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Factor XIII Deficiency Presenting As Persistent Umbilical Bleeding In Newborn - A Case Report

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ABSTRACT

Factor XIII, also known as fibrin stabilizing factor, plays an important role in hemostasis by stabilizing the clot. Factor XIII deficiency is a rare coagulation factor deficiency. It can be either congenital or acquired. It is inherited as an autosomal recessive disorder. It presents most frequently in newborn period with persistent bleeding from umbilical stump. We report a case of 4 day old neonate presenting with persistent umbilical bleeding. Routine haemostatic tests were normal and it was diagnosed by clot solubility test. Infant was treated with FFP.

KEYWORDS Factor XIII, clot solubility test, umbilical bleeding,FFP.

Introduction

Plasma factor XIII is a heterotetramer (FXIII-A2B2) that plays an integral role in hemostasis by catalyzing the cross-linking of fibrin, a variety of integrins within the platelet membrane and matrix proteins throughout thrombus formation, thus strengthening and stabilizing the blood clot.[1] Factor XIII deficiency is a rare coagulation deficiency with an incidence of about 1 case per 2–5 million. Only few cases are reported in literature. The first case of congenital FXIII deficiency was reported in Switzerland in 1960[2]. Factor XIII Deficiency is an inherited bleeding disorder, inherited in an autosomal recessive pattern[3] Umbilical bleeding is a characteristic and frequent finding occurring in 80% of cases [4]. So being a rare disease and presenting most commonly in newborn period with umbilical bleeding we report a case of Factor XIII deficiency diagnosed in a newborn.

Case report:

A 4 day old male infant born to a second degree consanguineously married primigravida mother presented with history of persistent and prolonged bleeding from umbilical stump. There was no history of trauma and no history of drug intake in mother, no family history of bleeding. No history of bleeding from other sites like skin, gastrointestinal tract, immunization site. Infant was given 1mg Vitamin K intramuscular at birth. On examination heart rate was 150 per minute and BP was 66/45 (50mm Hg), respiratory rate was 48per minute. CRT was less than 3 seconds. On examination anterior fontanelle was open measuring 2x2cm.. Bleeding from the umbilical stump was present. No petechiae or purpura were present. Systemic examination was normal. Baby was active, tone and newborn reflexes were normal. Baby was admitted and detailed laboratory evaluation was done. Hemoglobin was 8.5gm%, total leukocyte count was 9850cells /cu mm, platelet count was 3.74lakhs/ cu mm. Neonate's blood group was' O' positive, and platelet aggregation was seen on finger prick smear. Coagulation profile showed bleeding time 2 minute, clotting time 5 minute 45seconds, PT 10.9seconds (control-11seconds).APTT was 34.4seconds (control-30seconds), thrombin time 12.7 seconds (control-15). Mixing studies for PT/APTT showed features consistent with factor XIII deficiency. Factor VIIIC assay was 66.1 IU/dl , factor IX assay was 49.5 IU/dl , and test for factor XIII (urea solubility test) was positive. Baby was given FFP following which bleeding stopped. Baby was also given packed RBC transfusion for anemia. Infant was discharged and advised for FFP or cryoprecipitate infusion every 3-4 week interval.

Discussion

Factor XIII is also known as fibrin stabilizing factor. It is required for normal fibrin clot formation. It acts in the terminal phase of the coagulation cascade, after thrombin has converted fibrinogen to fibrin. Half life of factor XIII is 5-7 days and hemostatic level is 2-3% activity. In the absence of factor XIII, a clot is easily soluble, so its deficiency leads to prolonged bleeding. Factor XIII deficiency can be either congenital or acquired .Congenital deficiency of factor XIII was first described in 1960 by Duckert [2]. Factor XIII deficiency is a rare congenital coagulation abnormality of which only 200 cases are reported till 2002[5]. The disease is transmitted as an autosomal recessive trait and is more common in countries with high rate of consanguineous marriages[6]. Disease can affect both male and female. Acquired deficiency of factor XIII is seen in the acute stages of Henoch Schonlein purpura (HSP), active stages of ulcerative colitis and Crohn's disease and in the presence of inhibitors against factor XIII. Factor XIII deficiency presents frequently with umbilical stump bleeding in 80% of cases[4]. It also presents with superficial bruises, bleeding into soft tissues and central nervous system bleeding. Rarely it can present with bleeding from the gums, into muscles and joints, cuts, scrapes or bleeding after surgery. Other clinical manifestations are delayed separation of umbilical stump beyond 4 weeks, poor wound healing, recurrent spontaneous abortions in women.

The platelet count, bleeding time, prothrombin time, APTT, thrombin time, and whole blood clotting time are within normal limits. Screening tests for factor XIII deficiency are based

on the observation that there is increased solubility of the clot because of the failure of cross linking. The normal clot remains insoluble in the presence of 5M urea, whereas in a patient with factor XIII deficiency, the clot dissolves. Specific immunoassays for factor XIII confirms the deficiency.

Factor XIII deficiency is treated with cryoprecipitate or fresh frozen plasma (FFP). Pasteurized FXIII concentrates are also available which are safe and have higher titer of FXIII (about240 units/vial). Life-long prophylactic therapy every 4-6 weeks by 10-20 U/kg FXIII is recommended in patients with severe FXIII deficiency to prevent life-threatening spontaneous bleeding[6].

Conclusion

Factor XIII deficiency is the coagulation factor deficiency that cannot be detected by classical haemostatic tests. A newborn presenting with persistent umbilical stump bleeding should be screened for factor XIII deficiency when routine coagulation tests are normal.

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