Hemophilia C management in obstetric anesthesia

ABSTRACT
Coagulation alterations might represent a problem in obstetric anesthesia considering that they may contraindicate neuraxial techniques and worsen a case of uterine atony with more severe bleeding if they are not correctly recognized and treated. We report the case of a parturient diagnosed with severe factor XI deficiency during the delivery progress. In this case, non-steroidal anti-inflammatory drugs and neuraxial techniques were avoided and intravenous patient-controlled analgesia with boluses of remifentanil was used for pain management. Treatment with tranexamic acid and fresh frozen plasma was initiated and the absence of urgent factor XI availability was notified. Due to no progression of labor, cesarean section was required and a general anesthesia was performed. During the procedure, uterine atony occurred. Uterine massage and several uterotonic drugs were needed to control it. The patient remained stable and the delivery was accomplished without further incidents. The objective of this report is to present the pain, coagulation and bleeding management of a patient with hemophilia C in our obstetric department and to alert for the need of multidisciplinary work to successfully approach this type of patient.

Key words: Coagulation disorders; factor XI; hemophilia C; obstetric anesthesia; obstetric bleeding; postpartum hemorrhage; uterine atony

Introduction
Coagulation alterations can pose a problem for the anesthesiologist in the obstetric scope, where may contraindicate neuraxial techniques, which are considered the gold standard, and constitute a risk factor for postpartum hemorrhage (PPH), which is responsible for the 8% of maternal deaths in developed countries, being uterine atony (UA) its principal cause.

We submit the case of a 27-year-old woman with an isolated Activated Partial Thromboplastin Time (APTT) prolongation detected at the beginning of labor who developed PPH secondary to UA.

Case Report
A 27-year-old woman, 66 kg, 40 + 3 weeks pregnant, nulliparous, allergic to acetaminophen, was admitted to our hospital in labor. A blood analysis was performed, showing a starting hemoglobin (Hb) of 13.8 g/dl and an APTT prolongation of 50.9 s with an APTT ratio of 1.79 that corrected completely (29 s) with a factors mixture.

Faced with this situation, the Hematology service was consulted, who re-interrogated the patient. She only referred a persistent bleeding after tooth extraction, denying any...
history of spontaneous bleeding, familiar hemorrhagic diathesis nor iron or prior transfusion therapy. They also carried out a coagulation factors study, which revealed a severe deficiency of factor XI (FXI) (0.8% level), diagnosing type C hemophilia (TCH). Consequently, they recommended avoiding instrumental delivery and contraindicated any neuraxial technique or non-steroidal anti-inflammatory drugs (NSAIDs) administration. They started treatment with tranexamic acid (TA) 1 g/6 h and fresh frozen plasma (FFP) 15-20 ml/kg. They confirmed with Pharmacy service the urgent unavailability of FXI, so in the event of massive bleeding unresponsive to previous measures, they indicated assessing factor VII (FVII) treatment 15-30 µg/kg.

In collaboration with the Obstetrics service, it was decided to use intravenous (IV) patient-controlled analgesia with 0.2 µg/kg boluses of remifentanil following the hospital protocol and maintaining an expectant attitude.\[3\]

However, given the lack of progression of labor due to pelvic-cephalic disproportion, a cesarean section under general anesthesia was performed. Before entering the operating room, two 18 G peripheral venous lines were cannulated and antibiotic prophylaxis, gastric protection, 1 g of TA aforementioned and 1500 ml of FFP were administered.

Standard monitoring and urinary catheter were placed, and the radial artery was cannulated for invasive blood pressure monitoring. Balanced general anesthesia was performed with rapid sequence induction with propofol 2.5 mg/kg and succinylcholine 100 mg IV. The patient was intubated with Sellick maneuver, direct laryngoscopy (Cormack II) and a secured 7 mm endotracheal tube. Sevoflurane 2% was used for maintenance.

