Factor-X deficiency; a rare disorder to be looked for in cases of congenital bleeding tendency

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Submission date: 27-Mar-2018 12:14PM (UTC+0500)
Submission ID: 936893326
File name: 18270-72589-1-ED.docx (26.85K)
Word count: 1203
Character count: 6867

Title

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Key words

Bleeding disorder, factor-X deficiency, inherited

Dear Editor;

Factor X deficiency is an autosomal recessive disorder which is quite rare and involves coagulation cascade. People with this disorder present with a myriad of early life bleeding complications. We report here a case, who presented with bleeding complications at different stages of his life but was diagnosed very late.

A 23-year-old male presented to the medical emergency department of our hospital with complaints of hematuria for five months, black stools for ten days, and bleeding from nose for four days. He had a history of recurrent bleeding from different sites, starting from the time of his circumcision on seventh day of his life. The circumcision wound bled so severely that his wound had to be sutured to achieve hemostasis. At the age of 11 years, he developed severe epistaxis, for which he remained admitted in the hospital for 15 days and received transfusion of a standard pack of red cell concentrate (RCC). At 12 years of age, he was re-admitted for a massive hematoma in right leg after getting injection from a quack that resulted in weakness of his right leg due to nerve compression. After seven years, he was operated upon for the drainage of psoas abscess. During operation, he developed severe bleeding, and had to be transfused with 18 pints of fresh frozen plasma (FFP), and one pack of RCC. He remained admitted in the hospital for almost seven months until his wound healed completely after daily wound wash and aseptic dressings. Through all his visits, the patient never reported fever, night sweats or weight drop. He had no history of tobacco smoking, drug or alcohol abuse.

He was born to consanguinous parents. One of his elder sister had complaints of heavy menstrual bleeding since menarche but was not yet investigated. He was not taking any medication affecting coagulation function.

On examination, he had marked palmar and conjunctival pallor. He was vitally stable. No petechiae or gingival anomalies were seen on oral cavity examination. Abdominal examination showed scar mark of drainage of psoas abscess and associated incisional hernia. There was no lymphadenopathy nor abdominal organomegaly. Rest of the systemic examination was unremarkable.

His laboratory evaluation revealed a hemoglobin of 11.2 g/dL (normal range: 12.9–16.1 g/dL)[2], and a normal platelet and total leucocyte count. The prothrombin time (PT) was 30 s (normal: 15 s) and activated partial thromboplastin time (aPTT) was 62 s (normal: 33 s). His D-dimers were >250 ng/mL D-Dimer Units (normal: ≤ 250 ng/mL D-Dimer Units) but the fibrinogen level was not decreased, excluding the possibility of disseminated intravascular coagulation (DIC). The serum total proteins were in the normal range. PT and aPTT mixing studies corrected with a 1:1 mix with normal plasma (1). The assessment for serum antinuclear antibody, antinuclear cytoplasmic antibody, and C_3, C_4 complement levels showed normal values. Serological tests for rheumatoid factor and hepatitis B and C were non-reactive. The levels of different coagulation factor were tested and only factor X levels were decreased i.e. 13% (normal: 50-150%)

He was managed with 6 pints of FFP because factor X concentrates were not available. (Figure-1A) He was discharged after ten days following complete resolution of bleeding. Prior to discharge, he was properly counseled about the disease and the management options, and was advised to seek immediate medical care in case of bleeding from any site.

Seven months after discharge, he presented again to the hospital with non-healing wound, and purulent discharge from the site where psoas abscess was surgically drained. After diagnostic imaging, the patient was diagnosed to have enterocutaneous fistula that was excised surgically

and right hemicolectomy with ilio-colic anastomosis had to be done. The wound of the surgical incision did not heal, and purulent discharge persisted. The patient was again operated upon for exploration. The surgeon found multiple adhesions of descending colon and small-gut. There were many small-gut tears and long fistulous communications in the right hepatic flexure. The adhesions were broken, affected portion of the small gut and descending colon were removed, and tube colostomy was done in the right hypochondrium while ileostomy was constructed in the left hypochondrium. (Figure-1B). The wounds for ileostomy and colostomy kept on bleeding for three months before coming to an arrest, and he had to be transfused with 4-5 pints of FFP every week. The patient is now getting food orally, and stable on home medications and colostomy.

Factor X is the first enzyme that is involved in the coagulation cascade for the formation of fibrin. Factor X deficiency has an estimated prevalence of 1 in 5 -10 x 10^5 in the general population (1). Families that adhere to consanguineous marriage traditionally, are more likely to carry the disease (1). Pakistan has a reported incidence of 3.5%, 6%, and 26.1% for factor X deficiency in three different reports about patients with bleeding disorders (2-4). The manifestations of the disease can become evident at any age; however, the symptoms are more severe if the disease presents itself during infanthood. The symptoms are noticeable only in homozygote individuals and are combinations of easy bruisability, hemorrhages in soft tissues and joint cavities, epistaxis, hematuria and excessive menstruation (5). Differential diagnoses of factor X deficiency include von-Willebrand disease, deficiency of factors II, IX, V, VII,VIII, XI, DIC, hemolytic-uremic syndrome, dysfibrinogenemia, cryoglobulinemia, Cushing syndrome, immune thrombocytopenic purpura, Waterhouse-Friderichsen syndrome, Osler-Weber-Rendu Syndrome, scurvy, thrombotic thrombocytopenic purpura, and vitamin K deficiency.

The laboratory findings pertinent to the disease include prolonged PT and aPTT. The goal of treatment in factor X deficiency is to restore circulating factor X levels to 10-40% of the normal. Therapeutic measures may include infusion of FFP and prothrombin complex concentrates. The prognosis of X deficiency depends on gravity of the disease at presentation measured through estimation of factor X levels. Low levels of factor X are associated with increased chances of life-threatening complications (6).

In conclusion, factor X deficiency, though rare, is a life-threatening disease. Its knowledge is important to differentiate it from other disorders of coagulation. Timely diagnosis of the condition will save the patient from unnecessary interventions (e.g. factor VIII concentrate injections), and will lead to adequate management.

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Figure legends

Figure-1: 1A: Figure showing the patient being transfused with fresh frozen plasma at initial presentation. 1B: Figure showing the patient with right tube colostomy and left ileostomy

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