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CASE REPORT

Diagnostic Dilemma in Peripartum Management of von Willebrand Disease: a Case Report

Megha Garg[1] · Uma Pandey[1] · Lalit Prashant Meena[2]

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Introduction

Von Willebrand's disease (vWD) is the most common inherited bleeding disorder in humans with an incidence of 1–2% in the general population [1]. Von Willebrand's disease is an autosomal hereditary bleeding disorder associated with a quantitative or qualitative defect of Von Willebrand factor (vWF) [2]. The vWF transports and stabilises factor VIII and facilitates adhesion of platelets to the endothelium. The disease is classified as type-1 in patients with decreased amount of vWF (quantitative deficiency), type-2 in patients with structural defect of vWF (qualitative deficiency) and type-3 in cases with no vWF function or protein [3]. (Table 1). The incidence of haemophilia A is 1 out of 10,000 male births, while of haemophilia B is 1 out of 30,000 male births with the prevalence ranging from 5.4 to 14.5 per 100,000 male births. The severity of the bleeding symptoms depends on the degree of vWF and FVIII reduction and other factors [4]. The management of vWF disease patients depends on the type of vWF disease, factor levels, symptoms, surgery in future, etc.

For females planning pregnancy, pre-conceptional counselling is important. After conception, multidisciplinary team approach is essential. VWF and factor VIII levels should be monitored in each trimester and also before planning delivery. During delivery if factor levels are low, they can be given Desmopressin, Factor infusion (factor VIII-vWF concentrates), etc. The peri-partum and post-partum period is very crucial for such females due to high chances of bleeding that might happen during and after childbirth. So, the challenge of managing such patients is the correct and timely diagnosis, availability of factors (FVIII, vWF) and efficacious care during antenatal, intrapartum and post-partum period.

Case Summary

An antenatal female of 23 years primigravida, IVF conceived, known case of hypothyroidism and Hepatitis C at 36 weeks + 1 day of gestation was referred to our hospital (tertiary care hospital) because the patient was apparently believed to have "Haemophilia A", i.e. factor VIII deficiency. The patient was diagnosed as Haemophilia A in childhood when she had some bleeding episodes (through gums, nose) and received factor VIII infusion for the same after which her bleeding episodes subsided. Throughout adolescence and adulthood, the patient never had any repeat bleeding episodes, no heavy bleeding during menses and no bleeding episodes in the antenatal period. None of her family members suffered from any similar disease.

After arrival at our hospital, physicians and haematologists of our hospital were consulted regarding confirmation of the diagnosis of the patient as Haemophilia is uncommon in females. A thorough laboratory work was done and her Hb was 12 g/dl, aPTT- 32.3 s (C-35 s), INR- 0.90, PT- 29.2 s, factor VIII-5.00% and vWF 3.60%, vWF: Ristocetin cofactor

Megha Garg is a Junior Resident Department of Obstetrics and Gynaecology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India; Uma Pandey is a Professor Department of Obstetrics and Gynaecology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India; Lalit Prashant Meena is is a Professor Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

✉ Megha Garg
megha.garg01@gmail.com

[1] Department of Obstetrics and Gynaecology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

[2] Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

Table 1 Classification of von Willebrand disease (VWF)

S.No	Type of von Willebrand disease	Description
1	Type 1	Partial quantitative deficiency of VWF
2	Type 3	Virtually complete deficiency of VWF
3	Type 2	Qualitative deficiency of VWF
	Type 2A	Qualitative variants with decreased platelet-dependent function associated with the absence of high and intermediate-molecular weight VWF multimers
	Type 2B	Qualitative variants with increased affinity for platelet GPIb
	Type 2M	Qualitative variants with decreased platelet-dependent function not caused by the absence of high-molecular weight VWF multimers

Table 2 Coagulative profile of the patient on arrival to the hospital

1	aPTT	32.3 (30–40 s)
2	PT	29.2 (11–13.5 s)
3	INR	0.90 (normal < 1)
4	Factor VIII value	5.00%(low)
5	VWF value	3.6% (low)
6	VWF: Ristocetin cofactor activity	2.1%(low)

activity: 2.1%. (Table 2) The patient was thus diagnosed as a case of von Willebrand Disease and not Haemophilia, which the patient was known to be suffering since childhood. Since the patient reported to us late in pregnancy, genetic study could not be done earlier but sample for genetic testing was sent.

On obstetrical examination, the patient has severe oligohydramnios (AFI < 2 cm) with decreased foetal movements. So, a decision to deliver the baby was taken. Haematologists were consulted and preparations were done for the Caesarean section. Pre-operatively she was given four units fresh frozen plasma (FFP) and von Willebrand factor combined with factor VIII infusion at 40 IU/kg and 20 IU/kg respectively, 12 h prior to Caesarean section as she was a very high risk for intra-op and post-op bleeding. (Fig. 1). The dosage was calculated as per mother's weight, which was 70 kg.

