

Routine Preoperative Coagulation Screening Detects a Rare Bleeding Disorder

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Factor X deficiency is a rare hereditary coagulation disorder. We report a case of congenital factor X deficiency diagnosed preoperatively in an 8-yr-old female child scheduled to undergo corrective surgery for congenital thoracolumbar kyphoscoliosis. Her preoperative coagulation profile revealed prolonged prothrombin time and activated partial thromboplastin time values. Further evaluation showed functional activity of factor X was <8% of the normal activity and was corrected to 10%–40% of the normal activity with fresh frozen plasma. IV tranexamic acid was also administered to reduce intraoperative blood loss. There were no postoperative bleeding complications. This case emphasizes the need for routine preoperative coagulation screening, at least for major surgical procedures.

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Congenital factor X deficiency is an extremely rare autosomal recessive disorder affecting both genders. There are only 50 reported cases in the world literature, the incidence being 1:500,000–1,000,000 population.¹ The plasma levels of factor X in normal healthy individuals range from 8 to 10 $\mu\text{g}/\text{mL}$. The functional activity of factor X required for surgical hemostasis is 10%–40% of the normal activity.² Patients with mild to moderate deficiency remain asymptomatic until stressed by trauma or surgery. Subclinical coagulation disorders that are not evident from the patient's history and clinical examination would be revealed only on biochemical assessment. However, there is insufficient evidence to recommend routine preoperative coagulation screening for all patients undergoing surgery. This case of asymptomatic mild factor X deficiency with deranged coagulation screening on preoperative evaluation is reported to emphasize the need for routine preoperative coagulation screening in patients undergoing major surgery.

CASE REPORT

An 8-yr-old female child weighing 20 kg, born to consanguineous parents presented to the orthopedic department with congenital thoracolumbar kyphoscoliosis and second lumbar hemi vertebra for corrective surgery. There were no associated co-morbid conditions. There was no history suggestive of coagulation deficiencies including easy bruising, nose bleed, hematoma, and excess bleeding after minor

trauma or neurological deficits. There was no history of fever, jaundice or exposure to toxic substances or drugs interfering with coagulation or platelet function. There was no family history of bleeding disorders. On general examination, there was no evidence of petechiae or ecchymotic patches, joint swelling or organomegaly. The preoperative investigations of the child were normal except the prothrombin time (PT) (176.6 s-control 13 s) and activated partial thrombin time (APTT) (99.8 s-control 30 s), which were abnormally prolonged. The hematologist was consulted and the child was evaluated for coagulation disorders. An isolated factor X deficiency with functional activity of <8% of normal was discovered. The child was premedicated with syrup trichlofos- 50 mg/kg orally. Central venous and arterial catheters were placed and pressures were monitored. After standard induction of anesthesia and tracheal intubation, the child was placed in a prone position with proper padding of pressure points and eyes. Proper care was taken to optimize the position to minimize bleeding due to venous congestion. Factor X was replaced in consultation with a hematologist using fresh frozen plasma (FFP) 20 mL/kg, given after induction and before surgical incision to achieve hemostatic levels (10%–40%) of factor X activity. A bolus dose of tranexamic acid (10 mg/kg) and a continuous infusion (5 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) were given to reduce blood loss. Propofol infusion was titrated to maintain a mean arterial blood pressure of 50 mm Hg. Posterior hemivertebrectomy of L2 with T12-L4 Mossmiami pedicle screw fixation with posterior spinal fixation was performed. An intraoperative "wake up" test was performed to identify any spinal cord injury before fusion of the spine was performed. The patient was hemodynamically stable throughout the procedure, which lasted for 6 h. Hemostasis was secured without any difficulty. Intraoperative blood loss was about 300 mL and one unit of whole fresh blood was transfused. The patient was mechanically ventilated for 6 h and tracheally extubated after reversal of residual neuromuscular blockade. The patient's postoperative course was uneventful. There was no wound hematoma or excess blood loss in the drain. Postoperatively, one unit of FFP (3–6 mL/kg) was transfused daily for 2 wk to maintain hemostatic functional activity of factor X, as the half-life of factor X in plasma is 34–40 h. Functional activity of factor X was 8% and 23% on the 5th and 10th postoperative days. The patient was discharged on the 17th postoperative day, with instructions to prevent injuries and

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a reminder to communicate factor X deficiency at any future surgical procedures. Follow-up after 1 mo showed no fresh neurological, hematological or wound-related complications. The parents were evaluated for functional activity of factor X and found to have 48% and 54% of normal.

