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Case Reports

Epidural Labor Analgesia in Parturient with von Willebrand's Disease Type IIA and Severe Preeclampsia

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VON WILLEBRAND'S disease (vWD) presents special risks to the parturient and demands additional attention be paid to her periapartum course. We are aware of two previous case reports of epidural labor analgesia in patients with vWD, [1,2] both in patients with type I (80% of all cases), which normalizes during pregnancy. We report a case of type IIA vWD complicated by severe preeclampsia and its management during the puerperium.

Case Report

A 36-yr-old woman, gravida 2 para 0020, was diagnosed with vWD during her teenaged years. She was characterized as vWD type IIA based on factor VIII activity (FVIII:C), von Willebrand's factor antigen (vWF), ristocetin cofactor activity (RCF), and a von Willebrand's

factor multimeric assay. She had a family history of vWD. After her diagnosis, she was treated with desmopressin (1-deamino-8-p-arginine vasopressin [DDAVP]) before surgical interventions and had no hemorrhagic complications. This pregnancy was notable for multiple nosebleeds, some of which required chemical cautery.

A hematology consultation was performed at 27 week's gestation. Laboratory evaluation revealed prothrombin time (PT), 11.5 s (normal range, 11.3-13.3 s); activated partial thromboplastin time (aPTT), 29.8 s (normal range, 20.1-32.9 s); FVIII:C, 72% (normal range, 54-195%); vWF, 89% (normal range, 50-150%); RCF, < 25% (normal range, 50-150%), consistent with variant (type II) vWD. Because there were no data from a DDAVP challenge, the hematologist recommended Humate P (Armour Pharmaceutical, Kankakee, IL), an intermediate purity FVIII concentrate, before delivery or any invasive procedure [3] and continuation for 6 days postpartum to prevent secondary postpartum hemorrhage. [4] This concentrate is rich in vWF, RCF, and FVIII:C. [5] Humate P has a lower risk of viral transmission than cryoprecipitate and has the highest concentration of vWF of any blood product, and therefore has been recommended as the preferred blood product for the treatment of vWD. [6,7] Incidence of postpartum hemorrhage in patients with vWD is 18.5% and 20%, respectively, for primary and secondary. [8] The goal for transfusion was to keep RCF > 50% (i.e., in the normal range).

At the same time as the hematology consultation, she was seen by the Division of Women's anesthesia, because the patient desired to have an epidural block for labor analgesia. The patient was informed that the option may or may not be feasible, depending on her coagulation status at the time of delivery.

At 35 week's gestation the patient was admitted for induction secondary to the development of severe preeclampsia. The patient complained of increased edema in her hands, face, and feet. Other symptoms included occassional headaches, scotomata, and blurry vision. Her admitting vital signs were blood pressure, 133/84 mmHg; pulse, 79 beats/min; oxygen saturation by pulse oximetry (SpO_2), 99% on room air. Laboratory results showed the following: urine protein, 1 + to 3 +; platelet count, 196,000/mm (^{3}); hemoglobin, 11.9 g/dl; hematocrit, 35%; and white blood cell count, 9,700/mm^3. Coagulation studies on the morning of her induction showed a FVIII:C of 115%, a vWF of 122%, and an RCF of <25%.

The patient was treated with magnesium and was given misoprostol as a cervical preparation and oxytocin intravenously to start her labor. When she became uncomfortable and requested an epidural block for labor analgesia, she received her first dose of Humate P (30 U/kg), and RCF was drawn 11 h later. RCF was 112%, and a lumbar combined spinal epidural block was placed without incident. Intrathecal dosing was 2.5 mg bupivacaine and 25 [micro sign]g fentanyl. An infusion of 0.1 ropivacaine with 2 [micro sign]g/ml fentanyl and 1:400,000 epinephrine was maintained at 10 ml/h.

Vaginal delivery of a healthy boy occurred 6.5 h later. Brisk bleeding prompted manual

extraction of the placenta, uterine massage, administration of intravenous oxytocin, and intramuscular 15-methyl prostaglandin F_2 [Greek small letter alpha], 250 [micro sign]g. RCF was 96% 30 min before delivery. Estimated blood loss was 450 ml. The epidural infusion was discontinued at this time. Within 1 h, the patient was regaining normal sensation and motor tone in her lower extremities. Her next dose of Humate P was given 8.5 h postpartum; RCF was 68% 2 h before transfusion. Two hours later, the epidural catheter was pulled with no sign of bleeding. RCF was again 68% 2 h later.

The patient continued to receive Humate P every 12 h for 48 h postpartum, then once a day until postpartum day 6. The change from every 12 h to every 24 h was prompted by supratherapeutic RCF on postpartum day 2 (104-128%). There were no additional bleeding episodes, and the patient was discharged to home on postpartum day 3.

Discussion

von Willebrand's disease is an autosomal dominant disease with several subtypes and mild and severe forms. The disease was first described by Erik von Willebrand more than 70 yr ago. It is a functional or quantitative deficiency of the protein vWF, which has two roles. It assists in platelet adherence to exposed collagen under disrupted endothelium and promotes platelet aggregation. Its second function is to act as a carrier protein for FVIII and to protect FVIII from premature activation and degradation. von Willebrand's disease is associated with prolonged bleeding time and decreased platelet adhesiveness, FVIII:C, cWF, and RCF. This patient has vWD type IIA, which means that she has a deficiency of the large molecular weight portion of the FVIII/vWF complexes. In other words, her vWF protein is abnormal in size, morphology, and activity, rather than being a quantitative deficiency, as in the case in type I.

In a normal pregnancy, FVIII:C and vWF increase at term by 200 and 375%, respectively, [9] and RCF increases by >400% of baseline. [10] For this reason, most type I patient achieve normal vWF and FVIII:C levels at term, obviating the need for specific therapy at the time of delivery. [5] In a parturient with vWD type IIA, FVIII:C and vWF reached 100% of normal levels for nonpregnant people, but only 50% of the normally higher levels of pregnancy. [10] At 35 1/7 weeks' gestation, this patient's clotting factor concentration and activity and had not yet peaked given the normal course. It was necessary to treat with blood products to maintain therapeutic vWF activity and normal platelet function. Other patients with vWD have been treated with epidural analgesia for labor, [1,2] but only in type I disease with normalization of coagulation status only caused by their pregnancy.

Our patient had improvement and normalization of FVIII:C and vWF, but no improvement in RCF at her pre-term induction. Her obstetric management required transfusion with a vWF-containing preparation. This allowed normalization of her coagulation profile, such that we could provide the patient with epidural labor analgesia. Although DDAVP was used in the past on this patient before surgery without bleeding complications, and has been used

to successfully treat parturients, [11] there were no DDAVP challenge data available, and our hematologist preferred not to do a challenge while the patient was pregnant. Postpartum follow-up revealed a response to DDAVP challenge with supranormal RCF, FVIII:C, and vWF.

von Willebrand's disease is uncommon (1:10,000) especially type IIA. Its combination with preeclampsia and a labor epidural block was never before reported. Normalization of coagulation studies in the peripartum period, either with the physiologic changes of pregnancy [1,2] or the use of DDAVP, have been reported in conjunction with labor epidural block. Here we used transfusion of intermediate purity FVIII concentrate to normalize coagulation studies with success. Further experience with such patients would be needed before any clinical recommendations can be made regarding the administration of an epidural block for analgesia in labor in patients with von Willebrand's disease.

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