Anaphylactic Reaction to Cryoprecipitate in a Patient with Von Willebrand Disease During Factor Correction for Elective Cesarean Section

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A 40-year-old patient with Type I Von Willebrand Disease presented for elective cesarean section. At the operating theater before delivery, while receiving cryoprecipitate, she developed an anaphylactic reaction requiring resuscitation. Once she was hemodynamically stable, factor VIII/VWF concentrates were administered and operative delivery performed, with a good maternal and fetal outcome.

Key Words: Von Willebrand disease, cesarean section, cryoprecipitate, anaphylactic reaction, B-Lynch suture.

Introduction

Von Willebrand Disease (VWD) is the commonest inherited bleeding diathesis in pregnancy.[1] The endothelial derived Von Willebrand Factor (VWF) promotes platelet activation, platelet adhesion at the site of vascular injury and is the carrier protein for Factor VIII. Types 1, 2 and 3 have been described, with Type 3 being responsible for the most severe bleeding manifestations.[2]

Case Report

A 40-year-old patient, G2P2C1 at 37 weeks of gestation, with a history of type 1 VWD was scheduled for elective cesarean section (CS), at a tertiary care university hospital. She had been diagnosed with VWD at the age of 3. The patient had been free of bleeding complications from the time of diagnosis into adult life. She had had a prior CS under general anesthesia. During infusion of cryoprecipitate for factor correction, she had developed a mild anaphylactic reaction. She had responded to an adrenaline infusion and the IV cryoprecipitate had been continued to achieve the targeted factor level. Surgery had been uneventful, with no bleeding complications. She also gave a history of bronchial asthma and was well controlled on a salbutamol inhaler.

The patient had been followed-up during this pregnancy by the hematology and transfusion medicine teams. They had recommended a reduced dose of cryoprecipitate, in combination with human factor VIII/VWF concentrate prior to surgery. Her VWF level prior to delivery was not assessed. In the morning of surgery, IV access was established, hydrocortisone 100mg IV was administered and monitoring was commenced. Human factor VIII/VWF concentrate was infused to achieve half the targeted correction, without any adverse

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events. Following this, a slow infusion of cryoprecipitate was commenced. Soon after starting the infusion, the patient complained of shortness of breath, experienced a fall in blood pressure to 80/40 mmHg, and developed facial swelling. The infusion was immediately discontinued, a bolus of 100mcg of adrenaline was administered IV and an adrenaline infusion was commenced. She was nebulized with salbutamol in oxygen, and given 200mg of hydrocortisone. The patient's vital signs stabilized on therapy. It was decided to achieve the targeted factor correction with human factor VIII/VWF concentrates. Fetal Doppler assessment at this time confirmed fetal heart activity at a rate of 130bpm but a reduced diastolic blood flow in the umbilical artery. Surgery commenced approximately 2 hours after the initial reaction to cryoprecipitate. The patient had an uneventful general anesthetic. A healthy baby with 1 and 5-minute Apgar scores of 8 and 9 was delivered and cord blood was sent for factor assay. An infusion of syntocinon was commenced, ergometrine 0.6mg and cefuroxime 1g were given IV. Tranexamic Acid 1g was administered IV and continued for 4 days postoperatively. In addition to routine surgical closure, a B-Lynch suture[3] was applied to the uterus, due to a degree of uterine atony. Complete hemostasis was achieved. At the conclusion of surgery, the trachea was extubated and the patient was transferred to the ICU. Thromboelastography results in the ICU were within normal limits. She continued to daily receive 50% factor correction with human factor VIII/VWF concentrates daily for 4 days.

Her postoperative course was complicated by two episodes of bleeding per vagina requiring transfusion with 3 units of blood and a right lower lobe segmental consolidation and a small pleural effusion. Antibiotics and chest physical therapy were continued. She was discharged from hospital on POD 10.

Discussion

Erik Von Willebrand described the disease in 1924 and it is the commonest hemostatic disorder of pregnancy.[1] VWF level usually increases in normal pregnancy. Three types of VWD are recognized according to the inheritance pattern and severity.[2] Type 1 is the mildest form of the disease, has an autosomal dominant inheritance and causes a deficiency of normal VWF. Type 3 is the most severe form of the disease, with an autosomal recessive inheritance and results in virtual absence of VWF. Patients with type 2 VWD have a defective VWF and inheritance can be either autosomal recessive or dominant. Acquired variants of VWD have been associated with autoimmune diseases and malignancy.[4]

Management depends on prior diagnosis, type of VWD, VWF levels and potential for bleeding. The mildest form of VWD in obstetric practice may only manifest with excessive bleeding at the time of delivery. Desmopressin (D-amino D-arginine vasopressin), a synthetic analogue of vasopressin, promotes the release of VWF from vascular endothelium.[1,2] Desmopressin may be sufficient for treatment in the mildest forms of the illness. Due to its potential for placental vasoconstriction, it is not recommended in patients with Pregnancy Induced Hypertension. However, in most instances, supplementary treatment with cryoprecipitate or viral inactivated factor concentrates is indicated.[1,2,4] Cryoprecipitate is currently formulated in saline and theoretically has minimal risk of precipitating serious allergic reactions. This was a major concern in our patient, as she had experienced an anaphylactic reaction previously. The decision to cautiously attempt correction of VWF levels using cryoprecipitate, under steroid cover, was

made on the recommendations of transfusion service. This was based on the fact that only a mild reaction encountered previously. However anaphylactic reaction did occur which needed to be managed with an ongoing live pregnancy. The Vasoconstrictor adrenaline is the standard drug used in the management of anaphylaxis. Its use in our patient may have caused the reduction in placental blood flow.

Platelets carry 10% of VWF in circulation and platelet transfusions have been used for factor correction.[4] Tranexamic Acid administered orally at the onset of labor, and IV during operative delivery and continued IV into the postoperative period, is a valuable therapeutic adjunct to prevent thrombolysis and peri-partum hemorrhage.[1] In our patient, a degree of uterine atony was noted during surgery, despite maximal medical therapy. In order to minimize the risk of a massive postpartum haemorrhage requiring re-exploration and possibly emergency hysterectomy, a B-Lynch uterine suture[3] was placed to promote hemostasis. Though she experienced continued bleeding per vagina, we believe this maneuver proved successful in preventing serious sequelae.

Anaphylactic reactions are said to be common in IgA deficient patients, with an occurrence of 1:700, but the levels have not been assessed in this patient. She would have benefited, if the levels were assessed, because we could have used IgA deficient donor products and avoided the reaction.

Conclusion

The successful management of a mother with type 1 Von Willebrand's disease presenting for elective cesarean section is described. 50% Factor correction with cryoprecipitate was complicated by an anaphylactic reaction and merits caution.

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