The same dose of vWF and FVIII at 40 IU/kg and 20 IU/kg, respectively, was repeated half an hour before the Caesarean section. Immediate pre-operative PT-INR, vWF and FVIII levels were tested and were found to be as-vWF- > 120%, FVIII-71% and INR-1.00. Spinal anaesthesia/epidural anaesthesia were not given due to risk of bleeding. General anaesthesia was given to the patient and the Caesarean went well with minimal blood loss was around 100–200 ml. She gave birth to a male baby who had no evident sign/symptoms of bleeding. Testing of the baby for bleeding disorders was planned. Intraperitoneal and a superficial drains were put during abdominal closure. There was no significant immediate post-operative blood loss. The patient was kept

Fig. 1 Factor VIII and Von Willebrand factor combination used for the patient. Each vial contained 435 IU vWF and 235 IU of factor VIII

on vWF and factor VIII infusion (at the rate of 40 IU/kg and 20 IU/kg respectively) 12 hourly for the first 3 post-operative days and alternate day vWF and FVIII levels were tested. The levels were satisfactory and the patient had no significant bleeding from any site. The drains were removed on post-operative day 2. On post-operative day 4 and 5, the patient was given 30U/kg vWF infusion and 15 IU/kg factor VIII 12 hourly. On post-operative day 6 and 7, she was infused with vWF (20 IU/kg) and factor VIII (10 IU/kg) 24 hourly. (Table 3) Alternate day vWF and factor VIII levels were measured. (Table 4) The levels were within normal range. The patient had no significant bleeding throughout the post-op period. The factor infusion was stopped from post-operative day 8 and vWF level and FVIII levels dropped

Table 3 Frequency and dosage of factors infusion given to the patient

		Von Willebrand factor (vWF)	Factor VIII	Frequency
Pre-operative	12 h pre-operatively	40 IU/kg (40*70 = 2800 IU)	20 IU/kg (20*70 = 1400 IU)	Bolus
	Half an hour before Caesarean	40 IU/kg (40*70 = 2800 IU)	20 IU/kg (20*70 = 1400 IU)	Bolus
Post-operative	Day 0–3	40 IU/kg (40*70 = 2800 IU)	20 IU/kg (20*70 = 1400 IU)	12 hourly
	Day 4–5	30 IU/kg (30*70 = 2100 IU)	15 IU/kg (15*70 = 1050 IU)	12 hourly
	Day 6–7	20 IU/kg (20*70 = 1400 IU)	10 IU/kg (10*70 = 700 IU)	24 hourly

Table 4 Post-operative von Willebrand factor and factor VIII values

Day of surgery	Factor VIII value	VWF levels	Hb levels
Day 0	71%	> 120%	12.0 g/dl
Day 1	81%	> 120%	
Day 3	91%	> 120%	9.0 g/dl
Day 5	79%	100%	
Day 7	68%	100%	
Day 13	6%	6.94%	

after which she was transfused with 6 units of fresh frozen plasma (FFP). On post-operative day 13, the patients factor levels dropped to her baseline levels (vWF-6.94% and FVIII-6.0%). The patient never had any significant bleeding from any site throughout her hospital stay. In the post-operative days, the patient was not administered non-steroidal anti-inflammatory drugs (raises chances of bleeding in patients with vWF disease).

On post-operative day 14, patient's stiches were removed and the stiches were healthy with no bleeding. The patient was discharged as she was fine and was called for follow-up with her pending genetic study. She returned after 1 month and was doing fine and the genetic study confirmed the diagnosis to be "von Willebrand Disease type 2,3"; homozygous type.

Discussion

Patients of Von Willebrand disease are prone to high amounts of bleeding throughout their life. The chances of bleeding in such patients in the antenatal period are 10 times more as compared with normal women. The risk of bleeding is also comparatively high during parturition and also in the post-partum period. Therefore, healthcare providers should be vigilant for complications that they arise to such patients in the antenatal period, during delivery and in the post-partum period.

Sometimes physicians are unable to correctly diagnose patients with bleeding disorder which may result in delay in treatment/ wrong treatment as happened with our patient. Hence, the diagnosis of patients with bleeding disorders should always be confirmed and other specialities should be sought consultation from when in doubt.

The treating doctors should be always ready in case the patient bleeds and blood and blood products, factors for infusion (vWF, FVIII) should be arranged and should be readily available in case of any bleeding episode during or after surgery. There have been cases reported for management of vWF disease in pregnancy in which management was done with Desmopressin, vWF concentrates depending on the factor levels [3]. In our patient, we could provide timely and adequate factors infusion to the patient and did vigilant monitoring of the patient with regular factor level measurement which could have helped our patient and the whole delivery procedure went uneventful.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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About the Author

Dr Megha Garg is a final year Junior resident in the Department of Obstetrics and Gynaecology in Institute of Medical Sciences, Banaras Hindu University.