CASE REPORT

Bali Medical Journal (*Bali Med J)* 2020, Volume 9, Number 3: 600-602
P-ISSN.2089-1180, E-ISSN: 2302-2914

Published by DiscoverSys

Management of von willebrand disease in pregnancy in resource-limited settings: a case report

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ABSTRACT

Background: Von Willebrand's disease (VWD) is the most common autosomal dominant bleeding disorder. Pregnancy and delivery in patient with VWD possess significant clinical challenges.

Case description: a 24-year-old woman who will undergo labor with a history of VWD. The patient was planned for induction of vaginal delivery and has been given intranasal desmopressin, cryoprecipitate, and factor VIII from before delivery to 5 days after delivery. Labor occurs without excess bleeding. The patient was monitored for 6 days after delivery, and there is no complication of excessive bleeding.

Conclusion: This case emphasizes how to manage Von Willebrand's disease in pregnancy with limitation in the examination and therapeutic option, also the importance of joint management from the hematologist, obstetrician, starting from the antepartum, delivery, and postpartum phases.

Keywords: pregnancy, von Willebrand disease, bleeding

Cite this Article: Mariadi, I.K., Sudjana, K., Wibawa, I.D.N. 2020. Management of von willebrand disease in pregnancy in resource-limited settings: a case report. *Bali Medical Journal* 9(3): 600-602. DOI: 10.15562/bmj.v9i3.2044

INTRODUCTION

Von Willebrand disease (VWD) is an autosomal dominant bleeding disorder caused by quantitative or qualitative disturbances in Von Willebrand factor (VWF), that act as platelet-binding adhesive protein in the exposed sub-endothelial region and carries factor VIII (FVIII) in the circulation. Clinical manifestations of VWD are bleeding from mucocutaneous and soft tissue. The severity of the bleeding depends on the level of VWF dan FVIII in circulations.[1,2]

The heterogenicity of the phenotypes and pathophysiological mechanisms associated with VWD, pregnancy, and delivery in VWD presents significant clinical challenges. There is a change in VWD disease pattern in pregnancy compared to patients with VWD in general, so a careful evaluation is needed to determine the appropriate therapy in VWD patients with pregnancy and delivery plans.[3,4]

In this report, the author describes the experience of handling von Willebrand patient's case with pregnancy with limited examination and treatment options.

CASE REPORT

A female patient, 24 years old, with a history of VWD since 2014 when the patient was 17 years old planned for labor. The patient complained of frequent gum bleeding since childhood. There are no complaints about prolonged or excessive menstruation. There are no complaints regarding bruising of the joints.

The patient already been tested for VWF antigen (VWF:Ag), ristocetin-induced platelet aggregation (RIPA), and Factor VIII in 2014 with results of 1% (50%-160%), 50 (normal aggregation against ristocetin), and 12% (60%-150%) respectively. Complaints of gum bleeding occurred until now.

The patient is the first of four children. The second and third children of the patient's family had the same complaint as the patient, namely gum bleeding that often occurred. The patient's first brother was a male with the same complaint but was said to have died from excessive bleeding from the nose and mouth. The patient's second brother is a male who also has the same complaint and has been diagnosed with VWD. The patient's parents were said not to have the same complaint as the patient.

In the first control at Sanglah General Hospital, the patient was 33 weeks pregnant with no abnormality at the fetal examination and movement. The patient was given tranexamic acid and was planned to reexamine VWF Antigen and prepare for delivery using vaginal delivery methods, preparation of desmopressin, and cryoprecipitate. Repeated VWF antigen was 2% (50% -160%).

The patient was then hospitalized at 40 weeks' gestation in preparation for delivery. Laboratory

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Received: 2020-08-23
Accepted: 2020-10-01
Published: 2020-10-30

tests were performed with WBC 9.54 x 10^3 / uL,% ne 79,% ly 15.1, Hb 8.49 g / dL, HCT 31.11%, MCV 75.7 fL, MCH 20.6 pg, PLT 334 x 10^3 / uL, PPT 13.0 seconds, APTT 71.1 seconds, INR 0.91, BT 1.30 minutes, BUN 6.8 mg / dL, SC 0.54 mg/dL, SGOT 19.4 U/L , SGPT 5 U/L. Transfusion of packed red cell was given before delivery and was planned to give desmopressin spray 300 mcg 2 hours before delivery, cryoprecipitate 5 bags 2 hours before delivery, and continued 5 bag/day, and factor VIII 1000 units 2 hours before delivery.

