Factor X Deficiency In Pregnancy: An Obstetricians Nightmare

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Abstract:
Congenital isolated factor X deficiency is a very rare autosomal recessive disorder. The incidence of factor X deficiency is 1 in 10,00,000 in the general population. Pregnancy with factor X deficiency may present with recurrent antepartum and peripartum haemorrhage including recurrent episiotomy site haematoma. Complete absence of Factor X is lethal.
Here we report a case of severe factor X deficiency who was referred to our institute at 38 week of gestation. She had history of recurrent episiotomy site haematoma in previous pregnancy and multiple episodes of antepartum haemorrhage in present pregnancy. She was managed successfully with a planned haemostatic strategy at our institute.
No specific guidelines for managing such cases are available till date. In our opinion, patients with severe Factor X deficiency can have a normal pregnancy outcome with dedicated multidisciplinary approach and a planned delivery at a tertiary care center.

Keywords:
pregnancy, Factor X deficiency, PCC, FFP, management, postpartum haemmorhage, tertiary care center

Introduction:

The most common congenital bleeding disorder affecting females is Von Willebrand disease. Factor X deficiency is an uncommon cause of bleeding disorder in pregnancy; very few cases are reported. Factor X has an important role in intrinsic as well as extrinsic pathways of coagulation, so its deficiency leads to impaired thromboplastin time and prothrombin consumption. Therefore, factor X deficiency affects both prothrombin time (PT) and activated partial thromboplastin time (aPTT). In this article, we discuss the difficult task of managing factor X deficiency during pregnancy.

Case report:

A 30-year-old second gravida with one live issue was referred to our high-risk pregnancy clinic at 38 weeks of gestation. She had been diagnosed with severe factor X deficiency and came to us for further management and delivery. During this pregnancy, she had threatened abortion associated with a 2 cm x 2 cm retroplacental hematoma. Due to recurrent episodes of spotting and deranged coagulation profile, she received multiple fresh frozen plasma (FFP) and cryoprecipitate transfusion during her antenatal period.
She has a history of petechiae formation and bruises after minor trauma. She also gives history of the formation of scalp hematoma twice in her childhood which was managed surgically. There was a

history of menorrhagia resulting in severe anemia, for which she required multiple blood transfusions. In her previous (2016) pregnancy, she had precipitate labor along with recurrent episiotomy site hematoma, which was surgically managed three times in same pregnancy, along with multiple blood and blood product transfusions and ICU care. She is the second sibling of a non-consanguineous marriage, and there is no history of any bleeding tendency in her parents or siblings.

Based on her history, she was admitted and further evaluated. Her PT was 59.6, International normalized ratio (INR) was 4.9 and aPTT was 57.9. Factor X level was 1.4% of normal, suggesting severe factor X deficiency. A multidisciplinary team approach was adopted. Isolated factor X replacement was impossible as it is not available in India. The patient had a history of transfusion reaction (itching, rashes, chest discomfort and breathing difficulty) with FFP on several occasions, so FFP transfusion was discouraged. Prothrombin complex concentrate (PCC) is available in our country, so PCC infusion was planned before elective labor induction. However, the patient went into spontaneous labor. Consequently, 1500 IU of PCC were infused during active labor. Each vial of PCC contains 500 IU. Seven vials of PCC were arranged. Coagulation was corrected within one hour of the PCC infusion and its effect persisted for 24 hours. Labor progressed very quickly and she delivered vaginally. Active management of the third stage of labor was performed. A post-placental Levonorgestrel-releasing intrauterine system (LNG-IUS) was inserted. The coagulation profile and factor X level were repeated after one hour of PCC infusion and were PT - 17.00, aPTT - 34.8, INR - 1.5 and the factor X level was 14%. The patient was monitored closely for bleeding. Her postpartum period was uneventful. The patient was given 1000 IU of PCC infusion on the second and third postpartum days. Her factor X level then rose to 40%. The infant was observed closely for the development of hemorrhagic complications. The patient was discharged on the fifth postpartum day with advice for the evaluation of the baby. Now the patient is following up in the postnatal clinic and pediatric outdoor patient department (OPD).

