



Anaesthesia Management of a Patient with Factor XI Deficiency

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Factor XI deficiency is an extremely rare disease presenting no clinical symptoms, unless there is an inducing reason such as trauma or surgery. Normally, factor levels are in the range of 70–150 U dL⁻¹ in healthy subjects. Although no clinical symptoms are seen, only high levels of aPTT can be found. Once a prolongation is detected in aPTT, factor XI deficiency should be suspected and factor levels should be analysed. With careful preoperative preparations in factor-deficient people, preoperative and postoperative complications can be decreased. In this case report, management of anaesthesia during total hip arthroplasty of a patient with factor XI deficiency is presented.

Keywords: Factor XI deficiency, anaesthesia management, total hip replacement

Introduction

Factor XI deficiency is a rare factor deficiency, and the encoding gene is located on chromosome 4. Spontaneous bleeding in patients with factor deficiency is rare, but major bleeding after surgery and traumas are possible. The values of isolated prolonged activated partial thromboplastin time (aPTT) should be a warning for factor deficiency XI (1). The basic method for treatment is the replacement of the missing factor (2). In this case report, the anaesthesia management of a patient with factor XI deficiency who was supposed to undergo a total hip replacement surgery is presented.

Case Presentation

The patient was informed, and permission was taken for this case report. The patient was a 59-year-old woman patient who had been followed for 2 years because of the lack of factor XI; she was evaluated prior to the left total hip replacement surgery. She stated that she also had allergic asthma and thyroid nodules in addition to factor XI deficiency. The patient's pulmonary function and thyroid functions were found to be within normal limits in the examinations performed. It was found that the diagnosis of the factor deficiency was made on the basis of the family history during a previous surgery; however, no prophylaxis was administered because the previous surgery was a minor surgical procedure and did not incur a serious complication.

It was observed in the haematological evaluation of the patient that the aPTT level was 77 seconds and the factor XI level was 9 U dL⁻¹ (normal values, 70–150 U dL⁻¹). Pre-operative haemoglobin was identified as 13.6 g dL⁻¹ and platelet count as 273 thousand mm³. The haematology department suggested the administration of 15–20 mL kg⁻¹ of fresh frozen plasma (FFP) prior to the intervention, 5 mL kg⁻¹ in the post-operative 12th hour and then 5 mL kg⁻¹ every 12 hours if the bleeding continued. After 6 units of FFP replacement was performed in the pre-operative period, the control aPTT value was measured as 32 seconds and the patient was taken to the operating room. Monitoring was performed with non-invasive blood pressure, peripheral oxygen saturation and 5-lead electrocardiography. The basal blood pressure was measured as 150/85 mmHg, heart rate as 78 min⁻¹ and SpO₂ as 97%.

Sedation was performed with an intravenous administration of 2 mg of midazolam and 100 µg of fentanyl in the patient for whom regional anaesthesia was decided. For antibiotic prophylaxis, 1 g of cefazolin sodium was intravenously administered. In total, 3 L min⁻¹ oxygen administration was started with a nasal O₂ cannula. After local anaesthesia was performed subcutaneously at the L4–L5 level in the left lateral decubitus position, the epidural space was reached with an 18 G Tuohy needle. By penetrating the dura with a 27 G pen-tipped needle through the needle, the free flow of cerebrospinal fluid was observed

and spinal anaesthesia was performed with 20 mg (4 mL) heavy bupivacaine. Then, after removing the spinal needle, the epidural catheter was placed and fixed. Selective spinal block was created by keeping the patient in the lateral decubitus position for 7 minutes. Then, she was given the right lateral position. After the spinal anaesthesia was confirmed, the surgery was initiated. While placing the intramedullary femoral prosthesis, nausea and vomiting occurred in the patient, whose intraoperative haemodynamics remained stable; thereupon, intravenous granisetron was administered and relief was provided. Intraoperatively, 2 units of FFP and 2 units of packed red cells were given. The intraoperative haemoglobin value was measured as 9.6 mg dL⁻¹. In total, 2000 mL of crystalloid solution was administered, and the intraoperative urine output was measured as 2 L. The surgery took a total of 210 minutes. An additional dose of anaesthetics was not required through the epidural catheter during the surgery. At the end of the surgery, the patient was given 2 mg of morphine through the epidural catheter as a routine protocol of our hospital, and patient-controlled analgesia was started with epidural bupivacaine.

