FACTOR-X DEFICIENCY: A RARE DISORDER TO BE LOOKED FOR IN CASES OF CONGENITAL BLEEDING TENDENCY

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ABSTRACT

Factor X deficiency is a rare, autosomal recessive disorder that involves the coagulation cascade. People with this disorder present with a myriad of early life bleeding complications. We report here a 23-year-old male, who presented with bleeding complications (prolonged bleeding from surgical wounds, unresolving hematomas, uncontrolled nasal bleeding, hematuria and hematochezia) at different stages of his life but was diagnosed very late for factor X deficiency after comprehensive evaluation for clotting factors. He was managed by repeated transfusions of fresh frozen plasma and detailed counselling. Factor X deficiency is a rare life-threatening disease and must be differentiated from other disorders of coagulation. The patients are advised to avoid activities with high levels of physical contact, unnecessary invasive interventions and drugs that remarkably affect liver functions and seek immediate medical care in case of bleeding from any site.

KEY WORDS: Hemorrhage (MeSH); Bleeding disorder (Non-MeSH); Factor X Deficiency (MeSH); Inherited (Non-MeSH); Blood Coagulation Disorders, Inherited (MeSH); Blood Coagulation Disorders (MeSH).

THIS ARTICLE MAY BE CITED AS: Ayaz F, Ayaz SB, Furrukh M. Factor-X deficiency: a rare disorder to be looked for in cases of congenital bleeding tendency. Khyber Med Univ J 2018;10(3):163-5.

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Date Submitted: March 16, 2018

Date Revised: September 11, 2018

Date Accepted: September 15, 2018

INTRODUCTION

Factor X is one of the vitamin K dependent clotting factors. It plays a crucial role in the coagulation cascade as the first enzyme in the common pathway of thrombus formation. The gene for the factor X is present on the long arm of chromosome 13. Factor X synthesis occurs in liver. [1]

Factor X deficiency is an autosomal recessive disorder which is quite rare and involves coagulation cascade. Homozygous factor X deficiency has an incidence of 1: 1,000,000 in the general population. Heterozygotes are often clinically asymptomatic. Acquired factor X deficiency is rare, but when it occurs it is usually in association with amyloidosis. People with this disorder present with a myriad of early life bleeding complications.[1] We report here a case of factor X deficiency, who presented with bleeding complications at different stages of his life but was diagnosed very late.

CASE REPORT

A 23-year-old male presented to the medical emergency department of our hospital with complaints of dark-colored urine 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 long 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. After operation, bleeding from surgical wounds did not halt. Therefore, he had to be transfused with 18 units of fresh frozen plasma (FFP) and one unit 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 loss. He had no history of tobacco smoking, drug or alcohol abuse.

He was born to consanguineous parents. One of his elder sisters had complaints of heavy menstrual bleeding since menarche but was not investigated then. 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 or abdominal organomegaly. The joints examination did not reveal any swelling, erythema, tenderness or limitation of active or passive movements (Figure-1A).

His laboratory evaluation revealed a hemoglobin concentration of 11.2 g/dL (normal range: 12.9-16.1 g/dL), platelet count of 160×10^9/L (normal range: 150 to 450×10^9/L) and total leucocyte count of 6×10^9/L (normal range: 4.5 to 11.0×10^9/L). The prothrombin time (PT) was 30seconds (control: 15seconds) and activated partial thromboplastin time (aPTT) was 62 seconds (control: 33 seconds). His D-dimers were >250 ηg/mL D-Dimer units (normal: ≤250 ηg/mL D-Dimer units) but the fibrinogen level was 200mg/dL (normal range: 150-400 mg/dL) that excluded the possibility of

disseminated intravascular coagulation (DIC). The serum total proteins were in the normal range. On mixing studies, the aPTT corrected with normal plasma.[2] 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 for factor VIII and factor IX were 90% and 80% respectively. Only factor X levels were found to be low i.e. 13% (normal: 50-150%).

He was managed with 6 units of FFP because factor X concentrates were not available and was discharged ten days later following complete resolution of bleeding. Prior to discharge, he was counseled about the disease and the management options and was advised to avoid activities with high levels of physical contact, unnecessary invasive interventions e.g. intramuscular or intravenous injections and drugs that affect liver functions considerably. He was instructed to always inform his treating physician about his disease and 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 units of FFP every week. The patient is now getting food orally and stable on home medications and colostomy.

