Management of pregnancy and emergency caesarean delivery in a patient with type IIB von Willebrand disease and severe preeclampsia: A case report and literature review

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Abstract

Main purposes of the study: To report an example of how concurrent von Willebrand disease type IIB disease and severe preeclampsia can be safely managed to and to review the current literature to evaluate management approaches that have proven safe and effective.

The basic procedures used: Report of case with a review of literature.

Conclusions: Through regular von Willebrand factor and platelet replacement during the prenatal period, immediately pre-delivery, and as needed intraoperatively and postoperatively, women with von Willebrand disease type IIB can safely undergo both normal spontaneous vaginal deliveries and caesarean deliveries, even with concurrent disorders like preeclampsia. Further studies with larger sample size are required to solidify management concepts in this disease concurrent with pregnancy.

Keywords

Complications, high-risk pregnancy, haematology, haemorrhage

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Introduction

Maternal inherited coagulation disorders during pregnancy can have devastating consequences for both the mother and the neonate if untreated. von Willebrand disease (vWD) is the most common inherited bleeding disorder, found in approximately 1% of the general population.¹ vWD can be classified as inherited (types I, II, III) and acquired. Type II vWD is further divided into IIA, IIB, IIM and IIN. In types IIA and IIB, there is an autosomal dominant disorder characterised by the production of abnormal von Willebrand factor (vWF), with vWD type IIB accounting for approximately 5% of cases. Type IIB vWD is unique from other forms of the disease in that it is characterised by a dysfunctional vWF with gain-of-function mutation conferring increased affinity for the platelet receptor GP Ib leading to moderate or severe thrombocytopenia. Although the autosomal inheritance pattern does not put women at higher risk of bleeding events and resultant complications than men, there is a higher frequency of symptomatic type II vWD in women because of the haemostatic challenges of menses, pregnancy and delivery, especially when operative delivery is required. We present a case of an early-term pregnant woman who presented for induction of labour for severe preeclampsia with vWD type IIB who ultimately required emergency caesarean delivery. Other cases of vWF IIB in pregnancy are also reviewed and management plans discussed.

Case

A 30-year-old gravida 1 para 0 at 37 and 4/7 weeks' gestational age presented to labour and delivery suite with complaints of new-onset headache and elevated blood pressure (170/110). Medical history was significant for vWD type IIB diagnosed in early childhood where profuse bleeding was noted following tonsillectomy and subsequent coagulation disorder workup was initiated. This patient denied any history of surgery apart from her tonsillectomy. Prenatal history was remarkable for anaemia for which ferrous sulphate was prescribed. This patient

was followed throughout her pregnancy for vWD by haematology and received platelet transfusions (HLA-matched single donor) for thrombocytopenia, Humate-P (600 IU vWF Ristocetin cofactor activity/250 IU coagulant factor VIII) as needed to maintain adequate plasma levels of each: the patient received infusions twice per week from 35 weeks to 37 weeks. No significant bleeding episodes were encountered throughout her pregnancy.

Throughout early pregnancy, this patient experienced thrombocytopenia with platelet counts 110 k/uL at 10 weeks, 47 k/uL at 20 weeks this was treated with platelet transfusion, and 61 k/uL at 29 weeks. At 35 weeks' gestation, this patient's platelet count was noted to drop to 15 k/uL. This drop was associated with an increase in coagulant factor VIII of 92% and vWF Ristocetin cofactor activity of 28% and associated gingival bleeding, which was treated with Humate-P 3000 IU (25 FVIII u/kg). Given the low platelet count with presence of minor bleeding, platelet transfusions were also given at this time.

On admission, FVIII and vWF assays were 96.3% and 113%, respectively. Cervical exam demonstrated a closed, long and posterior cervix. No uterine contractions were present and fetal heart tracing (FHT) was Category I (normal). Bedside biophysical profile (BPP) was performed and demonstrated a BPP of 8/10 due to an amniotic fluid index of 4 cm. Complete blood count (CBC) was ordered and revealed haemoglobin of 13.7 g/dL, haematocrit of 42.1% and platelet count of 110 k/uL. A spot protein/creatinine ratio was ordered and resulted as 1.1 mg/mg.

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Decision at this time was made to admit this patient for induction of labour in view of severe preeclampsia, oligohydramnios and thrombocytopenia. For delivery, a loading dose of Humate-P 3000 IU about 1–2 h before delivery and a maintenance dose of 2000 IU every 8–12 h was planned. Epidural anaesthesia was to be avoided to eliminate any risk of bleeding in the spinal canal. Labetolol was administered for blood pressure control, magnesium sulphate started for neuroprotection, and acetaminophen as needed for headache. Sequential compression devices were used for deep vein thrombosis prophylaxis with subcutaneous heparin to be ordered postpartum.

