Case Report

Management of a Pregnant Patient at Term with Von Willebrand Disease - III

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ABSTRACT

Von Willebrand disease (VWD) is a common inherited bleeding disorder involving a deficiency or abnormal function of a blood clotting protein called Von Willebrand factor (VWF). Women with VWD require monitoring during and after pregnancy. This case report describe management of a patient presenting with type III VWD at term and during labour. She had history of severe post-partum haemorrhage (PPH) after cesarean section in previous pregnancy and again had a risk of life-threatening PPH in the current gestation which was managed by appropriate planning and timely decision.
KEY WORDS: Von Willebrand's disease (VWD), Term, Labour, Post partum haemorrhage (PPH).

INTRODUCTION

In 1926, Erik Von Willebrand first reported an autosomally inherited mucocutaneous bleeding disorder in a large family from the Aland Islands off the coast of Finland. The disease was termed VWD, named after this original report. VWD is a common, inherited, genetically and clinically heterogeneous hemorrhagic disorder caused by a deficiency or dysfunction of the protein termed VWF. Consequently, primary hemostasis is impaired because of defective interaction between platelets and the vessel wall.[1] Its prevalence is 0.9 to 1.3% of general population.[2]

VWF is a large multimeric glycoprotein that circulates in blood plasma at concentrations of approximately 10 mg/mL. In response to numerous stimuli, VWF is released from storage granules in platelets and endothelial cells. It performs 2 major roles in hemostasis. First, it mediates the adhesion of platelets to sites of vascular injury. Second, it binds and stabilizes the procoagulant protein Factor VIII (FVIII).[1]

VWD can be classified into 3 main types.

Type 1 VWD (60-80% of all VWD cases) is a quantitative defect with decreased levels of VWF and Factor VIII. In this case Desmopressin is effective.

Type 2 VWD (20-30%) is a qualitative defect and the multimers are structurally abnormal. Desmopressin is only effective in type 2A.

Type 3 VWD is the most severe form of disease. VWF antigen and Factor VIII levels are less than 10%. Acquired VWD can occur in patients with autoantibodies i.e. Systemic Lupus Erythematosus and hypothyroidism.

During normal pregnancy, risk of bleeding is decreased due to increased levels of clotting factors, secondary to elevated hormonal levels, whereas in patients with VWD, levels of VWF are increased to lesser extent as compared to normal pregnancy. There may be a dramatic fall in these levels within first 24 hours of delivery, which explains the risk of PPH, and need for monitoring VWF and Factor VIII levels.[3]

CASE REPORT

A 32 years old unbooked patient, $G_2P_1A_0$ at 39 weeks of gestation with previous one caesarean section, known case of VWD-III, came through OPD for her routine antenatal checkup in Allied Hospital, Faisalabad. She had history of life threatening PPH in previous pregnancy, 6 units of blood and 4 Fresh Frozen Plasma (FFP) were transfused. She had strong family history of this disease. Her brother died during circumcision and her sister died due to heavy menstruation at menarchae. Her maternal cousins were also suffering from this disease. She had H/o moderate menorrhogia since menarchae and most of the time it got relieved by taking hormonal medication.

On general physical examination, she was a woman of average built and height, fully cooperative and a febrile. Blood pressure was 120/80 mm Hg with regular pulse, and pallor+. On abdominal examination, her fundal height was 36 week with longitudinal lie,

cephalic presentation head 5/5 palpable above pubic symphysis, palpable contractions were absent. On vaginal examination her bishop score was zero. Investigation showed her blood group to be O +ive, haemoglobin 9.2 gm/dl, random blood sugar level 66 mg/dl. Further clotting profile does not need to be discussed as she is a known case of VWD-III.

This was a very high risk pregnancy. So haematologist, physician and anesthetist were consulted and her relatives were counselled about the complications during labour, delivery and post partum period. They were also counselled about the need for multiple blood transfusions. The greatest risk of PPH was within 2 – 3 days post delivery when levels of VWF fall significantly.

She went into spontaneous onset of labour at 40 weeks. After 4 hours of labour, signs of fetal distress appeared. There were deceleration and non-reactive pattern on fetal cardiotocography. So emergency caesarean section was decided under general anesthesia. She delivered a male baby of 3.5 Kg with Apgar score 6/10, 8/10. Patient was transfused with 1 unit of cryoprecipate and 3 unit of fresh blood per operatively. Her uterus became atonic and she was bleeding profusely so obstetric hysterectomy was performed to save her life.

