Isolated Factor X Deficiency, A Rare Occurrence: Anesthetic Concerns And Perioperative Management

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Citation

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Abstract

Purpose: Congenital factor X (FX) deficiency is a rare inherited coagulation disorder. Anesthesiologists have limited experience in the prevention of the severe hemorrhagic diathesis caused by FX deficiency before surgical procedures.

Clinical features: A 20 year old, ASA grade III female patient was admitted with complaints of pain in the abdomen, polymenorrhagia and an abdominal mass. She was diagnosed as FX deficiency earlier. Presently, at the time of admission she had grossly deranged coagulation [prothrombin time (PT)-55.6 seconds (normal 12 seconds), activated partial thromboplastin time (aPTT)-52.7 seconds (normal 30 seconds)]. She was scheduled for exploratory laparotomy to confirm the diagnosis. Preoperatively, FFP 15ml/kg was transfused. On the morning of surgery in spite of receiving recommended dose of FFP as planned, PT was 20 seconds (normal 12 seconds). Further 4 FFP had to be transfused prior to induction of general anesthesia. After induction laryngoscopy and tracheal intubation was performed when adequate muscle relaxation was achieved to avoid any airway trauma. Injection Trenaxemic acid 2 gm intravenously was administered on the day of surgery and continued postoperatively. The postoperative plan was to transfuse 4 units of FFP 12 hourly for next 4-7 days with PT, aPTT monitoring. Postoperative analgesia was provided with IV tramodol (50 mg) 8 hourly and IV pethidine (37.5mg), phenargan (12.5 mg) for breakthrough pain.

Conclusion: In patients with FX deficiency, coagulation should be optimized preoperatively and continuously assessed in the perioperative period as in severe deficiency; the coagulation parameters may vary and be deranged in spite of seemingly adequate FFP transfusion.

Implication Statement: Patients with factor X deficiency require multidisciplinary approach including hematologist, gynecologist and anesthesiologist along with meticulous homeostasis during surgery and careful monitoring of blood coagulation in the postoperative period.

INTRODUCTION

Congenital factor X (FX) deficiency is a rare inherited coagulation disorder[1]. Recurrent intracranial hemorrhage with associated morbidity and mortality has been reported in fetuses and in neonates[2]. Women with FX deficiency may have severe menstrual bleeding, recurrent spontaneous abortion, placental abruption, premature births and excessive bleeding after delivery[3]. Anesthesiologists have limited experience in the prevention of the severe hemorrhagic diathesis caused by FX deficiency before surgical procedures[1]. Hence, we describe preoperative preparation and anaesthetic management of a patient with FX deficiency who was scheduled for exploratory laparotomy for pain abdomen and an intraabdominal mass.

CASE

A 20 year old, American Society of Anesthesiologist physical status (ASA) grade III female patient presented in the outpatient department of gynaecology with complaints of pain in the abdomen and polymenorrhagia for 4-5 years. The pain was diffuse all over the abdomen, severe in intensity and typically premenstrual. On abdominal examination, an irregular mass, firm to hard in consistency arising from the pelvis corresponding to 16-18 weeks of pregnancy could be palpated. She reported multiple episodes of joint pain and swelling due to hemarthrosis following minor trauma as well as easy bruisability, epistaxis and gum bleeding since 7-8 years of age for which she had been hospitalized several times and also received fresh frozen plasma (FFP). Eighteen months back she was admitted with pain in the abdomen and

lower chest. A diagnosis of corpus luteal cyst hemorrhage with hemoperitoneum, and hemothorax was made which was managed conservatively with administration of blood products. Subsequently she was diagnosed as having severe FX deficiency (levels < 1 % of normal).

Presentally at the time of admission she had grossly deranged coagulation profile [prothrombin time (PT)-55.6 seconds (normal 12 seconds), activated partial thromboplastin time (aPTT)-52.7 seconds (normal 30 seconds)]. Urine test ruled out pregnancy. In view of large intraabdominal mass, a differential diagnosis of malignant or hemorrhagic cyst, degenerated fibroid or Koch's abdomen was made. She was scheduled for exploratory laparotomy to confirm the diagnosis. After consultation with hematologist, it was planned to transfuse FFP 15ml/kg two days prior to surgery for correction of coagulation parameters. Once the coagulation profile was corrected, a subsequent continuous infusion of a total volume of 15ml/kg of FFP was to be administered over 8 hours finishing immediately prior to surgery. Further FFP was arranged for excessive intraoperative blood loss. Postoperatively 4 units of FFP were planned to be transfused 12 hourly for next 4-7 days with PT, aPTT monitoring. Injection Trenaxemic acid 2 gm slow intravenously was to be given on the day of surgery followed by 0.5 gm 6 hourly for next 48 hrs postoperatively. After the initial FFP transfusion the PT was corrected to 17.5 seconds and aPTT 36.5 seconds. On the morning of surgery inspite of receiving FFP as planned the PT was 20 seconds. Further 4 FFP had to be transfused prior to induction of general anesthesia. After induction of anesthesia, a smooth, atraumatic laryngoscopy and tracheal intubation was performed after achieving adequate muscle relaxation to avoid any airway trauma. Central neuraxial block, intramuscular injections and non steroidal anti-inflammatory drugs were avoided. Intraoperatively 4 units of FFP were transfused to control oozing. Bilateral ovarian hematomas containing large amount of blood clots (about 2 liter) beneath the ovarian capsule were detected and drained. At the end of the surgery, her trachea was extubated uneventfully. Post operatively on the day of surgery, PT was 16.9 sec (normal 12 seconds). Postoperative analgesia was provided with IV tramodol (50 mg) 8 hourly and IV pethidine (37.5mg), phenargan (12.5 mg) for breakthrough pain. Postoperative bleeding was within normal limits. The patient had an uneventful recovery and was discharged on postoperative day 6 with the advice to start oral contraceptive pills (OCPs) and follow up in gynecology and hematology clinics.