In the post-operative 4th hour, prophylactically, 2 units of FFP and 1 unit of packed red cells due to decreased haemoglobin (9.3 g dL⁻¹) were given. Control aPTT was measured as 28 seconds. The patient did not need any more replacement of another blood product. The mean VAS score of the patient was determined (twice a day) to be 2.5 in the post-operative first 48 hours. After the aPTT value was found to be normal, the epidural catheter was removed without any complication at the end of 48 hours. In the post-operative 96th hour, the patient, whose control aPTT value was found to be 33 seconds, was discharged with the recommendations of physical therapy.

Discussion

Factor XI deficiency (haemophilia C or Rosenthal's disease) was first described in 1953, and the incidence was reported as 1/1,000,000. The encoding gene is located on chromosome 4. The plasma level is about 70–150 dL⁻¹ in healthy adults. The ratio in patients with heterozygous deficiency decreases to 30–60 U dL⁻¹ and that in homozygous patients decreases to below 20 U dL⁻¹. Spontaneous bleeding is rare in the clinic, but major bleeding is possible after surgery and traumas. Therefore, the factor XI level should also be considered along with the isolated prolonged aPTT values in the pre-operative evaluation (1). The severity of bleeding may not correlate with the plasma factor XI level (3). The main treatment is to replace the deficient factor to control the bleeding. The factor levels of the patients supposed undergo an intervention should be brought to normal values with pre-operative replacement and should not be allowed to fall below 60 U dL⁻¹ by continuing the replacement in the intraoperative period. Factor levels are recommended to be kept in the range of 30–60 U dL⁻¹ for at least 2 weeks in the post-operative

period (1, 2). In this case report, the anaesthesia management of a patient with factor XI deficiency who was supposed to undergo a total hip replacement surgery is presented.

Factor XI deficiency is usually diagnosed with abnormal bleeding, which occurs during delivery, surgery or dental procedures (4). A high level of isolated aPTT often draws attention in the analyses. The factor level is observed to be low in detailed examinations, although the factor level may not always remain parallel with bleeding (1); however, it is generally accepted that bleeding might be more severe in cases where the factor XI level is below 15 U dL⁻¹. In our patient, the factor deficiency was diagnosed in the examinations after the factor XI deficiency was found in her family. There was no excessive and uncontrolled bleeding in previous surgeries or in her other medical history. Due to the existence of this diagnosis, she was assessed by the haematology department before the surgery so that the necessary tests and measures could be performed in advance. Regional anaesthesia is not recommended in patients with bleeding tendency due to primary or secondary causes. In these patients, regional anaesthesia is recommended to be performed only after achieving normalisation of the bleeding profile (5). This was used as an anaesthesia method in our patient, with the idea that the risk of bleeding would be converted to normal in the pre-operative period. Evaluating the bleeding profile and taking a careful anamnesis in patients without diagnosis before the surgery may enable the reduction of any possible complications.

The basic treatment in patients in whom a lack of factor XI was determined is to replace the missing factor. The minimum plasma factor XI level required for haemostasis is reported to be 15–30 mg dL⁻¹. However, care should be taken of the risk of any probable development of thrombosis after excess replacement (6). The preparation of concentrated factor XI is difficult and expensive. Therefore, the use of FFP is the first choice in cases that require the replacement of product (1). However, care should be taken of any conditions, such as allergies, volume overload and thrombosis, that may occur when FFP is used. It is known that bleeding due to factor XI deficiency is more common in the surgeries of the oropharyngeal area, nasal mucosa, prostate and urogenital areas, where fibrinolytic activity is known to be higher (3). The use of anti-fibrinolytic drugs, such as tranexamic acid showing an effect on multiple effect mechanisms or desmopressin, which is the anti-diuretic hormone analogue, has been applied in the treatment of bleedings for which the cause cannot be determined. It was reported that these drugs can also be used in bleedings due to factor XI deficiency. Desmopressin has also been shown to increase the activity of the FXI (4, 7-9). FFP was the preferred product in our patient for factor XI replacement. The replacement was performed with FFP infusions given in the pre-operative and post-operative periods. The implementation of tranexamic acid or desmopressin was not required in our patient.