Discussion:

Factor X deficient patients who are heterozygous are usually asymptomatic, though some may present with significant episodes of bleeding [1]. Patients who are homozygous for factor X deficiency disorder commonly present with intracranial hemorrhage and umbilical cord stump bleeding during the neonatal period. During adult life epistaxis, recurrent hemorrhagic ovarian cysts, spontaneous hemoperitoneum from ovulation, menorrhagia, petechiae or bruises from minor trauma or hemarthrosis may be the presenting complain [1]. Factor X levels between 10% to 35% of normal are usually adequate to achieve hemostasis [2]. In normal pregnancy, factor X level increases during pregnancy and returns to non-pregnant level by six weeks postpartum. This physiological rise of factor X is rarely seen in women with severe factor X deficiency [2]. Among the standard coagulation tests (PT, INR, aPTT, fibrinogen concentration and platelet count), patients with factor X deficiency usually present with prolonged PT, INR and aPTT. However, a functional assay for factor X activity must be performed to make a definite diagnosis.

Management of laboring patients with factor X deficiency is very challenging. Treatment for these patients aims to adequately replace factor X to prevent bleeding and to prevent overcorrection due to risk of deep vein thrombosis. Therefore, the therapeutic management options are replacement using either transfusion of FFP or PCC infusion or plasma containing vitamin K dependent factors or infusion of factor X. Correction of factor X in such patients should be done in active labor [3]. The factors present in FFP are II, VII, VIII, IX, X, XI and Von Willebrand factor. FFP is administered as a loading dose of 10 to 20 mL/kg followed by three to six mL/kg every 12 to 24 hours. PCC contains four vitamin-K dependent coagulation factors—II, VII, IX, X, protein C, protein S, and protein Z. It also contains heparin which prevents activation of these coagulation factors. The dosage of PCC is 50–125 IU/kg. Not more than two to three doses should be administered in the first 36–48 hours because of an increased risk of thrombosis [4].

As opposed to FFP, PCC is rapid to reverse, safe and doesn't contain leukocytes, so there is less chance of reaction. Use of PCC infusion in obstetric hemorrhage limits the use of blood products and prevents transfusion-related complications and fluid overload. Allergic reactions and thromboembolic events like pulmonary embolism, deep vein thrombosis and stroke are a few

complications related to PCC [4]. Factor X should not exceed 50% as it may lead to thromboembolic complications. Relative contraindications of PCC are history of disseminated intravascular coagulation (DIC), recent history of myocardial infarction or stroke. Additional medications like tranexamic acid and epsilon-amino caproic acid can be used for additional benefit as they are antifibrinolytic.

The mode of delivery should be decided as per obstetric condition of the patient. There is no contraindication for vaginal delivery in cases of coagulation factor deficiency. The delivery must be managed in a tertiary care center with a multidisciplinary team approach and availability of blood, blood components, and factor concentrates.

Krkovic et al. treated a similar patient with FFP transfusion [2]. She had an elective caesarean section. Choissi et al. reported the case of a 30-year-old primigravida with factor X deficiency and factor X replacement was done by plasma exchange [4]. Kumar and Mehta et al. described a factor X deficient woman during her four pregnancies. She was treated successfully with FFP in her first pregnancy and factor X concentrate in subsequent pregnancies [5]. Taxiera et al. discussed a factor X-deficient woman who was managed successfully with PCC infusion [6]. Konje et al. reported a similar case of a woman who developed retroplacental hematoma during pregnancy. She was treated with PCC infusion and there were no complications during her delivery by caesarean section [7]. Van Dievoet et al. were the first to report a similar case with defects only in the extrinsic pathway. The patient was managed successfully with vitamin K supplementation [8].

Conclusion:

Our case is one of the few reported cases managed successfully by PCC infusion. We can say from our experience that a patient with severe factor X deficiency can have a normal pregnancy outcome with dedicated multidisciplinary care and planned delivery. LNG-IUS can be used for contraception. Vasectomy should be the preferred mode of sterilization when the partner is unaffected. Genetic counseling should be offered to all patients and their families.

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