Labor and delivery in a patient with hemophilia B

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ABSTRACT

Hemophilia B is a rare X-linked disorder that may cause dramatic bleeding. Women account for only 3.2% of those clinically affected. The X-linked inheritance frequently delays the diagnosis in women and may expose the patient to an increased risk of adverse events. There is limited experience with these patients during labor and delivery. A 28-year-old primiparous woman with hemophilia B (bleeding phenotype) delivered a male infant by an unplanned cesarean delivery under general anesthesia following treatment with factor IX and normalization of her coagulation parameters, guided by thromboelastography. Postpartum vaginal bleeding required transfusion of two units of packed red blood cells. Factor IX supplementation continued for one week. Once diagnosed with hemophilia B, a multidisciplinary approach and advanced antenatal planning can increase the likelihood of a safe delivery. Neuraxial approaches and cesarean delivery are recommended only after normalization of the coagulation profile. The male fetus of a hemophilia A or B patient requires special attention. Operative vaginal delivery and invasive fetal monitoring should be avoided. Thromboelastography is an excellent technique to assess parturients with bleeding disorders or peripartum hemorrhage and may be underused.

Keywords: Hemophilia B; Labor and delivery; Coagulation; Cesarean section; General anesthesia; Thromboelastography

Introduction

Hemophilia A and B are X-linked recessive disorders of coagulation with a prevalence of 1 in 10 000 and 1 in 100 000, respectively. Bleeding results from decreased activity of factor VIII in hemophilia A and factor IX in hemophilia B. Factor activity of <1% is classified as severe, 1 to 5% as moderate, and 5 to 40% as mild. The X-linked inheritance pattern results in men expressing the disease and women typically being carriers. Under rare circumstances a woman can also show a bleeding phenotype. For this to occur, the normal X-chromosome must be inactivated. The rarity of this event explains the low frequency of women with clinical hemophilia.

Case report

A 28-year-old primiparous woman with hemophilia B (Christmas disease) presented for cesarean section. One year before delivery she presented to the University of Florida, Department of Hematology and Oncology for investigation of a bleeding disorder. She had a history of easy bruising and menorrhagia. Her family history was negative. At age 16 she suffered recurrent bleeding for three months following tonsillectomy. She was diagnosed with von Willebrand disease by her local hematologist and received desmopressin perioperatively for minor procedures such as tooth extractions. Despite desmopressin, bleeding would often continue for several days. One year before this presentation she had been treated at another facility for a retroperitoneal hematoma secondary to an ovarian cyst. She required blood transfusions and factor replacement following documentation of low factor IX levels; however, it was unclear if this was due to a consumptive coagulopathy or a production defect.

Tests were performed including factor activities of II, VIII and IX, a platelet function assay, and a ristocetin cofactor assay. These tests were chosen to evaluate for von Willebrand disease, confirm factor IX deficiency, ensure that another vitamin K-dependent (factor II) was normal, and to exclude hemophilia A (factor VIII). All tests were normal except the factor IX activity, which was 11% (normal: above 60%) leading to the diagnosis of mild hemophilia B. Now pregnant for the first time with an uncomplicated pregnancy, a multidisciplinary treatment plan was established. She was to receive factor IX supplementation only in the case of bleeding or if a cesarean delivery was necessary. The patient was not in favor of neuraxial anesthesia. Additionally, because she was carrying a male fetus, an operative vaginal delivery and invasive fetal monitoring were both relatively contraindicated. After a normal antenatal period, the patient went into spontaneous labor at 39 weeks. However, at 6 cm cervical dilation labor arrested despite oxytocin augmentation. Her most recent
factor IX activity was 12% with an activated partial thromboplastin time (aPTT) of 43 s (normal range 25–35 s). The decision was made to perform a cesarean delivery under general anesthesia with factor IX supplementation using 9090 U of recombinant factor IX based on body weight administered intravenously 30 min before incision.

A thromboelastogram (TEG) drawn before factor supplementation showed an increased R-interval of 16.7 mm (normal 5–15), consistent with a coagulopathy (Fig. 1). The TEG was rechecked after factor IX administration and demonstrated normalization with an R-interval of 9.2 mm; aPTT was 35 s (Fig. 2).

The delivery of the baby via cesarean section was uneventful. Estimated blood loss was 800 mL and a 40-U oxytocin infusion in the operating room produced effective uterine contraction.

Factor IX supplementation was decreased in dose and frequency over seven days postpartum. However, she experienced vaginal bleeding on days 1 and 2 due to uterine atony. There was no incisional bleeding, which would have been expected with inadequate recombinant factor IX replacement. Her hematocrit fell to 18% and she received 2 units of packed red blood cells. Her subsequent hospital course was uneventful. As she was able to ambulate after her delivery and her body mass index was <30 kg/m², she did not receive pharmacological thromboprophylaxis. Acetaminophen and opioids were used for postoperative analgesia.

