Case Report

Near fatal spontaneous intraperitoneal bleeding: A rare manifestation in a congenital factor X deficiency carrier

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Abstract

Congenital factor X (FX) deficiency is a rare coagulation disorder of autosomal recessive inheritance, characterized by bleeding of variable severity. Bleeding severity generally correlates with the level of FX functional activity and severe bleeding usually occurs in moderate and severe deficiency, when FX coagulant activity is <5%. FX activity above 10% is infrequently associated with severe bleeding. Here we report the rare occurrence of life-threatening massive spontaneous intraperitoneal bleeding with hypovolemic shock, resulting from spontaneous rupture of an ovarian luteal cyst in a 25-year-old FX deficiency carrier woman, with a FX activity of 26%. She was managed successfully conservatively, with fresh frozen plasma and packed red blood cell transfusions and she showed gradual improvement. The case is being reported to discuss the diagnosis and management of this rare inherited coagulation disorder.

Keywords: Bleeding, factor X, hemoperitoneum, luteal cyst, rupture

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Introduction

Factor X (FX) deficiency is a rare inherited coagulation disorder of autosomal recessive inheritance. Severe FX deficiency, resulting from homozygous state, is a rare coagulation disorder with an estimated worldwide incidence of 1/10 lakh births.[1] Prevalence of FX deficiency carrier state (heterozygous state) may be as high as 1/500 population.[2] The bleeding manifestations are variable and their severity depends on functional activity of FX and genetic mutation in a given patient.[3] Most common manifestations include mucocutaneous bleeds such as cutaneous bruising, epistaxis, gum bleeds and menorrhagia in females.[4] Severe bleeding events such as hemarthrosis, intracranial and gastrointestinal bleeding, as seen in hemophilia, generally occur in those with severe (FX activity <1%) disease, but are uncommon in moderately severe (FX activity between 1% and 5%) disease. Mild disease (FX activity between 5% and 10%)[4] can be asymptomatic or can be associated with minor mucocutaneous bleeds. Heterozygote carriers (FX activity between 10% and 30%) rarely can have minor mucocutaneous bleeding manifestations, after trauma or surgery.[3] Here we report the rare occurrence of life-threatening massive spontaneous intraperitoneal bleeding with hypovolemic shock, most probably following rupture of an ovarian cyst in a 25-year-old woman with FX deficiency carrier state (FX activity: 26%).

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Case Report

A 25-year-old, unmarried woman presented to emergency department with complaints of sudden onset severe abdominal pain, vomiting and low grade fever for 36 h. On admission to intensive care unit, she was found to be pale and anxious. Examination revealed tachycardia (heart rate: 120/min), tachypnea and blood pressure (BP) of 90/60 mm Hg, with postural drop. Distention of abdomen, with diffuse tenderness and sluggish bowel sounds was noted. Abdominal sonography revealed moderate ascites, fluid in pouch of Douglas and an ill-defined cystic right adnexal mass, with internal echoes. Diagnostic abdominal paracentesis confirmed hemoperitoneum. Laboratory

evaluation revealed severe anemia (Hb: 2.2 g/dl, hematocrit: 7%), total leucocyte count: 11,600/µl, with 80% polymorphs, platelet count of 184 × 10^3/µl, blood urea nitrogen: 40 mg/dl, serum creatinine: 1.6 mg/dl, normal serum electrolytes, serum bilirubin: 0.9 mg/dl, aspartate transaminase: 78 U/l, alanine transaminase: 41 U/l, alkaline phosphatase: 72 U/l, serum protein: 6 g/dl, serum albumin: 3 g/dl, prothrombin time (PT): 16 s (control: 13 s) and activated partial thromboplastin time (aPTT): 64 s (control: 28–32 s). Urinary pregnancy test, serum fibrin degradation products and D-dimer assay were negative.

She gave history of prolonged bleeding from minor skin cuts and wounds, from age of 7 years. There was no history of umbilical stump bleeding after birth, spontaneous skin or mucosal bleeds, joint or muscle bleeds, blood product transfusion and her menses were normal. One-month prior to the current admission, she had profuse bleeding following dental extraction, needing local application of BotroClot™ (hemocoagulase) for hemostasis. Coagulation work-up, done few days later, after Vitamin K administration, had shown normal bleeding time (2 min 30 s) and PT: 14 s (control: 13 s), but aPTT: 53 s (control: 29 s) was prolonged. Hemoglobin: 12.2 g/dl, platelet count (244 × 10^9/l) and aggregation studies were unremarkable. Mixing study with 1:1 mixture of patient's plasma with normal pooled plasma and aged serum corrected the aPTT, but mixing with adsorbed plasma failed to correct aPTT. Mixing with FIX and FVIII deficient plasma corrected the aPTT and aPTT based assay, using FX deficient plasma, revealed FX activity of 26%. Her only sibling, an 18-year-old brother, had complaints of large cutaneous ecchymoses and excessive bleeding after minor trauma, starting from 5 years of age and he had suffered an episode of hemarthrosis of left knee following trauma. His coagulation work-up revealed FX activity of 8%. Her parents were asymptomatic and had a nonconsanguineous marriage. No other relatives on her maternal or paternal side had abnormal bleeding.

