Recurrent venous thromboembolic event in a sever factor X deficient patient without any correlation to Pro-coagulant product usage

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OBJECTIVES

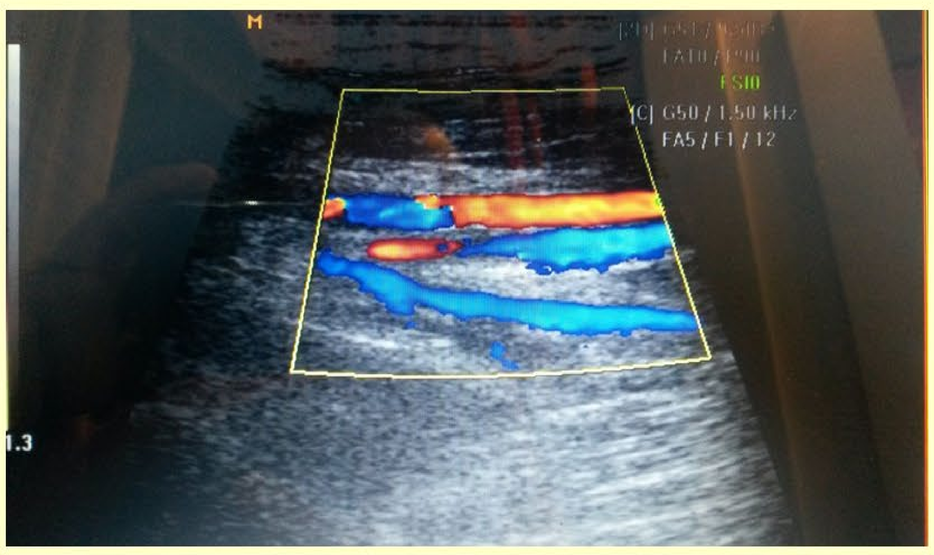
Factor X deficiency is a rare autosomal recessive bleeding disorder in children , with a prevelance of 1 in 2 million. Worldwide, about 1400 cases were reported till now . There is a wide spectrum of clinical symptoms ranging from minor bleeding , hemarthrosis to life threatening hemorrhagia . The diagnosis of FX deficiency is based on using PT and APTT, RVVT or chromogenic assay to measure the coagulant activity of FX (FX:C) and then if possible by immunoassay to detect plasma FX antigen levels (FX:Ag).No thromboembolic event has ever been reported which had not been related to treatment with coagulant products. Here we report a patient with a severe factor X deficiency disorder presenting with recurrent venous thromboembolic events.

Table-1

PT	50sec
APTT	70sec
Mixing PT	15.5sec
Mixing aPTT	31.1sec
Factor X level	0.3%
Mutation	p.Gly363Ser

Table-2

TEST	RESULT
Anti phospholipid IgG	2 u/ml
Anti beta-2 glycoprotein- IgG	2 u/ml
Anti beta-2 glycoprotein-IgM	4 u/ml
Anti phospholipid IgM	3 u/ml
ANA	Neg
Anti ds DNA	24
Anti cardiolipin IgG	3u/ml
C3	138 mg/dl
C4	31 mg/dl
Protein C Activity	78%
Protein S Activity	32%
Factor V Leiden	NL
MTHFR C677	NL
MTHFR A1298C	Mutated, Heterozygous
Prothrombin G20210	NL
Homocystein	10.7 umol/L
D-Dimer	0.1ug/ml
Plasma -FDP	Neg
HLA B5	Neg
HLA B8	POS
HLA B27	Neg
HLA B51	Neg
HLA B5	Neg



Case Report

An 8 year old boy with sever factor X deficiency was referred to Mofid Children hospital with a severe abdominal pain . The diagnosis of factor X deficiency disorder was made at 3 years old age based on bruising in the extremities and by coagulation test findings and FX level=0.3% and confirmed by molecular studies at the age 6 Y by finding a p.Gly363Ser mutation (Table 1). He was admitted with the main differential diagnosis of appendicitis or intra abdominal bleeding. In his physical exam. the patient didn't have any finding except for an abdominal pain without guarding or point tenderness.. Radiologic findings didn't correlate with the suspected diagnosis. After a couple of hours the patient's abdominal pain subsided and he claimed a localized severe inguinal pain. The ultra sound colored Doppler showed a decrease in the venous blood flow and a large venous thrombosis in the common femoral vein extending to the right safenous vein.(Fig-1) During the previous 2 months he didn't have any plasma of PCC transfusion. . A comprehensive lab tests did not show any significant finding except for a protein S activity=32% which was not clinically significant . (Table 2). The patient was treated simultaneously with FFP and LMWH (enoxaparin). After clinical and radiological improvement the patient continued a total short course of treatment for about 45 days and then stopped due to the tendency to bleeding. Two weeks after the cessation of FFP and LMWH the patient referred to our clinic with a severe upper extremity pain. The colored Doppler ultra sound showed again a thrombosis in the left brachial vein. The patient was treated again with FFP and LMWH for one month till completely improved Radiologic and clinical findings.

After two years the patient had again a deep venous thrombosis in the left femoral vein. The previous therapy was given for 45 days. No clinical or laboratory findings were able to justify these episodes. Continuous therapy with FFP and LMWH or vitamin K antagonists were not possible due to the bleeding risks, lack of monitoring data and the refusal of the patient. Since that time the patient had pain episodes in his extremities but neurologic or rheumatologic findings did not yield a specific diagnosis. At the meantime the patient is not treated with any anticoagulant therapy or blood product, and is being observed for on demand therapy

CONCLUSIONS

We just found two explanation for recurrent VTE events in our case despite of extensive assays. Our patient had a mild decrease in Prot. S activity which might be due to a heterozygote protein S deficiency, however it is unusual to cause a VTE in young children especially in repeatedly in a bleeding tendency status. Although he was heterozygote in MTHFR A1298C mutant, the homocysteine levels in both admissions were normal.however it might be supposed to be high before, due to some fasting condition. Since there is no underlying disorder in our patient ,co-inheritance of the above conditions was the sole explanation for for his presentation, even if dose not convince well.

the most problematic issue in this case were his management during the VTE events because LMWH was not expected to be efficious in Severe FX deficient patient, and warfarin therapy could not be monitored by PT and INR.So we tried to use a combination of antithrombotic treatment with FFP simultanously until the clinical response.

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