On 1st post operative day she was transfused 2 FFP and 2 unit of fresh blood. On 2nd post operative day she was again transfused with 1 unit of blood and 2 FFP. Her post operative investigations were satisfactory. Her VWF post operatively which was less than according to national haemophilia foundation guideline i.e. post operative level of VWF antigen should be 80 – 100% of normal. Desmopressin infusion was not used as it was of no use in her case. She was discharged on 7th post operative day on antifibrinolytics and haematincis. On 15th post operative day she presented with moderate per vaginal bleeding. On ultrasonography vault haematoma was diagnosed which was drained through vaginal route. She was transfused with 2 unit of blood and 1 unit of FPP after her drainage of haematoma.

DISCUSSION

VWD disease is the most common hereditary bleeding disorder.[4] Diagnosis is difficult. There may be history of nose bleed, heavy menstrual bleeding, heavy and prolong bleeding following surgery or childbirth, or a family history of bleeding disorder. On investigations, platelet count is normal with prolonged bleeding time and Activated partial thromboplastin time (APTT), decreased levels of VWF and Factor VIII, reduced platelet adhesion and increased ristocetin cofactor levels.

Patient with this disease is at high risk of severe hemorrhage during delivery and postpartum period. So management should be teamwork of an experienced obstetrician, pediatric consultant and hematologist. Purpose of management is appropriate antenatal care, delivery by least traumatic yet safest method for both mother and baby and meticulous control of PPH by replacement of clotting factors by blood and blood products as their levels falls quickly after birth.

During antenatal period, due to stress, there is relative increase in Factor VIII and VWF factor levels and risk of bleeding is decreased. Donors of cross matched blood should be arranged.

Patient should be given a list of medications to be avoided. This list includes: over-the-counter medication like aspirin, ibuprofen, naproxen, antihistaminics and ethanol; antiplatelet agents i.e. dipyridamole, ticlopidine, NSAID; antimicrobials i.e. penicillins, cephalosporins, nitrofurantoin hydroxychloroquine; Cardiovascular medications like propranalol, frusemide, calcium channel blockers, quinidine and others like caffeine, tricyclic antidepressants, phenothiazines, valproate and heparin. Acetaminophen can be used for fever and headache.[5]

After 36 weeks, delivery is impending at any time so hematologist should be consulted again. Factor VIII and VWF levels should be done and any disturbance of clotting factors should be corrected. Cryoprecipitate, FFP and Factor VIII concentrates should be reserved in blood bank for the time of delivery. Patient should be advised to report in labor room immediately if she has labor pains, vaginal watery discharge or bleeding or decreased fetal movements. During labor, intramuscular injection, aspirin, and non-steroidal anti-inflammatory drugs are not given. Fetal scalp electrodes and instrumental delivery are contraindicated. Factor VIII and VWF levels are checked 24 hours prior to delivery. General aim is to maintain VWF level above 70% for vaginal delivery and above 90% for c/s.[6]

In case of bleeding and disturbance of coagulation profile, treatment should be done to raise VWF levels. Desmopressin causes release of VWF and Factor VIII from storage sites in type 1 VWD. It is administered intravenously as an infusion in 50 cc saline about 0.3 ug/kg to maximum of 20 ug/kg hours over 20-30 min

or by nasal spray. Blood and plasma-derived products can be used for replacement. Otherwise, FFP and cryoprecipitate can be given but they carry risk of transmission of viral problems. Fibrinolytic inhibitors e.g. E-aminocaproic acid and transamic acid are found to be useful. Estrogen has also been found to be useful to increase VWF level.

Regarding use of spinal or epidural anesthesia during labor and delivery, there are no available guidelines. They carry risk of spinal hematoma causing cord compression and may be used if coagulation screen is normal. Scalp hematoma, bleeding after intramuscular vitamin K injection and umbilical bleeding are infrequent complications in affected infants.[7, 8]

Genetic counselling of parents should be done preferably by a pediatrician. Type I and 2 VWD are usually inherited in autosomal dominant pattern i.e., a person has 50% chance of passing the disease to the offspring. Type 3 is inherited as autosomal recessive.[9] Genetic testing of child at birth is not recommended according to the guidelines available but it can be done to remain on the safe side.[2]

The optimal dose and duration of prophylactic therapy will depend on the type and severity of VWDs, mode of delivery and clotting factor level at term. The frequent observation that most post partum haemorrhage occur after a reduction in dose or discontinuation of therapy underscores the importance of close monitoring for several weeks after delivery.

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