DISCUSSION

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 $5\text{-}10\times10^5$ in the general population. Families that adhere to consanguineous marriage traditionally, are more likely to carry the disease.[2] Pakistan has reported frequencies of 3.5%, 6%, and 26.1% for factor X deficiency in three different reports about patients with bleeding disorders.[3-5] 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

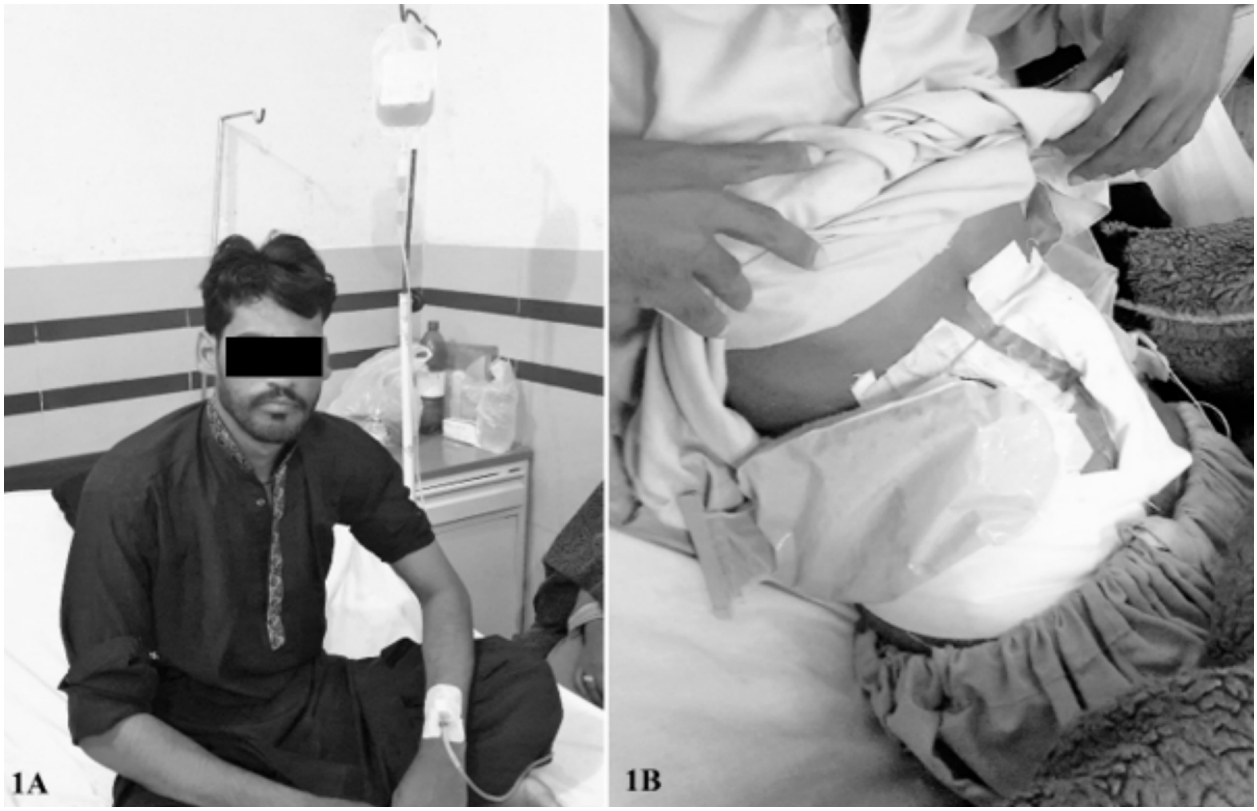

Figure 1: The joints examination did not reveal any swelling, erythema, tenderness or limitation of active or passive movements (Figure-1A); tube colostomy in the right hypochondrium and ileostomy in the left hypochondrium. (Figure-1B)

bruising, hemorrhages in soft tissues and joint cavities, epistaxis, hematuria, and excessive menstruation.[2] 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 factor 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. Because of risk of hemorrhage following trauma, the affected individuals are advised to avoid activities with high levels of physical contact and unnecessary invasive procedures. They are also instructed to inform the treating physician about their disease once diagnosed. The use of alcohol and drugs that affect liver functions is limited. All diagnosed patients must receive factor replacement therapy during operative procedures to avoid post-operative bleeding complications.

In our patient, the hematoma in right thigh and nerve compression could have been prevented if he could have avoided intramuscular injection in right thigh. Prolonged bleeding from surgical wounds might possibly be averted by pre-operative evaluation of factor X levels and perioperative transfusion of FFP.

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AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

FA & MF: Concept & study design, acquisition of data, final approval of the version to be published.

SBA: Analysis and interpretation of data, drafting the manuscript, critical review, final approval of the version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE

NIL

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