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Case Report



Inherited Factor XII Deficiency—What Is the Real Concern for Neuroanesthesiologist: Bleeding or Clotting

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Abstract

Factor XII deficiency is a rare disorder that can complicate the perioperative management of a patient. Factor XII plays an important role in the activation of intrinsic pathway of coagulation; the deficiency, therefore, results in prolongation of activated partial thromboplastin time (aPTT). This aPTT prolongation is expected to cause increased bleeding during surgery. However, on the contrary, in vivo isolated factor XII deficiency is associated with increased risk of thromboembolism (this risk being higher than the risk of bleeding). We report the perioperative management of a patient with factor XII deficiency who underwent cervical vertebral fusion (C₁–C₂) for atlantoaxial dislocation.

Keywords

- ▶ factor XII
- ▶ surgery
- ▶ bleeding
- ▶ thromboembolism

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Introduction

Inherited bleeding and clotting disorders can complicate the intraoperative anesthetic management especially in neurosurgical procedures where significant amount of blood loss is expected. Perioperative management of patients with these disorders remains a challenge to the neuroanesthesiologist. Of all these disorders, factor XII deficiency is extremely rare and is usually diagnosed incidentally when a prolonged activated partial thromboplastin time (aPTT) is observed during preoperative evaluation. We report the perioperative management of a patient with factor XII deficiency who underwent cervical vertebral fusion (C₁-C₂) for atlantoaxial dislocation (AAD).

Case Report

A 38-year-old male, weighing 38 kg and height of 160 cm, presented with increasing neck pain with tingling and numbness of both upper limbs. The patient was moderately built and had pallor. The muscle power was 3/5 at the right wrist and 4/5 at the left wrist joint. Airway examination showed restricted mouth opening (<1 finger breadth) and a Modified Mallampatti Class IV. Echocardiography was normal and the pulmonary function tests showed moderate restrictive lung disease. After magnetic resonance imaging, a diagnosis of ankylosing spondylitis with AAD was made. He was planned for posterior fusion of C₁-C₂ with lateral mass screws.

During evaluation, hemoglobin (Hb) of 7.3 g/dL and a prolonged aPTT value (73 seconds) with a normal platelet count (4.12 lakhs/cu mm) and prothrombin time (12.8 seconds) was observed. The test was repeated twice and consecutive values were high. Patient denied any history of prolonged bleeding after injury. Hematologist diagnosed him with anemia and reduced levels of factor XII (18 IU/mL, normal value—50 IU/mL). Factor VIII, factor IX, protein C and S assays were normal. Mixing studies were performed to rule out the presence of factor XII inhibitors. Mixing patient's plasma and test plasma in the ratio of 1:1 led to shortening of aPTT indicating the absence of factor XII inhibitors. Therefore, aPTT prolongation was due to deficiency of factor XII. The patient was started on hematinics and a follow-up was planned after 2 weeks.

On re-evaluation, the reduction in factor XII levels (28.9 IU/mL) and mild prolongation of aPTT (44 seconds) persisted and Hb improved to 8.2 g/dL. Literature search revealed that there were no guidelines with respect to the range at which correction of aPTT is recommended in factor XII deficiency.¹ Also, there is no consensus for minimum desired factor XII level for hemostasis *in vivo*.¹ Hence, surgery was scheduled.

Adequate blood and blood products were reserved. Patient was counseled about the nature of the condition, expected complications, and informed consent was taken. We did not transfuse fresh frozen plasma (FFP) preoperatively and plan was to transfuse, based on intraoperative blood loss, to avoid unnecessary complications of blood product administration. Awake orotracheal fiberoptic intubation was performed. Anesthesia was thereafter induced; adequate venous access and invasive arterial line were secured. An intermittent pneumatic compression device (IPCD) was placed to prevent venous thrombosis. A close watch was maintained for abnormal bleeding. However, no abnormal bleeding occurred and

surgery lasted 9 hours. A total blood loss of 500 mL occurred that was replaced with two units of packed red blood cells and Hb was 8.6 g/dL at the end of surgery. After reversal of neuromuscular blockade, motor power was 4/5 in both upper limbs and 5/5 bilaterally in the lower limbs. Patient was not extubated in view of difficult airway, nature of surgery, and prolonged procedure time and was shifted to intensive care unit. Patient was extubated the next day, mobilised and started on enoxaparin 60 mg subcutaneously once a day with daily screening for occurrence of deep venous thrombosis (DVT). The postoperative course was uneventful and patient was discharged on 5th postoperative day.