DISCUSSION

FX deficiency is an autosomal recessively inherited coagulation disorder[4]. It is amongst the rarest of the inherited coagulation disorders, with an estimated incidence of 1:500,000; its heterozygous asymptomatic form is more common with frequency of 1:500[1,2,5].

FX deficiency may be caused by complete deficiency of the protein, presence of a nonfunctional protein or presence of decreased amounts of functional protein. Acquired deficiencies of factor X may occur with anticoagulant therapy, liver disease, vitamin K deficiency, and secondary to administration of drugs such as phenytoin. Paraproteinemias like amylodosis can also cause FX deficiency[2,6,7].

FX deficiency is characterized by prolongation of PT, aPTT, with normal bleeding time and thrombin time as well as decreased levels of FX antigen or FX activity[8,9]. Russell viper venom time (RVVT) is prolonged with this disease and it can help differentiate factor VII and X deficiency as this agent activates factor X directly[4].

Deficiency of FX may present similar to any coagulation factor abnormality i.e. epistaxis, hemarthrosis and gastrointestinal blood loss (bleeding ranges from mild to severe)[4]. Mild deficiency (6-10%) may be identified incidentally and the patient may complain of easy bruising or menorrhagia[10]. Moderately affected patients with levels 1-5% of FX may bleed only after hemostatic challenge like trauma or surgery[10]. Severe deficiency (<1%) can present in the neonatal period with umbilical stump bleeding[10] and bleeding in deep subcutaneous tissues, muscles, joints or body cavities (hemoperitoneum, hemothorax) hours or days after injury and is unaffected by local measures[11]. Female patients with these levels may have severe menstrual bleeding and bleeding after a delivery or repeated episodes of hemoperitoneum due to the ruptured corpus luteum cysts[12,13]. Our patient though had severe deficiency, only manifested with hemarthrosis and gum bleeding at seven years of age and with corpus luteal cysts hemorrhages once she had reached menarche. These recurrent episodes of hemoperitoneum secondary to ruptured corpus luteum may be prevented by suppression of ovulation with the OCP as was advised in our patient[12,13].

Knight et al reported that FX levels of 9-17 percent are required to prevent minor bleeding in response to normal everyday knocks or injuries. In patients with severe FX

deficiency who present for emergency surgery for hemoperitoneum, 35-50% levels of FX is needed to achieve hemostasis during surgery and levels need to be maintained between 10 to 20% for 6 days postoperatively[14].

The best replacement therapy for factor X deficiency is FX concentrates but due to the unavailability and high costs in many developing countries, FFP has been the main stay of therapy. A loading dose of 15-20 ml/kg followed by 3-6 ml/kg twice daily is recommended aiming to keep FX levels above 10-20%[10]. Because of long half-life of FX (20-40 hrs) [2], the levels can be maintained by infusions of FFP every 12 hours. In neonates, FX levels can be elevated by exchange transfusion to avoid hypervolemia[15]. Therapeutic plasma exchange (PLEX) with concomitant administration of IV immunoglobulin (IgG) and steroids are reported to be effective in acquired FX deficiency[2,16].

Takabe K et al managed FX deficiency in a patient with amylodosis by administration of recombinant human factor VIIa and a Prothrombin complex (PCC). It contains the highest concentration of FX[7,17,18]. The disadvantage of this technique is that the degree of elevation of FX level is extremely variable with added risk of thromboembolic complications and the development of inhibitors. The advantages of PCC over FFP include reduction in the volume infused and decreased risk of viral contamination. The PCC can be stored in a lyophilized form and used for home administration[2].

In our patient FFP remained the mainstay of treatment as FX concentrates are not usually available in our set up. We monitored PT to achieve adequate levels of FX as specific FX levels are not easily done in our institute. We transfused FFP perioperatively as recommended to maintain FX with in acceptable limits to achieve hemostasis. In our patient even after transfusion of recommended dose of FFP, on the day of surgery the PT was prolonged. So we had to transfuse more FFP to keep PT within normal limits and to prevent excessive blood loss during surgery. So even FFP transfusion should be carried on and monitor PT, aPTT to assess coagulation parameters on the day of surgery.

Our patient was also administered injection tranexamic acid 2 gm IV stat and continued in the postoperative period. Tranexamic acid is a competitive inhibitor of plasminogen activation and at high concentration, an inhibitor of plasmin. In women with menorrhagia, 15mg/kg 8 hrly (1gm 6–8 hourly) may be effective when taken for the duration of the menstrual period[10].

To summarize, good clinical assessment including thorough history and examination helped us in the detection and relevant laboratory investigation confirmed the diagnosis of hematological disorder. Coagulation should be optimized preoperatively and continuously assessed in the perioperative period as in severe deficiency, the coagulation parameters may vary and be deranged inspite of seemingly adequate FFP transfusion. Careful hematological management, including specific factor replacement, is essential. The importance of multidisciplinary approach including a hematologist, gynecologist and anesthesiologist along with meticulous homeostasis during surgery and careful monitoring of blood coagulation in the postoperative period cannot be overemphasized.

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