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Case report

Factor IX deficiency (Christmas disease)

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Introduction

Hemophilia B is the second most common type of hemophilia.^{1,2} It is also known as factor IX deficiency, or Christmas disease. It was originally named “Christmas disease” after the first person diagnosed with the disorder back in 1952. Hemophilia A is 7 times more common than hemophilia B, occurring in about 1 in 25,000 male births in US and 1 in 30,000–60,000 in India.^{3,4} All races and economic groups are affected equally. Hemophilia B is inherited as an X-linked recessive disorder, where males are affected, with females being carriers.

Here we present a case that manifested with adult onset spontaneous gastrointestinal and gingival bleeding at 32 years of age.

Case report

A 32-year-old male presented with obscure gastrointestinal bleed, pain abdomen, vomiting, hematemesis and melena of 4 years duration. These symptoms were intermittent and were

happening once or twice per month. There was history of easy fatigability. There were few episodes of bleeding from gums which were spontaneous, but there was no history of purpuric spots, bleeding from deep tissues and joint bleeding. For these symptoms the patient was managed initially in a local hospital with repeated blood transfusions. Later, the patient was referred to a tertiary center, where complete work up was done. His hemogram revealed normal hemoglobin, WBC and platelet counts. Peripheral blood smear was also normal. Stool examination revealed presence of occult blood with no ova/cyst. His initial coagulation studies detected normal bleeding and prothrombin time, and a prolonged activated thromboplastin time (APTT). His liver function tests were normal. Total protein, albumin and globulin levels also were normal. Ultrasound abdomen and mesenteric angiography were normal. Chest X-ray, CECT abdomen, and renal function tests were normal. Tagged RBC scan was also normal. Explorative lap revealed blood in jejunum up to the colon. Upper GI endoscopy revealed edematous duodenal bulb folds with mild duodenitis, for which he was treated with antipyloric drugs. Colonoscopy revealed patchy loss of vascularity in proximal rectum for 15 cm. Rectal

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biopsy was normal. Earlier reports of any clotting factor assays were not available. However since for the last 3–4 months, symptoms were occurring more frequently, the patient was admitted to our hospital for further work up. A detailed coagulation work up revealed normal bleeding time, normal prothrombin time, normal russel viper venom test, prolonged APTT and normal thrombin time (TT). Tests for fibrinogen degradation products and D-dimer were negative (Table 1).

An isolated cause for prolonged APTT can be due to deficiencies of factor VIII, factor IX, factor XI or factor XII, and Von Willebrands disease. It could also be due to the presence of circulating anticoagulants (inhibitors). Heparin can also cause prolongation of APTT but in this scenario TT will also be prolonged (more sensitive marker). Circulating anticoagulants or inhibitors affecting the APTT may act immediately or be time dependent. Normal pooled plasma mixed with plasma containing an immediately acting inhibitor will have little or no effect on the prolonged clotting time. In contrast, if normal pooled plasma is added to plasma containing a time dependent inhibitor, the clotting time of later will be substantially shortened. However, after 1–2 h, correction will be abolished, and the clotting time will become increased again. To detect both types of inhibition, normal and test plasma samples are mixed in equal volumes and tested for APTT immediately as well as after incubation at 37 °C for 120 min.¹ In our patient clotting time became normal with addition of normal pooled plasma and remained so with and without incubation, thus ruling out the presence of inhibitors and suggesting a deficiency of factor IX. Thereafter factor VIII and factor IX were assayed, and were found to be 100% and 9%, respectively (normal value is 60–120% for both). With these reports, the patient was diagnosed as severe factor IX deficiency. Presently patient is on Epsilon aminocaproic acid and it is planned to start him on factor IX concentrate. Epsilon aminocaproic acid is an antifibrinolytic agent, which enhances plasminogen activation by binding to the lysine residues of plasminogen.

Discussion

Factor IX deficiency (hemophilia B) is a hereditary blood coagulation disorder. Females with one defective factor IX gene are carriers (they don't have symptoms). In women who are carriers, their male babies have a 50% chance of having the disease, while their female babies have a 50% chance of being a carrier. It is caused by a deficiency of a blood plasma protein called factor IX. Without enough factor IX, the blood cannot

clot properly to control bleeding.^{2,5} There are several types of hemophilias, including hemophilia A and B. Hemophilia A is 7 times more common than hemophilia B. Hemophilia B is the result of a deficiency of clotting factor IX. The severity of symptoms can vary, and the severe forms become apparent early on. Bleeding is the main symptom of the disease and sometimes, though not always, occurs if an infant is circumcised. Additional bleeding problems usually show up when the infant becomes mobile. Symptoms include bleeding into joints and associated pain and swelling, blood in the urine and stool, bruising excessive bleeding following circumcision, gastrointestinal tract and urinary tract hemorrhage, nosebleeds, prolonged bleeding from cuts, tooth extraction and during surgery and at times spontaneous bleeding. APTT is prolonged, prothrombin time is normal, bleeding time is normal, fibrinogen level is normal, factor VIII level is normal and factor IX is reduced. Standard treatment is infusion of factor IX concentrates to replace the defective clotting factor. The amount infused depends upon the severity of bleeding, the site of the bleeding, and the size of the patient.³ Hepatitis B vaccine is recommended for individuals with hemophilia B because they are at increased risk of developing hepatitis due to exposure to blood products. Depending on the severity of the disease, factor IX concentrate may be given prior to dental extractions and surgery to prevent bleeding. The prognosis is usually good with treatment. Most people with hemophilia are able to lead relatively normal lives. A small percentage of people develop inhibitors of factor IX, and may die from loss of blood. People with hemophilia B should establish an ongoing relationship with a hematologist, especially one associated with a hemophilia treatment center. The ability to have quick and easy access to medical records describing their level of factor IX, history of transfusions (including the type and amount), any complications they've had, and the type and amount of any inhibitors can be lifesaving in the event the person with hemophilia is in an emergency situation.

Conflicts of interest

All authors have none to declare.

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Table 1 – Laboratory data of patient.

Tests	Patient	Control
PT (s)	13	11–16
APTT (s)	50.1	26–40
TT (s)	16	15–19
RVVT (s)	15	15
Factor VIII (%)	100	60–120
Factor IX (%)	9	60–120
FDP (μg/ml)	Negative	<5
D-Dimer (μg/ml)	Negative	<0.5