Discussion

Severe hemorrhage is a leading cause of morbidity during childbirth. It is therefore clear that coagulation disorders must be identified before labor. Parturients with a bleeding phenotype of hemophilia A or B present much less frequently due to their X-linked inheritance pattern. In fact this pattern may lead to delayed or improper diagnosis as in our patient where mild hemophilia B, with a factor IX activity of 11% resembled von Willebrand disease. Irrespective of the diagnosis, a multidisciplinary approach is essential for patients with coagulation disorders. A treatment plan should be established and accepted by the parturient before labor and delivery.

The anesthesiologist will most likely be involved during the peripartum period. There is little available in the literature regarding neuraxial techniques in parturients with inherited coagulation disorders. Choi et al. reviewed the literature describing neuraxial techniques (block or lumbar puncture) in patients with common bleeding disorders. Of those patients with known hemophilia A or B, factor activity was increased to normal before the needle was inserted; there were no maternal complications; however, an infant with unrecognized hemophilia suffered a spinal hematoma causing paraplegia.

Chi et al. found encouraging results in pregnant women with inherited bleeding disorders. Following the normalization of coagulation defects, either by intervention or spontaneously, neuraxial anesthesia was not associated with increased complications compared to the normal population. However, patients and coagulation must be monitored. Of note, this analysis did not include patients with the bleeding phenotype of hemophilia B and unlike patients with von Willebrand disease, factor levels in patients with the bleeding phenotype of hemophilia B do not normalize during pregnancy. Our patient opted against a neuraxial technique. Factor IX administration was reserved in case of operative delivery or severe hemorrhage during pregnancy or vaginal delivery. A cesarean delivery was deter-

Fig. 1 Thrombelastogram (TEG) before factor IX administration: prolonged R-interval.
mined to be the best option after the arrest of cervical dilation. Factor IX was administered as per hematology recommendations. As this was not a true emergent cesarean, incision was made 30 min after factor IX administration. A TEG was obtained before and after the administration of factor IX to monitor effect and to exclude further coagulation disturbances. Using TEG to monitor coagulation is well established in cardiac and hepatic surgery. The R-interval, which reflects the function of the coagulation factors, was prolonged initially, consistent with a factor deficiency. In contrast, the R-interval normalized after factor IX administration, indicating that this factor was responsible for the initial prolongation. Additional coagulation defects were essentially excluded.

Had our patient requested neuraxial analgesia for labor, we would have first corrected her coagulation. This would have provided the added advantage of normalized coagulation in case she required a true emergent cesarean section where time would have been limited to correct her coagulopathy. This could also be advantageous in patients with hemophilia presenting with a difficult airway.

Factor IX was administered for seven days postpartum. This is consistent with the observations of Yang and Ragni in 16 deliveries with hemophilia B undergoing labor and delivery. The use of thromboprophylaxis is controversial in this patient population. These patients should be closely monitored. While there are no recommendations addressing the use of thromboprophylaxis, reports have demonstrated that patients with hemophilia are at risk for thrombosis, especially when undergoing surgery. The bleeding defect will usually be corrected with plasma concentrates during the perioperative period and puts the patients at risk for thrombosis, especially if they undergo procedures such as joint arthroplasty. Based on the risk of thrombotic events and the level of correction of the bleeding disorder, it could be suggested that these patients should undergo thromboprophylaxis with mechanical devices and pharmacological prophylaxis with heparin. The use of non-steroidal anti-inflammatory drugs in the perioperative period is also controversial; however, celecoxib and ibuprofen have been beneficial when administered under surveillance.

In summary, we recommend that parturients with bleeding disorders be identified before they are in active labor. A multidisciplinary treatment plan should be established and specific coagulation factors should be readily available.

References

Acute starvation in pregnancy: a cause of severe metabolic acidosis

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ABSTRACT
We report a case of starvation-induced metabolic ketoacidosis in a previously healthy 29-year-old, nulliparous woman at 32 weeks of gestation. She was admitted to hospital with mild preeclampsia associated with persistent nausea and vomiting that progressed to severe preeclampsia requiring urgent control of hypertension before caesarean delivery. Prolonged and severe vomiting limited oral caloric intake and led to starvation ketoacidosis, characterised by ketonuria and a raised anion gap metabolic acidosis that required intensive care support. Despite significant metabolic derangement the patient appeared clinically well. Intravascular volume was replenished. Fluid restriction used as part of our preeclampsia treatment regimen delayed the therapeutic administration of sufficient dextrose, which rapidly corrected her metabolic derangement when commenced after delivery. Electrolyte supplementation was given to prevent re-feeding syndrome. Both mother and baby were discharged without sequelae.

Keywords: Starvation; Ketoacidosis; Re-feeding; Preeclampsia; Pregnancy

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Introduction
We describe an unusual presentation of starvation-induced high anion gap metabolic ketoacidosis in a third trimester pregnancy complicated by preeclampsia. The