Discussion

Factor XII also known as Hageman factor is synthesized in the liver. It is a single chain glycoprotein with molecular weight of 80,000 daltons, half-life of 60 hours, and normal plasma concentration of 50 IU/mL (30 µg/mL).¹ Factor XII deficiency can be both inherited (autosomal recessive) and acquired. Acquired causes include nephrotic syndrome, sepsis, and disseminated intravascular coagulation. The overall prevalence of the disorder is ~1.5 to 3.0%, with severe factor XII deficiency (activity <1%) in a minority.²

Factor XII deficiency is one of the causes for prolongation of aPTT. Other causes of prolonged aPTT include deficiency of coagulation factors VIII, IX, X, XI, V, or II; deficiency of factors for contact phase activation; Von Willebrand disease, liver disease, vitamin K deficiency; therapeutic anticoagulation; and autoimmune diseases (due to anti-phospholipid antibodies). Whenever isolated prolongation of aPTT is encountered, management involves identification of the cause (with specific assays) and correcting it, administration of recombinant clotting factors, factor concentrates, FFP, or cryoprecipitate as per the clinical manifestations.³

Factor XII, prekallikrein, and high-molecular-weight kininogen are important for activation of contact phase of coagulation. Factor XII is activated by plasma kallikrein during endothelial injury. Activated factor XII is the first component of intrinsic pathway of coagulation. Also, fragments of factor XII activate plasminogen during the initiation of normal fibrinolysis. Therefore, factor XII deficiency affects coagulation as well as fibrinolysis.

In our patient, the activity of factor XII was 31% of mean normal range with mild prolongation of aPTT. In patients with severe factor XII deficiency, aPTT values may exceed 120 seconds. Unlike previous literature reports, we did not transfuse FFP for normalization of aPTT.⁴ This is justified by the fact that although factor XII plays an important role in activation of coagulation cascade *in vitro*, its role is very negligible in *in vivo* coagulation activation and extrinsic pathway is sufficient for activation of coagulation pathway in humans.¹ Thus, even severe form of isolated factor XII deficiency does not cause hemostatic problems perioperatively, and prophylactic transfusion with FFP/cryoprecipitate is not warranted. This also explains why there was no abnormal bleeding intraoperatively in our patient. However, the factor XII levels were not very low and there was only a mild prolongation of aPTT in our case.

Factor XII deficiency inhibits fibrinolysis and therefore can lead to thromboembolic complications.⁵ Patients with isolated factor XII deficiency have a high rate of venous thromboembolism and arterial thrombosis, leading to life threatening complications such as pulmonary embolism and myocardial infarction.⁶ In addition, surgical trauma and immobilization increase the risk of thromboembolic complications. This necessitates the use of thromboprophylaxis perioperatively (mechanical and pharmacological) and early aggressive mobilization postoperatively.⁷ We used IPCD intraoperatively and in the postoperative period, low molecular weight heparin, early mobilization, and daily screening for DVT was done in addition to continued use of IPCD.

In conclusion, patients with factor XII deficiency are at high risk of thromboembolism for which vigilant monitoring and measures for thromboprophylaxis should be undertaken perioperatively. The risk of bleeding, although present, is not so alarming. The prophylactic correction of prolonged aPTT should be given a second thought.

Conflict of Interest

None declared.

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Case Report



Dilated Cardiomyopathy and Prone Position: An Anesthetic Challenge

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Abstract

Keywords

- ▶ cardiac resynchronization therapy device
- ▶ dilated cardiomyopathy
- ▶ prone position

The anesthetic management of a patient with dilated cardiomyopathy (DCM) for non-cardiac surgery is challenging due to associated congestive heart failure, malignant dysrhythmias, sudden cardiac arrest, implanted rhythm devices, and thromboembolism. We report successful conduct of a case of DCM on cardiac resynchronization device with Cauda equina syndrome (CES) under general anesthesia in prone position. The anesthetic concerns specific to the pathophysiology of DCM are also discussed.

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