During the procedure, UA was observed. To control it, the patient required uterine massage, 1 g extra of TA, 2 g of IV fibrinogen, 10 IU of IV oxytocin bolus + 40 IU oxytocin/500 ml of saline/4 h infusion, 0.2 mg of intramuscular methylergometrine, 0.25 mg of intrauterine carbopect and 1000 µg of intra-rectal misoprostol, following the hospital PPH protocol.\[4\] The sevoflurane was diminished to suboptimal concentration (0.6%) to avoid its muscle relaxant effect.\[5\] A total of 500 ml of colloids, 1500 ml of crystalloids, 1 mg of midazolam and 300 µg of fentanyl after fetal extraction were administered. The patient remained hemodynamically stable and an arterial blood gasometry showed unremarkable findings apart from Hb 9.9 g/dl and lactate 4.6 mmol/l.

Finally, eduction and extubation occurred without incident. She went to the obstetric resuscitation room for surveillance where a new blood sample verified progressive decrease in lactate, Hb of 10.6 g/dl, APTT of 38.2 s and APTT ratio 1.35. Hematology recommended continuing TA 500 mg/8 h, reintroducing FFP only if new invasive procedures or major bleeding occurred, adding elastic compression stockings for thromboprophylaxis and urged to study the newborn. For pain management, a 20 mg morphine with 1.25 mg droperidol elastomer and metamizole 2 g/8 h were prescribed. The patient was discharged without further complications.

**Discussion**

FXI deficiency, also known as TCH, is a rare disease linked to chromosome 4,\[4\] with variable inheritance and a 1/1,000,000 inhabitants incidence,\[6,7\] reaching 1/450 people in Ashkenazi population.\[7\] Its defect causes an intrinsic coagulation pathway alteration that should be suspected when an isolated prolongation of APTT is present with normal prothrombin time.\[6,8\]

Clinically, spontaneous bleeding is rare and routine treatment is not necessary, but the risk of bleeding may always be assessed according to the characteristics of the surgery and FXI levels,\[6,7\] which should be around 30% prior to intervention.\[8\]

General recommendations consist in multidisciplinary management,\[6\] NSAIDs avoidance and FXI activity stimulators administration, such as desmopressin (0.2-0.4 µg/kg IV or subcutaneously).\[6,7\] Antifibrinolytics such as TA (15 mg/kg/8 h IV) may be useful in minor bleeding cases, while factor replacement through FFP (15-20 ml/kg, followed postoperatively by 5 ml/kg/12-24 h)\[6,8\] and FXI (10-15 IU/kg, with a half-life of 2-4 days) should be reserved for major bleedings.\[6,7\] In absence of response, FVII (15-30 µg/kg) may be considered for massive bleedings.\[7\] Aside from this, the presence of inhibitory antibodies should be discarded in previously exposed patients with very low level of FXI before a new dose,\[8\] being useful the anti-inhibitory coagulant complex administration.\[8\]

Regarding the analgesic technique, the information is scarce and based only on series or case reports, so it is impossible to make a general recommendation. However, given the risk of epidural hematoma and secondary paraplegia, epidural anesthesia is contraindicated,\[7\] except if prophylactic therapy is given.\[6,8\] Conversely, subarachnoid anesthesia is considered safer and can be used if correction of the APTT is verified.\[6,8\] Nevertheless, FFP or FXI administration is not advised only to perform a neuraxial technique.\[7\]

Furthermore, it is essential to identify risk factors for UA and PPH (such as prolonged labor, uterine distension or...
coagulation disorders among others), as well as know its sequential management, which includes uterine massage, oxytocin perfusion and several uterotonics along with more invasive measures such as radioembolization or surgical treatment.\(^\text{[2,9]}\)

**Conclusions**

In case of TCH, desmopressin, TA and FFP administration, apart from FXI, have proven usefulness. Moreover, in pregnant women, it is advisable to be familiar with the management of UA, since we must consider them at high risk of developing PPH. Overall, a multidisciplinary strategy is fundamental to reduce the complications when coagulation alterations are present.

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**Conflicts of interest**

There are no conflicts of interest.

**Informed Consent**

Informed consent from patient was obtained to report this case.

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