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CASE REPORT

Anesthesia strategy for factor X deficiency coagulopathy: case report

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Abstract Factor X deficiency ranks among the rarest coagulopathies and has a variable presentation spectrum. We intend to present a proposal for anesthesia protocol for individuals with the coagulopathy. The excision of an ovarian neoplasm was proposed for a 26-year-old, female, ASA II patient, with congenital Factor X deficiency. Physical examination and lab tests were normal, except for Prothrombin Time (PT) 22.1s (VR: 8–14s), International Normalized Ratio (INR) 1.99 (VR: 0.8–1.2) and Activated Partial Thromboplastin Time (aPTT) 41.4s (VR: 25–37s). We concluded that a history of bleeding should always be investigated, along with a pre-anesthetic coagulation study.

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Introduction

Blood coagulation occurs due to the sequence of physical, biochemical, and cellular reactions in a series of phases, culminating in the formation of a platelet and fibrin plug at the site of vascular injury, and continuity of activated procoagulant substances at the injury site. Given that the concept of “coagulation cascade” describes only a set of chemical reactions that lead to the formation of a clot, it does not fully explain hemostatic events *in vivo*.¹

Factor X (FX), or Stuart-Prower Factor, is a vitamin K-dependent plasma glycoprotein synthesized in the liver, and plays an essential role in the coagulation cascade, as it is

activated either by the extrinsic pathway (Tissue Factor FVIIa), or by the intrinsic pathway (FXIa and FVIIIa), and is the first enzyme in the common pathway of thrombin formation.²

Congenital FX deficiency is an autosomal recessive disease with an incidence of 1:1000000. Total or partial FX deficiency causes an impairment of clot formation, leading to a hemorrhagic condition that presents with hemorrhagic symptoms of variable severity.²

The diagnosis of this disorder is based on the measurement of functional FX activity (FX:C) and FX plasma antigen (FX:Ag) levels by immunoassay, Prothrombin Time (PT), and Activated Partial Thromboplastin Time (aPTT).² It is important to check for vitamin K deficiency or an acquired deficiency, more often seen in elderly patients, as part of the differential diagnosis.³

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The classification of the deficiency is based on the results of immunological and functional assays: the parallel reduction of FX and FX:Ag indicates Type I deficiency, usually caused by a defect in glycoprotein synthesis or in the abolition of protein secretion. The discrepancy between low FX:C and normal FX:Ag indicates Type II deficiency, that is, a normal or minimally reduced release of non-functioning FX.

FX deficiency can be mild, moderate, or severe. Mild FX deficiency (FX:C 6–10 IU.dL⁻¹) is characterized by easy bruising and/or menorrhagia and is usually diagnosed during routine laboratory testing or by a family history. In moderate FX deficiency (FX:C 1–5 IU.dL⁻¹), hemorrhage occurs with trauma or surgical aggression, and is therefore usually diagnosed after the hemostatic challenge has occurred. Severe FX deficiency (FX:C < 1 IU.dL⁻¹) may appear in neonates (e. g., central nervous system hemorrhage or umbilical stump) and tends to exhibit the most severe phenotype.³

From a clinical point of view, as this is a very heterogeneous bleeding disorder, measuring FX:C based on PT prolongation and aPTT suffices for the correct diagnosis of FX deficiency, but not to predict clinical phenotype, particularly in patients with moderate or mild impairments, as the presentation can range from severe to completely absent symptoms.²

In the past, bleeding episodes in patients with FX deficiency were treated with Prothrombin Complex Concentrate (PCC) or Fresh Frozen Plasma (FFP). However, the concentrations of FX in FFP are low and, therefore, large volumes are required to achieve FX replacement, and there may be a risk of overloading the circulatory volume. Other adverse events associated with FFP are allergic reactions, thromboembolic complications, and transfusion-related lung injury. PCC contains factors II, IX, X, and some factor VII, so it also presents a risk of thromboembolic complications.³

Therefore, current guidelines recommend using single factor concentrates when available for patients with rare bleeding disorders. Thus, Plasma-Derived FX concentrate (pdFX) is approved for on-demand and prophylactic treatment of bleeding episodes, as well as for perioperative management for patients with hereditary FX deficiency. However, it may not be available at all hospitals.⁴

The present case report aims to describe the anesthetic and perioperative management of patients with FX deficiency, presenting suggestions for strategies in the perioperative care of surgical patients with this rare coagulopathy.

Case report

A planned excision of an ovarium neoplasm was proposed for a 26-year-old, female, ASA (AMERICAN SOCIETY OF ANESTHESIOLOGISTS) physical status II patient, with a personal history of non-stratified Factor X deficiency without immuno-hemotherapy follow-up. The diagnosis was made at 7 years of age, during a pre-anesthetic consult, by lab tests with increased TP and aPTT, leading to the diagnosis of congenital FX deficiency by gene sequencing, given there was no history of family hemorrhage events. There was no history of previous surgeries, despite the proposal of amygdalotomy, that was not performed due to risk of hemorrhage inherent to surgery on a patient with coagulopathy. The physical exam was uneventful, and the patient weighed 56 kg and measured 159 cm. Preoperative lab tests revealed hemoglobin of

13.9 g.dL⁻¹ (VR: 12–15 g.dL⁻¹); hematocrit of 39.4% (VR: 34.7–46.0%); 162,000 platelets (VR: 150,000–440,000); TP 22.1s (VR: 8–14s); International Normalized Ratio (INR) of 1.99 (VR: 0.8–1.2), and aPTT of 41.4s (VR: 25–37s).