On July 15th, 2020, vaginal induction of labor was carried out, but there was no progress in labor, so the cesarean section was performed with indications of failed induction. A baby girl weighing 3,540 grams was born, and there was no excess bleeding in the patient. Desmopressin, cryoprecipitate, and factor VIII were given for 5 days after the patient gave birth. The patient and baby were then evaluated for 6 days at Sanglah General Hospital, and there was no excessive bleeding in the birth canal.

DISCUSSION

Women naturally have physiological changes in menstruation, pregnancy, and childbirth that can cause profuse bleeding without specific bleeding disorders. Pregnancy itself is classified as a hypercoagulable condition due to an increase in factor VII, X, fibrinogen, and plasminogen activator 1, accompanied by a decrease in protein S, which works as an adaptive mechanism to prepare for labor. During pregnancy, levels of VWF and FVIII increase significantly in normal women with the highest rates in the third trimester, with levels usually more than 100 IU/dL at delivery.[5,6]

One study showed that women with VWD have risk of experiencing antepartum bleeding 10 times more likely (OR 10.2; 95% CI 7.1-14.6). Based on this data, the management of VWD in pregnancy should not only focus on the time of delivery but during preconception, antepartum, delivery, and postpartum.[7]

Delivery and postpartum period possessed a high risk of bleeding in VWD woman. The risk of bleeding during vaginal delivery or cesarean delivery is low if the VWF and FVIII levels are above 50 IU / dL. Women with mild type 1 VWD can give birth in a community hospital with a hematologist's direction. For patients with severe type 1, type 2, and 3 VWD, delivery should be done in a health facility with an obstetrician, hematologist on-site, has facilities for checking coagulant factors, supporting transfusion and adequate pharmacy and has appropriate hemostatic agents.[8]

The method of delivery was chosen based on the consideration of the obstetrician. Vaginal and cesarean delivery have the same safety for mothers and babies if maternal coagulation factors are within normal limits. Intracranial bleeding in fetuses with VWD is rare; however, precautions must be taken. Delivery should be carried out by the traumatic method to a minimum by preventing a long second-stage phase or, if necessary, proceed to cesarean delivery. The use of forceps and vacuum should be avoided to minimize the risk of hematoma and intracranial bleeding.[9]

In patients with VWD type 1 with FVIII or VWF levels <30 U / dL at delivery, desmopressin is required to increase coagulation factor levels prior to epidural injection delivery. Desmopressin has a maximal effect on coagulation factors 30-60 minutes after intravenous administration (0.3 µg / kgBW) and 90-120 minutes after intranasal administration (<50 kg, 150 µg;> 50 kg, 300 µg). Desmopressin is given 3-4 days postpartum because of the decrease in VWF levels that occur after delivery.[5,10]

In pregnant patients with type 2 VWD with levels of FVIII:C and VWF:Ag 30-50 IU / dL, desmopressin can be given after umbilical clamping and continued for 3-4 days after that. Patients with VWD type 2, FVIII / VWF concentrates for at least 3 days are required. In pregnant patients with Type 2B VWD there will be an increase in the multimers level, abnormally increasing the affinity of Ib on the platelet surface, causing thrombocytopenia. In this case, platelet transfusion in pregnant women indicated a platelet count <30.000 / µL. In pregnant patients with Type 2N VWD in whom late pregnancy FVIII levels do not reach normal values, desmopressin and VWF concentrates may be given if desmopressin is not sufficient. Patients with VWF type 3 do not have elevated levels of FVIII and VWF during pregnancy due to the absence of endothelial deposits. In this case, a VWF/FVIII concentrate is required during pregnancy and at delivery to prevent excessive bleeding.[5,10]

In areas where there is no VWF concentrate infusion, the use of cryoprecipitate which has about 80 units of FVIII in one standard unit, can be administered in life-threatening situations. Cryoprecipitate carries a risk of transmission of infectious agents, so its use is only given when concentrated plasma is not available.[11]

In the postpartum condition, the VWF and FVIII levels fell below baseline immediately after delivery. VWF and FVIII levels should be monitored from the first to the fifth day postpartum. Bleeding complications in the postpartum period are minimal if the VWF and FVIII levels are above 50 IU/dL. Oral antifibrinolytic agents can be given during this period to prevent PPH due to excessive lochia.[12]

In this case, the patient was a woman with pregnancy and suffering from VWD. The patient has received joint management from the hematologist, obstetrician, starting from the antepartum, delivery, and postpartum phases. There are no adequate available examination and treatment options so that the patient gets only the available therapy. However, the delivery was successful with the therapy given without any meaningful complications to either the mother or the baby.

CONFLICT OF INTEREST

The author declares there is no conflict of interest regarding the publication of the current case report.

ETHICAL CONSIDERATION

The patient had received information and signed informed consent regarding data publication before any data collection.

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