Case Report

Congenital Factor X Deficiency

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Introduction

Inherited clotting factor X deficiency is one of the rarest inherited coagulation disorders. It is characterized by spontaneous mucous membrane bleeding, unusual bleeding following major or minor trauma, and menorrhagia. Factor X or Stuart-Prower factor is the first enzyme in the common pathway of thrombus formation. It is synthesized in liver and requires vitamin K for synthesis. Gene for factor X is located on chromosome 13 (13q34)\(^1\). Factor X is the first member of thrombin pathway. It cleaves prothrombin yielding active thrombin. It is inactivated by protein Z-dependent protease inhibitor (ZPI). Defects in this protein leads to increased factor Xa activity and a propensity for thrombosis.

Factor X deficiency was first noted in 1950s by two independent groups. This deficiency may be congenital or acquired. Congenital factor X deficiency is an autosomal recessive disorder\(^2\). Acquired deficiency is seen in liver disease, amyloidosis, myeloma, leprosy, severe burns and respiratory tract infections\(^3-5\).

Congenital factor X deficiency is considered very rare in Western literature. About 50 cases have yet been described. This deficiency affects one individual per 500000 to 100000 population worldwide\(^6\). It is common in areas where consanguinity is frequent like Pakistan and India. In a local case report, 3.5% subjects who were evaluated for bleeding disorder had factor X deficiency. This case report describes three members of a family who were found to have factor X deficiency.

Case Report

A 16-year-old teenager was admitted with recurrent spontaneous mucosal bleeding and easy bruising since birth. For these complaints he had been receiving blood transfusions and fresh frozen plasma previously without any definite diagnosis. He also complained of breathlessness on exertion and difficulty in walking due to pain in right knee. There was history of severe umbilical cord bleeding and prolonged bleeding following circumcision as well.

He was product of consanguineous marriage. He had five siblings, two of whom had related but milder problems. An elder brother was having repeated episodes of similar spontaneous mucosal bleeding and easy bruisingibility while the elder sister frequently required blood transfusions for massive menorrhagia. Other three siblings and rest of the family did not have similar complaints.

On examination he was markedly pale. He had multiple bruises and chronic synovial inflammation of right knee joint. Except for hyperdynamic circulation rest of examination was unremarkable. His haemoglobin was 2.4g%. Platelet count was 25000/mm\(^3\). Bleeding time was normal. Hess test was negative. Prothrombin time (PT), activated thromboplastin time (APTT) and thrombin time (TT) were all prolonged. Coagulation factor assays showed marked factor X deficiency (<1% of normal activity). Workup of other two siblings also revealed factor X deficiency (1-10% of normal activity).

During his hospital stay he started complaining of pain and swelling in thigh, which on evaluation turned out to be hematoma. He was administered fresh frozen plasma at a dose of 10 ml/kg body weight. He also received blood transfusions and hematinics. Both these interventions led to marked improvement of his complaints. He was also administered first dose of hepatitis
B vaccine. He and other family members were counselled appropriately. He was discharged with advice for regular follow up.

**Discussion**

Congenital factor X deficiency is of two types. In type I there is reduced synthesis of factor X, while type II is a qualitative defect associated with production of dysfunctional molecule. Point mutation and splice site mutation cause type I disease where as missense mutation cause type II disease. Missense mutations are common cause of acquired factor X deficiency. Complete deficiency is incompatible with life.

Levels of factor X deficiency determine the severity of bleeding. Subjects with >10% of normal factor X have few problems. Those with 1-10% of normal factor X have mild to moderate bleeding and individuals with <1% of normal factor X have severe bleeding. It is generally considered that factor X deficiency in Pakistani subjects is not severe. Our index patient and his affected siblings had <1% and 1-10% of normal factor X activity respectively, indicating severe and moderate disease.

Factor X deficiency can present at any age and with variable manifestations. Common presentations are umbilical cord stump bleeding, nose bleed, easy bruising, bleeding into soft tissues and muscles, GIT bleeding, menorrhagia, intracranial bleed, hemarthrosis, recurrent epistaxis and bleeding after trauma or surgery. Combination of duodenal telangiectasia with factor X deficiency presenting as recurrent melena has also been reported. Females are susceptible to early abortions. In our index case severe umbilical cord stump bleeding and prolonged bleeding following circumcision were earliest notable manifestations.

Investigations for congenital factor X deficiency include prolongation of coagulation time, PT, APTT, TT and Russell viper venom time. Bleeding time is normal. Factor X assays are confirmatory. Mutation analysis should also be performed. Assays for other coagulation factors are normal.

Morbidity reduction and prevention of complications are main aims of therapy in congenital factor X deficiency. Treatment has to be individualized for each patient. It generally consists of restoration of circulating factor X levels to 10-40% of normal. Fresh frozen plasma is used for this purpose. Prothrombin complex concentrates can also be used to increase factor X levels. Vitamin K administration is not helpful in congenital factor X deficiency. Genetic counseling and mutation analysis should be done.

Affected person should be vaccinated against hepatitis B. Activities involving severe physical effort should be limited. Females with severe deficiency or with history of early or recurrent miscarriage need aggressive replacement therapy during pregnancy. Prognosis is dependent on degree of factor X deficiency; affected persons with severe deficiency have increased chances of bleeding and related complications compared to the ones with less severe deficiency.

**References**