DISCUSSION

Factor X or Prower-Stuart factor is a vitamin K-dependent serine protease that serves as the first enzyme in the common pathway of thrombus formation. Hence, its deficiency results in severe bleeding disorders. The gene for factor X maps to the long arm of chromosome 13q. Normal plasma levels are 8–10 $\mu\text{g}/\text{mL}$. Functional activity for surgical hemostasis is considered to be 10%–40%.² The occurrence and frequency of bleeding symptoms correlates with the degree of factor X deficiency. Patients with factor X deficiency are categorized based on the functional activity of factor X as: mild deficiency with levels of 6%–10% activity may be identified incidentally and the patient may complain of easy bruising or menorrhagia; moderately affected patients with levels 1%–5% of factor X may bleed only after hemostatic challenge, such as trauma or surgery; severe deficiency with <1% activity can present in the neonatal period with umbilical stump bleeding and bleeding in deep subcutaneous tissues, muscles, joints or body cavities (hemoperitoneum, hemothorax), hours or days after injury and is unaffected by local measures.³ The majority of patients (56%) present with severe deficiency. The disease is more common in communities with social acceptability of consanguinity. In a report by Knight et al.⁴ a level of 35% of functional factor X activity was maintained during an emergency surgical exploration for hemoperitoneum. In another report⁵ for surgical repair of fractured femur, a level of 100% was achieved intraoperatively. Cesarean delivery in a woman with factor X deficiency was also reported.⁶ In all these surgical procedures, factor X was replaced by prothrombin concentrate complex (PCC) which attains higher functional activity of the factor. In our case, PT was done after the initial bolus dose of FFP for adequacy of replacement therapy, which was 15 s. A factor X assay was done postoperatively on two occasions as there was no visible bleeding. Acquired deficiency, though uncommon, can occur with liver disease, vitamin K deficiency, amyloidosis, multiple myeloma, mycoplasma pneumoniae, leprosy and exposure to methyl bromide. Transient deficiency of factor X was reported in an adult as intracerebral hemorrhage.⁷ Replacement therapy for factor X deficiency includes FFP (20 mL/kg as bolus and 3–6 mL/kg as maintenance) and PCC (15–125 U/kg). One unit of FFP will increase all clotting factors by 2% to 3% (Transfusion Medicine Update 1992) and is a better choice in elective surgery. PCC, which contains factors II, VII, IX, X, protein C, and trace amount of heparin, gives the best recovery of factor X and may be preferred in emergency procedures⁴. However, there

is a risk of thromboembolic complication when 2 to 3 standard doses are administered in 48 h.⁸ Vitamin K administration may be useful in certain patients with acquired factor X deficiency. Patients with inherited deficiency do not respond after vitamin K administration and, in fact, this nonresponse helps to establish the diagnosis of this disorder.³ Tranexamic acid, an inhibitor of fibrinolysis diminishes bleeding in patients with inherited coagulation disorders. It acts by protecting labile hemostatic plugs from fibrinolytic degradation.⁹ The ultimate goal of preoperative assessment is to reduce mortality and morbidity associated with surgery. The American Society of Anesthesiologists task force guidelines for preoperative evaluation (2002) revealed abnormalities in bleeding time, PT, partial PT, or platelet count in 0.8%–22.0% of cases ($n = 15$ studies). There was a change in clinical management in 1.1%–4.0% of the cases found to be abnormal ($n = 2$ studies). Findings for indicated coagulation studies were reported as abnormal in 3.4%–29.1% of cases ($n = 4$ studies). The incidence of routine coagulation testing abnormalities in obstetric patients and in patients scheduled for regional anesthesia has not been reported. Kaplan et al.¹⁰ opined that, in the absence of specific indications, routine preoperative lab tests contribute little to patient care and could reasonably be eliminated. Schein et al.¹¹ recommended stopping routine preoperative laboratory tests for patients before surgery. There have been no conclusive guidelines regarding the routine screening of a coagulation profile. This case is reported to emphasize the importance of routine coagulation screening, at least for major operations. Shah et al.¹² concluded that the scope of laboratory investigations in any child with a prolonged APTT should be tempered by clinical presentation and associated personal and family history. This child had no clinical history suggestive of coagulation disorder. She was born of consanguineous parents but there was no history of bleeding disorders in the family. The routine preoperative screening revealed abnormal PT and APTT. A normal clinical history and examination do not sufficiently exclude mild to moderate coagulation disorders. This child had a rare factor X deficiency. When stressed by trauma or surgery, these patients could develop unanticipated massive bleeding. An abnormal coagulation profile should alert physicians to the possibility of such disorders and help them proceed with further assessment to identify the deficiency and undertake corrective measures to avert a major catastrophe.

Although the incidence of factor X deficiency is rare, its existence should be remembered when patients present with bleeding diathesis or abnormal screening tests. Routine screening for coagulation disorders should be considered, at least for major surgical procedures as demonstrated in this case.

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