On the day of the surgery, based on the orientation of the immunohemotherapy specialist, before anesthesia induction, 600 mL of frozen fresh plasma and 1 g of tranexamic acid were administered at the initial intraoperative stage. Two units of red blood cells had been reserved and immunotherapy was alerted that massive transfusion protocol would be triggered if necessary. Two large caliber peripheral venous accesses (16G) were put in place on each one of the upper limbs.

We performed balanced general anesthesia, maintenance with 2% sevoflurane and monitoring with electrocardiogram, pulse oximetry, noninvasive blood pressure, capnography, anesthesia depth monitoring, and diuresis.

A laparoscopic approach was decided to decrease surgical aggression and to decrease risk of bleeding. During surgery, a total of 300 mL of Plasma Lyte was infused. To prevent nausea and vomiting, 4 mg of dexamethasone and 4 mg of ondansetron were administered and also, 1,000 mg of paracetamol and 100 mg of tramadol for postoperative analgesia. Surgical procedure time was 1 hour and 30 minutes with approximate blood loss of 200–300 mL.

Anesthesia and surgery were uneventful. The postanesthesia care unit stay was satisfactory during immediate postoperative follow-up. During the initial 12 postoperative hours, 1 g of tranexamic acid was administered, aimed at avoiding late postoperative bleeding. The patient remained in the hospital for 72 hours after surgery for hemorrhage surveillance.

Although the diagnosis of XF deficiency was confirmed, we were unaware of baseline levels; the *a posteriori* measurement result was 7.8% (VR: 70–120%).

Discussion

In rare hemorrhagic disorders, the major challenge is to maintain homeostasis during a surgical procedure, as there are constant blood losses with consumption and loss of the insufficient factor. Information available on the anesthetic and perioperative handling of FX deficiency seems limited, as the patient population is relatively small.

The present case describes a patient with FX deficiency proposed for programmed excision of an ovarian neoplasm. To optimize the outcome and minimize the risk of bleeding, a multidisciplinary approach with replacement of FX levels through FFP, a minimally invasive surgical approach, and longer-than-usual hospital stay for bleeding surveillance were used. Based on the result of the FX levels in the postoperative period and on the clinical evaluation of the patient, we considered that the patient presented a mild FX deficit. However, whatever the phenotype classification, FX levels must be restored when patients with this deficiency undergo a surgical procedure, as they are at risk of severe postoperative hemorrhage.^{3,4}

The importance of the pre-anesthetic evaluation that led to the diagnosis of the deficiency in this patient, reached prior to the hemostatic challenge posed by tonsillectomy, is

also noteworthy. If such an assessment had not occurred, there could have been serious consequences.

According to the current literature, some suggestions of anesthetic strategy and available therapeutic alternatives are proposed for the perioperative approach of factor X deficiency coagulopathy, namely: 1) Plasma-derived FX concentrate, approved in the United States and Europe, for the treatment and prophylaxis of bleeding episodes and for perioperative management of patients with hereditary FX deficiency. The prophylactic dose of 25 IU.kg⁻¹ is safe and effective, being administered 2–3 times a week, as its half-life is 29.4 hours. In addition, pdFX can be administered at higher doses to support perioperative management in patients with mild to severe deficiency^{3,4}; 2) Fresh Frozen Plasma 15–20 mL.kg⁻¹ in the immediate preoperative period, followed by postoperative maintenance of daily FFP transfusion (5 mL.kg⁻¹) for one week, may be sufficient to prevent bleeding complications after an elective abdominal surgical procedure²⁻⁴; 3) Prothrombin Complex Concentrate 15 to 20 IU.Kg⁻¹ in the immediate preoperative period followed by postoperative maintenance of 10 to 15 IU.Kg⁻¹ daily transfusion. Due to possible thromboembolic complications, FIX and D-Dimer levels should be monitored mainly in long-term treatments.^{2,4} To treat hemorrhagic events in patients with severe deficiency, 20 to 30 IU.kg⁻¹ should be administered once a day, which can be changed according to the type of hemorrhage and residual FX activity; 4) Epidural anesthesia is not recommended and is contraindicated in patients with factor X deficiency, unless prophylactic therapy with FFP is administered⁵; 5) Subarachnoid block is safer than epidural anesthesia in patients with coagulopathies⁵; 6) Use of antifibrinolytic drugs with tranexamic acid, desmopressin and fibrin glue^{2,4}; and 7) Choice of minimally invasive surgical techniques such as laparoscopy.

Therefore, our case report underscored changes in the anesthesia and perioperative approach for a laparoscopy

procedure with minor risk of hemorrhage, but that due to the rare deficiency, made the patient a hemostatic challenge. We also intend to alert toward existing hemorrhage disorders in patients without a personal or family history of hemorrhage, and to the importance of pre-anesthetic coagulation investigation and, also to the importance of investigating FX deficiency in the event of prolonged PT and aPTT of unknown cause.

Conflicts of interest

The authors declare no conflicts of interest.

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