



## CASE REPORT

# Perioperative Management in Patients with Factor XI Deficiency

**Antoine Legrand, Remi Bouquerel, Antoine Strzelecki, Benjamin Le Gaillard, Christophe Pelletier, Mireille Houadec and Edmundo Pereira de Souza Neto\***

Département d'Anesthésia, Centre Hospitalier de Montauban, France

\*Corresponding author: Edmundo Pereira de Souza Neto, Département d'Anesthésia, Centre Hospitalier de Montauban, 100 rue Léon Cladel, 82013 Montauban, France



## Introduction

Factor XI (FXI) is a plasma serine protease that contributes to thrombin generation primarily through proteolytic activation of factor IX. While FXI is necessary for normal coagulation *in vitro* systems individuals FXI deficiency have a variable bleeding risk that cannot be predicted from FXI antigen, FXI: Clotting activity, and activated partial thromboplastin time (APTT) [1-3]. The bleeding disorder in FXI-deficient patients has presented practical and conceptual challenges for clinicians [1-4].

In this article, we describe three cases of patients with FXI deficiency.

## Case Report

### Case 1

White French female patient, 56-years-old, 76 kg, 170 cm, was scheduled for a Left knee arthroplasty. Vital signs (blood pressure, temperature, oxygen saturation and Glasgow coma score) were normal. His ASA physical status was 2 and she had no treatment. Past medical history found a cervicobrachial neuralgia. Past surgical history consisted of bilateral hallux valgus, left knee arthroscopy, blepharoplasty and an ovarian ectopic pregnancy.

The patient had an history of abnormal clinical bleeding that needs a blood transfusion that were during the ovarian ectopic pregnancy surgery and for her two childbirth (vaginal delivery).

The complete blood count discovered only a low

hemoglobin count 10.6 g/dl. Prothrombin time (PT) was 100% (normal range: 70%-100%), activated partial thromboplastin time (APTT) with normal plasma [ratio 1:1] was 1.24 (Normal range: 0.80-1.20). Her laboratory evaluation revealed an FXI level quantitated at 41%.

A routine hematology consultation was obtained and a bleeding management strategy was established that was performing the surgical procedure with antifibrinolytic therapy with tranexamic acid (1 g twice a day, for 10 days), avoid nonsteroidal anti-inflammatory and use of Factor XI concentrates (Hemoleven®, LFB) only if bleeding.

The surgery was done without any problem, bleeding was about 200 mL and no transfusion was needed.

The patient remained in the post-anaesthesia care unit for 80 minutes and then returned to her hospital room. She was discharged from the hospital the day after surgery. No adverse events have been reported.

### Case 2

White French female patient, 33-years-old, 56 kg, 156 cm was scheduled for a tubal ligation. Vital signs (blood pressure, temperature, oxygen saturation and Glasgow coma score) were normal. His ASA physical status was 2, her treatment was Levothyroxine 75 µg. Past medical history found a hypothyroidism. Past surgical history consisted of two deliveries without complication, bilateral inguinal hernia, appendectomy, tonsillectomy without problem. A wisdom teeth extraction done in 2016 presented a hemorrhagic complication and laboratory evaluation found a factor

XI deficiency with a rate of 36%. There were no blood transfusions or pharmacologic agents given to promote hemostasis.

Her laboratory evaluation revealed an APTT at 1.27 (Normal range: 0.80-1.20), PT at 87% (normal range: 70%-100%) and a FXI level quantitated at 41%.

After a hematology consultation, it was decided to perfuse 1 g preoperative of EXACYL, to avoid NSAIDs and low-molecular-weight heparin. Hemoleven® was made available in the operating room. However, as the surgery was done without bleeding, Hemoleven® or transfusion was not needed.

The patient remained in the post-anaesthesia care unit for 80 minutes and then returned to her hospital room. As no adverse events have been reported, she was discharged from the hospital the day after surgery.

### Case 3

Black French female patient, 38-years-old, 90 kg, 165 cm, was scheduled for an urgent caesarean because failed operative vaginal delivery. Vital signs (blood pressure, temperature, oxygen saturation and Glasgow coma score) were normal without foetal suffering. His ASA physical status classification was 2. Her treatment was salbutamol if necessary and iron supplementation. Past medical history was a cured syphilis, allergic asthma, factor XI deficiency (discovered in previous pregnancy). She had no surgical history outside four normal deliveries.

In 2013, for the last delivery, FXI counts were 32%, Hemoleven® made available, but not used because no hemorrhagic complication. Delivery was done without hemorrhagic or obstetric complications.

Her laboratory evaluation realized 3 weeks before caesarean revealed a factor XI with 47% activity, an APTT at 1.12 (Normal range: 0.80-1.20) and a PT at 98% (normal range: 70%-100%).

Hematology consultation stated that her blood deficit was a physiological deficit during pregnancy, which does not require any particular conduct.

Caesarean was done under general anesthesia, because FXI counts were at 24%. An intravenous perfusion of 1 g of acid tranexamic was realized. The surgery was done without major bleeding and without the need to realize transfusion.

The patient remained in the post-anaesthesia care unit for 60 minutes before returned to her hospital room. She was discharged from the hospital the 4 days after surgery. No adverse events have been reported. Supplementation of an anemia by iron (Venofer®) (iron sucrose injection) was done.

