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Management of severe factor XI deficiency in pregnancy: A case report

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Abstract

Factor XI (FXI) deficiency is one of the rarest coagulation disorders with a frequency of 1:1,000,000. A 30-year-old woman, diagnosed with FXI deficiency at the age of 4, was admitted to our maternity service at 25 weeks of gestation. The patient had no history of hemorrhage or abnormal bleeding, and the clinical examination was unremarkable. Antenatal care was also normal. The parturient was admitted in early labor at 38 weeks of gestation. Despite the absence of clinical hemorrhagic syndrome, a transfusion of fresh frozen plasma combined with tranexamic acid was initiated once the active stage of labor was started. Management of FXI deficiency in pregnant women is a challenge due to its unpredictable bleeding tendency, and careful planning and knowledge of appropriate hemostatic management is pivotal for their care.

Keywords

Factor XI, factor XI deficiency, bleeding, hemostasis, pregnancy, delivery

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Introduction

Factor XI (*FXI*) deficiency (hemophilia C), first described in 1955, is a rare autosomal inherited multigenic disorder that affects only 1/1,000,000 of the general population but is more common in Ashkenazi and Iraqi Jewish populations.[1] The *FXI* is located on chromosome 4, several mutations have been described but the two genetic variants that account for over 90% of abnormal alleles in the Jewish population are Glu117 Stop (type II) and Phe283Leu (type III).[2,3] The FXI deficiency is characterized by reduced levels of coagulation FXI in plasma but the values do not reflect the importance of factor to hemostasis in an individual very well.[4]

FXI (Rosenthal factor) is a plasma glycoprotein that participates in the early phase of the blood coagulation cascade and plays an essential role in normal hemostasis and fibrinolysis.[2,5] The susceptibility to bleeding is not related to the severity of the deficiency even in the most severe forms, unlike coagulation disorders associated with FVIII or IX[6,7] Menstruation, pregnancy, abortion, and childbirth represent intrinsic hemostatic challenges for women with FXI deficiency.[7]

We present the *case* of a 30-year-old woman who presented with severe asymptomatic congenital FXI deficiency and try to analyze the impact of the use of hemostatic products in the management of pregnant patients affected by this type of deficiency.

Case

A 30-year-old, Arab, nulliparous, woman diagnosed with FXI deficiency was referred to our maternity service at 25 weeks of gestation to follow up on her pregnancy with specific healthcare. The diagnosis of FXI deficiency was made at the age of 4 after a preoperative assessment for tonsillectomy. She was also operated on an appendectomy at the age of 24 after prophylactic treatment with fresh frozen plasma (FFP); the operation was carried out without

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complications. The patient had no history of hemorrhage or abnormal bleeding, and there was no family history of bleeding disorders. The clinical examination was unremarkable. Antenatal care including several checkups, tests, and scans was normal. A pre-anesthesia evaluation was conducted at 36 weeks and a workup was requested to assess potential risk. The blood tests showed a prothrombin time of 97.3% (11, 4 s), hemoglobin of 11 g/dL, a platelet count of 243,000/mm^3, an activated partial thromboplastin time (aPTT) value of 46 s, and an FXI assay of 5%.

The parturient was admitted in early labor at 38 weeks of gestation. On admission, the aPTT was prolonged (patient-control ratio of 1.46), PT: 100% (11, 6 sec), aPTT: 43 s, platelets: 259,000/mm^3, hemoglobin: 10.4, and FXI level: 5%. At the start of the active stage of labor, a transfusion of coagulation factors using FFP was requested to achieve an FXI level over 50% and prevent a postpartum hemorrhage (PPH).

On the second day of hospitalization, a spontaneous rupture of membranes occurred and the patient was transferred to the delivery room. There was no clinical bleeding syndrome, but the patient was immediately started on FFP transfusion at 15 ml/kg because there is no clear consensus on the precise indications for FFP in the management of deliveries in patients with FXI deficiency. And because this was the first pregnancy with significant maternal stress, priority was given to the management of bleeding risk. No epidural anesthesia was administered due to patient preference (the patient wanted to experience childbirth without medication). Instead, intravenous morphine was administered as an analgesic alternative at a total dose of 6 mg with monitoring of respiratory rate, maternal saturation of peripheral oxygen (SpO2), and cardiotocography.

Three hours later, during the transfusion of the 4th FFP units, the patient delivered a healthy female baby weighing 2900 g and an Apgar score of 10 at both 1 and 5 min. We performed a vaginal delivery with a removal manual of the placenta and systematic uterine revision. An additional prophylactic oxytocin infusion and a slow IV of 1 g of tranexamic acid (TXA) over 20 min prevented maternal hemorrhagic complications, with no need for re-administration or oral relay as the patient remained stable.