The half-life of factor XI in the plasma is 2–4 days (3, 4). It is recommended that the surgery should be performed in the shortest possible time after the replacement. It should be known whether the other bleeding parameters are normal in patients who are supposed to undergo a surgery and any anti-platelet drugs being used should be discontinued for at least 1 week (3). The size of the surgery, the risk of bleeding and the factor level of the patient are important for the calculation of the amount of required replacement (3, 6). Pre-operative 20 mL kg⁻¹ and intraoperative 10 mL kg⁻¹ of FFP were given in our patient. The pre-operative aPTT value decreased to 32 seconds from 77 seconds. No different support treatment was required after the surgery.

Another alternative for factor replacement is the concentrates of factor XI. In addition to the fact that the increase in the level of factor XI is predictable when used in the recommended dose range, the long half-lives of these preparations facilitate their pre-operative use (6). However, when the concentrates of factor XI are given to patients with a very low level of factor XI, the formation of an inhibitor antibody may be observed. Therefore, when undetected factor levels are found in patients who have received FFP or concentrates of factor XI for any reason previously, antibody screening must absolutely be performed (6). In our patient, the factor XI level was quite low (9 dL⁻¹) and FFP was used for factor replacement. However, because there was no known history of replacement and as a significant improvement in aPTT was provided after FFP, antibody screening was not needed.

Conclusion

Factor XI deficiency is a rare disease. In the absence of a cause that can increase the bleeding, it may remain latent for many years. In these patients, unexpected heavy bleeding may occur during and after the surgery. Factor XI deficiency should be kept in mind in patients who have a predisposition for bleeding and pathology in laboratory tests. It is important to make pre-operative preparations in these patients carefully and to closely follow the bleeding during the surgery and particularly in the first post-operative 24 hours. Replacement must be performed in cases where the factor XI level is too low. Agents such as tranexamic acid or desmopressin can help reduce bleeding. We believe that a multidisciplinary organi-

sation in patient management can greatly reduce the complications that may occur.

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References

1. Singh A, Harnett MJ, Connors JM, Camann WR. Factor XI deficiency and obstetrical anaesthesia. *Anesth Analg* 2009; 108: 1882-5. [\[CrossRef\]](#)
2. Mansour J, Graf K, Lafferty P. Bleeding disorders in orthopedic surgery. *Orthopedics* 2012; 35: 1053-62. [\[CrossRef\]](#)
3. Oconnell MN. Factor XI deficiency. *Semin Hematol* 2004; 41: 76-81. [\[CrossRef\]](#)
4. Seligsohn U. Factor XI deficiency in humans. *J Thromb Haemost* 2009; 7: 84-7. [\[CrossRef\]](#)
5. Benzoni HT, Avram MJ, Green D, Bonow RO. New oral anticoagulants and regional anaesthesia. *Br J Anaesth* 2013; 111(Suppl 1): i96-113. [\[CrossRef\]](#)
6. James P, Salomon O, Mikovic D, Peyvandi F. Rare bleeding disorders - bleeding assessment tools, laboratory aspects and phenotype and therapy of FXI deficiency. *Haemophilia* 2014; 20: 71-5. [\[CrossRef\]](#)
7. Bolton-Maggs PH. Factor XI deficiency--resolving the enigma? *Hematology Am Soc Hematol Educ Program* 2009; 1: 97-105. [\[CrossRef\]](#)
8. Franchini M, Manzato F, Salvagno GL, Montagnana M, Lippi G. The use of desmopressin in congenital factor XI deficiency: a systematic review. *Ann Hematol* 2009; 88: 931-5. [\[CrossRef\]](#)
9. Obaji S, Alikhan R, Rayment R, Carter P, Macartney N, Coll P. Unclassified bleeding disorders: outcome of haemostatic challenges following tranexamic acid and/or desmopressin. *Haemophilia* 2015; Epub ahead of print. DOI: 10.1111/hae.12811. [\[CrossRef\]](#)