### Discussion

Factor XI (FXI) deficiency is an autosomal disorder

that should occur in equal numbers in men and women and may be associated with bleeding [1,3]. Homozygotes and compound heterozygotes will have a factor level of less than 15% and the expected FXI level in heterozygotes is 25-70% [1,3].

While the incidence of severe FXI deficiency in the general population is estimated at only 1 in a million persons, the disorder is common in Ashkenazi (East European) Jews, in whom the carrier frequency for an abnormal FXI allele is about 8%, and severe deficiency is present in one in every 450 persons [2-4].

Other terms for FXI deficiency include plasma thromboplastin antecedent deficiency, Rosenthal syndrome, and hemophilia C. The International Committee for the Nomenclature of Blood Clotting Factors proposed FXI, to distinguish it from the factors missing in hemophilia A (Factor VIII), hemophilia B (Factor IX), and Hageman trait (Factor XII) [1-3].

Patients with FXI deficiency do not need treatment or prophylaxis for routine functions or activities [1-3]. The treatment of FXI deficiency is not always straightforward because the bleeding tendency is unpredictable and does not correlate with residual enzyme activity [1-3]. The size of the surgery, the risk of bleeding and the factor level of the patient are important for the decision if the FXI should be replaced or not. However, it is generally accepted that bleeding might be more important in severe deficiency of FXI (FXI level < 15 to 20% of normal) [1-3,5].

The association between the amount of FXI in plasma as determined by the activated partial thromboplastin time (aPTT) and bleeding propensity is weak, aPTT may not be correlated with hemorrhagic tendency [1-3].

In general, treatments for FXI deficiency include FXI concentrate, fresh frozen plasma and the use of antifibrinolytic drugs or desmopressin. Desmopressin (0.3-0.4 µg/kg given intravenously or subcutaneously) has also been shown to increase the activity of the factor XI [2,6,7]. In cases with minor bleeding, tranexamic acid (15 mg/kg or 1 g, 3 times daily) can be considered [2,5]. In cases with severe bleeding, an initial dose of FXI concentrates (10-15 IU/kg) or fresh frozen plasma (20 mL/kg) can be given, with or without the addition of tranexamic acid, depending on the degree of bleeding. FXI concentrate should not be given along with tranexamic acid [2,7]. Combination of plasma and tranexamic acid has been suggested instead of FXI concentrate, but combined use of plasma and tranexamic acid remains a controversial practice [2,5]. Several reported cases use recombinant factor VIIa but it has been associated with thrombosis [5].

In parturient, some authors stated that FXI level should be maintained > 35% during labor and for 3-4 days after vaginal delivery and 6-7 days after caesarean section [1-3]. Bolton-Maggs, et al. [8] proposed that if

patients have 4 of the following symptoms, they can be classified as “bleeders”: 1 - Bruising tendency; 2 - Mucous membrane bleeding, epistaxis, gastrointestinal bleeding, and hematuria; 3 - Heavy menstrual bleeding requiring treatment; 4 - Any (excessive) bleeding postsurgery; 5 - Bleeding post dental extractions; 6 - Bleeding related to childbirth [8].

If FXI level during the third trimester is < 20%, FXI concentrate or plasma should be considered in symptomatic patients or patients with no prior hemostatic challenge. Prophylaxis using tranexamic acid should be considered [2,3,5].

If FXI level during the third trimester is between 20% and 70% and patient has a history of bleeding, or no prior hemostatic challenges, tranexamic acid can be considered [2,3,5].

In case where FXI activity during the third trimester is between 20% and 70% and patient had no prior bleeding despite hemostatic challenges, treatment should be considered only if abnormal bleeding occurs [2,3,5].

Actually, evidence on the choice of anesthesia technique in parturient with FXI deficiency is based only on case series and reports [2,4]. It is difficult to draw a recommendation in favor of a particular technique. However, the consequence of epidural hematoma with irreversible paraplegia may make it an unacceptable risk to be taken on the basis of current limited evidence [2,4].

The practice of prophylactic plasma transfusion to perform a neuraxial intervention is not advised because it may provide more risk than presumed benefit [2,5].

We had three patients with low FXI, but no major deficiency (under 15%) and we did not observe any hemorrhagic complication. A protocol was established in accordance with the specialized opinion and the actual knowledge of FXI deficiency and kind of surgery. Expectant treatment of a pregnant woman is controversial if a cesarean delivery is not planned. In our case, because it was not deep deficiency of FXI and no major risk of bleeding surgery, no prophylactic supplementation of FXI was judged necessary. Only general measures were established with perfusion of acid tranexamic, restriction use of medication with hemorrhagic potential and FXI concentrates available in necessary. This type of support can be used in case of other moderate FXI deficiency, and with there is no major risk of bleeding surgery. However, this does not preclude contacting a reference hematologic center.

## Conclusions

Factor XI deficiency is an autosomal disorder and replacements should be done based in the kind of surgery, the risk of bleeding and the factor XI level. Treatments for FXI deficiency include FXI concentrate,

fresh frozen plasma and the use of tranexamic acid or desmopressin. A multidisciplinary organization in patient management should be done to reduce the complications.

## Informed Consent

Written informed consent was obtained from patients who participated in this case report.

## Peer-Review

Externally peer-reviewed.

## Conflict of Interest

No conflict of interest was declared by the authors.

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