red cell indices and bleeding time (BT) were within normal limits. Prothrombin time (PT), activated partial thromboplastin time (aPTT) & thrombin time (TT) were prolonged which showed correction after mixing studies, done with normal pooled plasma (NPP) (which was prepared in house from 20 normal pooled plasmas). PT was found to be 66.4/13 s (test/control) with PT ratio of 5.1 & INR of 8.19; aPTT was 132.1/35 s (test/control) & TT was 37/16 s (test/control). Diluted Russell viper venom time (dRVVT) was also increased. He was further evaluated for Vit. K deficiency by doing functional (clot-based) assays for Vit. K dependent factors (Factor II, VII, IX and X) and individual factors, using Factor X deficient plasma. Results showed isolated deficiency of Factor X (i.e. < 1% of the normal value) (Normal level: 70–150%) (Tables 1 and 2).

The patient was diagnosed as severe Factor X deficiency and treated accordingly. Presently he is on regular follow up and is advised to take Fresh Frozen Plasma (FFP) in case of severe bleeding. Each unit of FFP contains approximately 220 iu of Factor X & each unit increase the Factor X levels by 2.5%. For hemostasis, 10–40% of normal level of Factor X is required.⁶

Discussion

Factor X is a vitamin K dependent glycoprotein. It is converted to an active form by Factor VII and calcium along with tissue thromboplastin in extrinsic pathway whereas, in intrinsic pathway, Factor IX, Factor VIII, calcium and platelet Factor 3 activates it. Factor X is also involved in the formation of 'prothrombinase complex' to convert prothrombin to thrombin on phospholipid surfaces of platelets along with Va (as it's co-factor) and calcium.⁷

Factor X deficiency can be congenital or acquired. Acquired deficiency of Factor X may occur with anticoagulant therapy, liver disease, drugs (e.g. phenytoin), paraproteinemia and amyloidosis.

Table 1 – Coagulation profile and mixing study of the patient.

Coagulation profile		
	Control (seconds)	Test (seconds)
Prothrombin time (seconds)	13	66.4
Activated partial thromboplastin time (seconds)	35	132.1
Thrombin time (seconds)	16	37
Mixing studies		
Prothrombin time (seconds)	13(seconds)	13(seconds)
Activated partial thromboplastin time (seconds)	35(seconds)	40.1(seconds)
Impression: correction with normal pooled plasma was observed.		

Table 2 – Factor studies of the patient.

Factor VII (%) (functional assay)	144% (normal 36%–185%)
Factor IX (%) (functional assay)	78% (normal 44%–127%)
vWF: Ag (immunogenic assay)	138% (normal 50%–160%)
Factor V (functional assay)	96% (normal 70%–150%)
Factor X assay (functional assay)	<1% (normal 70%–150%)

Interpretation: severe Factor X deficiency.

The diagnosis of Factor X deficiency is usually suspected when both the prothrombin time (PT) and activated partial thromboplastin time (aPTT) are abnormal and gets corrected with 1:1 mix with normal plasma.⁸ Functional activity of Factor X (FX: C) is quantified by performing prothrombin time – based assay, using rabbit thromboplastin and Factor X deficient plasma. Accordingly, patients are classified into three groups: severe (FX: C, <1%), moderate (FX: C, 1%–4%) & mild (FX: C, 6%–10%). Qualitative Factor X assay can be type 1 when both functional and immunological laboratory parameters are decreased (as proved to be in case of Mr Stuart) or type II in which Factor X protein is structurally normal but the functional activity is reduced, (as represented by Miss Prower).^{9,10}

Our case had severe Factor X deficiency (<1%) and in our country, sporadic cases of severe Factor X deficiency have been reported.¹¹ As the inheritance pattern of Factor X deficiency is autosomal recessive, our case was diagnosed as hereditary Factor X deficiency, since his parents had normal factor levels (>85%) and patient did not have any of the underlying acquired cause of Factor X deficiency. The child presented with haemarthrosis of right knee joint at one year of age, which is slightly unusual in such age group (as haemarthrosis occurs usually between 2 and 3 years of age, when the child starts walking). However, anecdotal cases have been reported in the literature.⁵

Because of the rarity of Factor X deficiency, evidence based management guidelines are lacking. For minor bleeding symptoms, topical therapies and anti-fibrinolytic agents may be sufficient whereas for more severe bleeding episodes, Factor X replacement therapy can be accomplished with fresh frozen plasma (FFP) or plasma derived prothrombin complex concentrates (PCC), which contains significant amount activated vitamin K dependent factors. Both of these treatments have their own side effects. While FFP have been associated with allergic reactions and transfusion related acute lung injury, PCC is associated with hypercoagulable complications such as DIC and venous thromboembolism.¹⁰ The biological half-life of infused Factor X is 20–40 h but varies among individual and with repeated dosing. Because of the long half-life, daily treatment may result in increasing levels and is not usually required.

Targeted level for treatment and surgery are not well established. Patient with Factor level of 10%–40% of normal have been considered adequate for hemostasis. Due to risk of thromboembolic phenomenon, Factor X levels should not exceed 50% of normal.

Conflicts of interest

All authors have none to declare.

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