The patient was admitted to the intensive care unit (ICU) for rigorous clinical and biological monitoring in our institution, and all women with a significantly high risk of PPH and morbidity are managed in the ICU. The initial workup on a postpartum day 1 showed PT 95% (11, 7 s), the aPTT was normal (32, 9 s), a fibrinogen level of 5.02 g/l, and an FXI level of 24% same level as immediately after FFP perfusion.

Follow-up was normal and the patient remained asymptomatic. Two days later, she was discharged from the ICU without complications. The patient refused to undergo genetic counseling for her baby during *the first months of birth as there was no urgency*, but it was scheduled during her first year.

Discussion

FXI plays an important role in the amplification phase of coagulation and inhibits fibrinolysis through activation of the thrombin-activatable fibrinolysis inhibitor. FXI deficiency is distinguished from hemophilia A and B by its occurrence in both sexes and by the absence of spontaneous bleeding into joints or muscles.[8] Clinical symptoms include bleeding occurring mainly in areas of high fibrinolytic activity: the urogenital tract or oral and nasal mucosa.[3,9] There is no correlation between coagulation factor activity level and clinical bleeding severity for FXI[1] and the most relevant risk factor for perioperative and obstetric bleeding prediction is a personal history of hemorrhage.[10] As FXI deficiency is often phenotypically silent, the presence of incidental findings is not uncommon.[11]

FXI deficiency is diagnosed by a prolonged activated partial thromboplastin time and low plasma levels of coagulant FXI.[4] The FXI level is less than 20% for homozygotes or compound heterozygous mutations and 20%–60% for heterozygotes.[2]

Despite there is no indication that FXI deficiency is associated with an increased risk of miscarriage, it is associated with an elevated risk of PPH in comparison with the general population (10%–22% vs 5–8% for primary and 7% vs 0.8%, respectively) and complication bleeding after termination of pregnancy.[2,10]

There is contradictory data in the literature concerning FXI levels during pregnancy, but several subsequent studies in FXI-deficient patients report no significant change over the course of pregnancy, in contrast to factor VIII and von Willebrand, which increase relatively during pregnancy.[4,11] However, measurement of FXI levels during the first and third trimesters remains essential for hematologists and anesthetists to decide the appropriate hemostatic prophylaxis during labor and delivery.[6] In the opinion of English authors, epidural anesthesia should be avoided in the presence of bleeding symptoms or severe deficiency but is not absolutely contraindicated.[12]

The mainstays of treatment for PPH prophylaxis in FXI-deficient patients include FXI concentrate, allogeneic plasma (FFP or other variants of it), and antifibrinolytics such as TXA or epsilon aminocaproic acid.[9] Desmopressin (DDAVP) is also commonly used for the *treatment and prevention of bleeding complications in patients with* FXI deficient but FFP remains the first-line treatment in many countries, despite its significant side effects: pulmonary edema, thrombotic events, immunization, and infection. Plasma-derived FXI concentrate, solvent-detergent-treated FFP, and aFVII are alternatives, but due to their high cost, they may not be accessible in some countries.[6,12] In our case, the patient had an FXI level of 5, and due to the unavailability of other products, it was decided to use FFP in combination with TXA for prophylaxis, after consultation and discussion with the patient.

Conclusion

The use of intrapartum prophylaxis may be useful in minimizing the risk and/or severity of PPH. Given the absence of recommendations for women with severe forms of the disease, care should be taken to consider FXI activity level together with the clinical presentation and history of bleeding before deciding the appropriate treatment. Pregnant patients with FXI deficiency should be managed by a multidisciplinary team that includes obstetrics, hematology, and anesthesiology.

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Author contribution

Rajae Tachinante, Mohamed Elkhorassani, and Mounia Yousfi: designed the study.
Fatima El Hassouni, Sofia Lahbabi, Rajae Tachinante, Mohamed Elkhorassani, and Mounia Yousfi: taking responsibility for patient follow-up, data management, and reporting.
Fatima El Hassouni, Sofia Lahbabi, Rajae Tachinante, Mohamed Elkhorassani, and Mounia Yousfi: taking responsibility for logical interpretation and presentation of the results.
Fatima El Hassouni and Asmae Bentaleb: drafting the article.
Sofia Lahbabi, Rajae Tachinante, Mohamed Elkhorassani, and Mounia Yousfi: reviewing the article for its intellectual content.

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Ethics approval

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Informed consent

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