Over the course of this patient's induction, recurrent variable decelerations were noted of FHT. Cervical exam at that time was 4 cm, 80% effacement, –3 station. Intrauterine pressure catheter was inserted and amnioinfusion started, but was ineffective in resolving decelerations. Late decelerations were later noted, the longest of which remained prolonged for 6 min before spontaneous recovery. Decision was made to proceed with emergency caesarean delivery under general anaesthesia. This decision was made for obstetrical indications rather than haematologic: to administer general anaesthesia was favoured because it would be faster to administer in the setting of an emergent delivery. Prior to procedure, patient was given Humate-P 3000 IU due to the possibility of acute surgical blood loss and potential progression to haemolysis, elevated liver enzymes and low platelet (HELLP) syndrome. The procedure was uncomplicated and infant delivered with APGARs 9 and 9 at 1 and 5 min, respectively. Estimated blood loss was 1000 mL and this patient did not require any intraoperative transfusions of blood products or further haemostatic agents. Immediate postoperative CBC revealed haemoglobin concentration of 10.7 g/dL, haematocrit of 32.2% and platelet count of 94 k/uL. Magnesium sulphate therapy was continued 24 h after delivery and discontinued without any acute events. No bleeding was encountered postpartum. The rest of this patient's postoperative course was uneventful and this patient was discharged home in stable condition on postoperative day 3.

Discussion

Eleven case reports/case series^{2–14} with a total of 18 patients were published during the periods of 1987–2016 that describe the evaluation and management of obstetric deliveries in patients with vWD type IIB, each with their own unique presentations and management. This report is the first report to our knowledge to have concurrent vWD type IIB with severe preeclampsia. It appears that prompt control of this patient's severe preeclampsia did not further exacerbate thrombocytopenia or ability to achieve haemostasis at time of caesarean delivery. Indeed, this patient did not progress to develop HELLP syndrome, which would undoubtedly have posed an even greater risk to this patient's operative delivery.

Of the cases reviewed, thrombocytopenia was present during pregnancy in most of the cases (14/18) and treatment with platelet transfusions was commonly reported. The cause of thrombocytopenia in these patients, according to recent report and review by Biguzzi et al.,¹⁴ is mainly due to increased production during the third trimester of dysfunctional vWF which characterizes type IIB vWD: this is evidenced by the presence of platelet clumps that was demonstrated on two previous studies where a parallel increase in intermediate molecular weight multimers and decreased platelets were shown in patients with vWD type IIB.^{2,3} Thrombocytopenia in these patients is further exacerbated by the physiological increase in plasma volume during the second trimester of pregnancy. Further, this present case complicated by severe preeclampsia further adds to the likelihood of developing thrombocytopenia, although there was no sudden decrease in platelets observed as a result. In this present case, this situation was ameliorated by frequent platelet transfusions.

Regarding the treatment of thrombocytopenia in pregnant patients with type IIB vWD, there are no specific guidelines and platelet

transfusion remains controversial. The efficacy of platelet transfusion is uncertain in the absence of a platelet count increase, although it was employed in this case. Other haemostatic agents, such as tranexamic acid, have been described in the use of this disease¹⁴ even in view of adequate levels of FVIII and vWF levels as prophylaxis for potential postpartum haemorrhage. It is generally an accepted principal that adequate prepartum haemoglobin/haematocrit levels are important in both patients affected by inherited coagulation disorders and those without given that anaemia is not only a risk factor for postpartum haemorrhage, but is associated with a higher likelihood of need for transfusion of blood products. In this present case, a modest drop in haemoglobin and haematocrit was observed to be 3 g/dL and 10.8%, respectively, and no transfusions were required postoperatively.

Throughout this patient's prenatal course, platelet transfusions were administered and the outcomes were favourable with severe bleeding episodes being avoided. It appears that decisions made regarding timing, dosing and duration of platelets and FVIII/vWF are guided by significantly abnormal values and, more importantly, presence of bleeding. So although there is no definitive evidence regarding these decisions, the presence of bleeding did prompt treatment. Future studies are needed to evaluate if these interventions are beneficial and necessary in these settings.

Management of the neonates of patients with vWD type IIB described in the literature favours factor replacement therapy and platelet transfusion as a recent case report and literature review by Proud et al.¹⁵ suggests. Burlingame et al.⁶ report the case of a 26-year-old female with type IIB vWD who delivered twins found to be thrombocytopenic with platelet counts of 12 k/uL and 14 k/uL. The infants were treated with infusions of Alphanate, a FVIII/vWF concentrate, and platelet transfusions and did not have haemorrhagic complications. Matthew et al.⁸ describe the case of a 22-year-old female with vWD type IIB who delivered a daughter found to be thrombocytopenic with 10 k/uL platelets. The infant was treated with Humate-P infusion and platelet transfusion and had no bleeding complications. These case reports establish a precedent for the use of factor replacement therapy and platelet transfusion in the management of neonates.

Conclusion

Maternal inherited coagulation disorders during pregnancy can have devastating consequences for both the mother and the neonate if untreated. There is a higher frequency of symptomatic vWD in women because of the haemostatic challenges of menses, pregnancy and delivery, especially when operative delivery is required. As evidenced by this case and review of the literature, through regular vWF and platelet replacement during the prenatal, immediate pre-delivery, and as needed intraoperatively and postoperatively, women with vWD type IIB can safely undergo both normal spontaneous vaginal deliveries and caesarean deliveries, even with concurrent disorders like preeclampsia. Further studies with larger sample size are required to solidify management concepts in this disease concurrent with pregnancy.

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Ethical approval

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Guarantor

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Contributorship

The manuscript's design and conception is by F Martingano and D Martingano. The manuscript was proofread by F Martingano and D Martingano.

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