Factor X deficiency and Pregnancy

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Factors X deficiency is a rare disorder, with only 50 cases reported to date. There are only a few published case reports of women with Factor X deficiency undergoing successful pregnancy, each with a unique clinical course and approach to management. In this case report, we describe the clinical course of a patient with severe Factor X deficiency who underwent a successful pregnancy and delivery.

Case Report
The patient is a 30-year-old woman who was diagnosed with factor X deficiency at menarche when she presented with symptoms of menorrhagia, requiring treatment with fresh frozen plasma and red cell transfusions. She was started on oral contraceptives, which helped to decrease the menstrual flow. Every 3 to 6 months she developed symptoms of hemarthrosis or painful bruising which required treatment with fresh frozen plasma or FEIBA (activated prothrombin complex concentrate).

At age 30, the patient decided that she wanted to become pregnant. The patient’s Factor X level was 2%. A detailed discussion about the possible risks of pregnancy was held between the patient and her hematologist. Despite the possible risk of a life-threatening bleed, the patient decided that she wanted to become pregnant and shortly thereafter conceived. Throughout the pregnancy, the patient was monitored closely by high-risk obstetrics and hematology. The first trimester of pregnancy was complicated by the development of a large hemorrhagic corpus leuteal cyst, seen incidentally on ultrasound. The patient was treated with FEIBA. Follow-up ultrasounds showed slow resolution of the cyst over the first trimester. The patient was subsequently followed with close observation, with plans to initiate treatment with factor replacement when the patient showed the first signs of labor.

There is no pure Factor X concentrate. Therefore available Factor IX products were assayed to determine which contained the highest ratio of Factor X to Factor IX within the product. Bebulin is a Factor IX complex which also contains Factor X, Factor II, and low amounts of Factor VII. The Factor X to Factor IX ratio in Bebulin was 0.44 and Bebulin was chosen for use for Factor X replacement.

At 35 weeks, the patient was admitted with uterine contractions and spotting. She was started on treatment with Bebulin. Factor X levels were maintained at 30% to 40% with every other day infusions. The contractions spontaneously ceased. The patient was monitored in the hospital with plans to induce labor at 37 weeks. The day of induction, Bebulin was given in order to increase the Factor X level to 70% and she subsequently was induced. Approximately 12 hours later, she gave birth to a healthy baby girl via vaginal delivery. The patient had a small vaginal laceration, which was repaired. Estimated blood loss was approximately 500 cc.

In the postpartum period, Factor X level was maintained at 30% to 40%. She was discharged, postpartum day 3, to receive Bebulin at home every other day until postpartum day 12.

Discussion
Factor X deficiency is a rare disorder of the clotting systems. It is characterized by severe episodes of bleeding, particularly if the Factor X level is less than 10%. Factor X is a vitamin K dependent clotting factor, which is a part of the final common pathway of the coagulation cascade. Factor X is converted to Factor Xa. The prothrombinase complex (Factor Xa...
+ Factor Va + phospholipid + calcium) convert prothrombin (Factor II) to thrombin (Factor IIa), which subsequently stimulates fibrinogen to fibrin. Patients with Factor X deficiency will have prolongation of the prothrombin time and partial thromboplastin time and a functional assay for Factor X will reveal a deficiency of the clotting factor.

There are only a few cases described in the literature of patients with Factor X deficiency undergoing successful pregnancies. The first case was reported by Brody and colleagues in 1960 in which they hypothesized improvement in Factor X deficiency. In pregnancy, the normal physiologic response is for a rise in Factor X levels to a peak of 163% of normal activity at 30 weeks. A second rise in Factor X levels to 173% of normal activity occurs 144 hours postpartum. The Factor X levels subsequently fall, returning to normal approximately 6 weeks after delivery. In the following cases of patients with severe Factor X deficiency, there was no improvement in the clotting factor deficiency with pregnancy.

Kunje and colleagues described a 22-year-old woman with Factor X deficiency whose pregnancy was complicated by the development of recurrent retroplacental hematomas. This patient was treated with Bioproduct Laboratory Factor IXA infusions, which is rich in Factor X (contains 500 iu Factor X, 500 iu antithrombin III, 550 iu Factor IX A, 600 iu Factor II and 5,000 iu heparin). Treatment was complicated by 2 transient episodes of chest pain and shortness of breath of unclear etiology. A healthy baby was delivered at 39 weeks by caesarean section.

Kumar and Mehta reported a case of 4 pregnancies in a woman with Factor X deficiency. The patient's first 2 pregnancies resulted in premature labor and delivery at 21 and 25 weeks. The babies subsequently died in the neonatal period. The patient was treated with fresh frozen plasma for acute bleeding episodes and received Konyne (Factor IX complex) prophylactically during the latter half of the second pregnancy. During the following 2 pregnancies, the patient was treated with prophylactic Factor X early in pregnancy. She developed premature labor, necessitating treatment to prevent premature contractions. She eventually gave birth to healthy 34-week-old and 32-week-old babies.

Rezig and colleagues describe a woman with Factor X deficiency who was treated with prothrombin complex concentrates (Kashadil) early in labor and during the peripartum period and delivered a healthy 33-week-old baby, with no excessive bleeding.

Lastly, Bofill and colleagues describe a 23-year-old woman with Factor X deficiency who received no factor replacement during the antenatal period. During labor and during the first postpartum day, the patient was treated with fresh frozen plasma. She had no excessive bleeding and the baby was healthy.

Review of this limited literature demonstrates the heterogeneity of the clinical course of patients with Factor X deficiency and pregnancy. Some patients required Factor X replacement early in the antenatal period while others were able to go through the entire pregnancy without factor replacement. Our patient developed premature labor at 35 weeks, which subsequently ceased with treatment with Bebulin (Factor IX concentrate with high levels of Factor X). The patient was hospitalized and treated with prophylactic Bebulin until delivery was induced at 37 weeks. The benefit of Bebulin over fresh frozen plasma is that Bebulin contains a higher concentration of Factor X than fresh frozen plasma, and therefore less volume is required to achieve a rise in Factor X levels. The safety of factor replacement in pregnancy is not known; however, based on these case reports, it appears that the offspring have suffered no adverse effects.

Consideration of pregnancy in patients with Factor X deficiency requires a detailed discussion of the possible risks of pregnancy and the heterogeneity of the clinical course. The risk of bleeding needs to be weighed against the risks of prophylactic factor replacement in the absence of symptoms. In the patients described to date, the risk of spontaneous hemorrhage has manifested as retroplacental hematomas or corpus luteal cyst hemorrhage. The risks of prophylactic factor replacement include the risk of hypercoagulability, as well as lack of knowledge regarding the safety of these products during pregnancy. In the present case, assays of available products allowed for rational dose scheduling that minimized hemostatic risks. A discussion of the risks and benefits need to be weighed with each individual patient.