She developed worsening hypotension (BP: 80/60 mm Hg) and urine output reduced during first 36 h. As she could not afford for prothrombin complex concentrates, she was managed conservatively with fluids, vasopressors and fresh frozen plasma (FFP) and 5 packed red blood cell units were transfused. There was gradual improvement of hemodynamic status and her urine output improved over next 24 h. Contrast computed tomography of the abdomen and pelvis [Figure 1] revealed a ruptured hemorrhagic corpus luteal cyst, with hemoperitoneum. She recovered gradually over a week and was discharged subsequently.

Discussion

Factor X is a Vitamin K dependent serine protease synthesized in liver. FX is activated to its active form (FXa) by FVIIa/tissue factor complex (extrinsic pathway) or by FIXa/FVIIIa complex (intrinsic pathway) and subsequently, along with FVa, platelet phospholipids and calcium ions, plays a crucial role in the final common pathway of coagulation cascade to convert prothrombin to thrombin.

Although severe bleeds involving central nervous system, gastrointestinal tract and haemarthroses have been reported earlier in FX deficiency,[2-4] spontaneous intraperitoneal bleeding resulting from rupture of corpus luteal cyst of the ovary has been rarely reported,[5-7] and these patients had severe disease. Severe and life-threatening spontaneous bleeding is uncommon when the FX activity is >1%.[2,4] The index patient, despite having FX activity >10%, had spontaneous life-threatening bleed. Genetic mutation and biologic activity of FX,[2,3] apart from quantity synthesized, determine bleeding severity. Genetic analysis and immunological assay to quantitate the FX antigen level could not be done in the index case for lack of facilities.

Diagnosis of congenital FX deficiency is to be suspected in a patient with compatible history and coagulation work-up showing prolongation of both PT and aPTT, which correct on 1:1 mix with normal plasma. However, cases of FX deficiency with normal

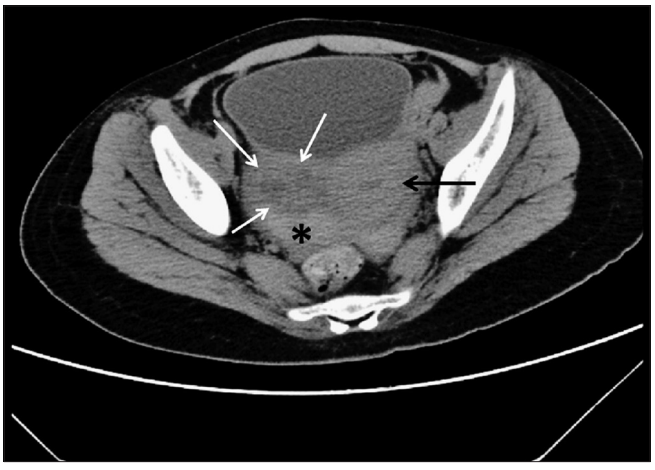

Figure 1: Contrast enhanced computed tomography of pelvis, showing a ruptured cystic right adnexal mass (white arrows), pushing the uterus (black arrow) to left; high attenuation within cyst (suggesting hemorrhage) and highly attenuated fluid (*) in the pelvic cavity, suggesting hemoperitoneum

PT, as in the index case, have been reported.[2,3] Freshly drawn blood (without heparin contamination) in a sodium citrate tube, with proper ratio of blood to citrate needs to be sent to a well standardized coagulation laboratory for valid results on functional FX assay. As the commercially available blue top citrate tubes are calibrated to maintain correct ratio of plasma to the sodium citrate up to a hematocrit of 55%, patients with a hematocrit >55% or <21% will not have correct ratio of plasma to citrate and hence coagulation studies may give erroneous results. Acquired FX deficiency can occur in liver disease, Vitamin K deficiency resulting from malabsorption, oral anticoagulation with Vitamin K antagonists, disseminated intravascular coagulation, myeloma, amyloidosis and acquired inhibitors to FX.[1] These conditions were excluded in the index case, based on clinical features and laboratory evaluation.

Management of moderate to severe bleeding in FX deficiency involves FX replacement, which can be accomplished by transfusion of FFP (10–20 ml/kg/day) or prothrombin complex concentrates.[2] FX concentrates[8] are not readily available. As FX has a biologic half-life of 20–40 h, once daily dosing is recommended. Recombinant FVIIa is considered not useful for treatment, other than in acquired FX deficiency associated with amyloidosis. Antifibrinolytics such as tranexemic acid and aminocaproic acid are used topically and systemically for control of mild mucosal bleeds.

To conclude, FX deficiency carrier state can rarely be complicated by life-threatening intraperitoneal bleeding from rupture of corpus luteal cyst and awareness of this rare coagulation disorder and its treatment is required for optimal management.

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