Proceedings of UCLA Health
-VOLUME 25 (2021)-

CLINICAL VIGNETTE

Von Willebrand Disease: Pathophysiology and Management of Acute Bleeding

Jessica Leung, MD and Thomas E. Blair, MD

Case Presentation

A 36-year-old male with past medical history of type II A Von Willebrand disease (VWD), hyperlipidemia, and lung nodules presented to the Emergency Department (ED) after a syncopal event.

Two months prior to admission, the patient had an uncomplicated dental extraction. Three days prior to admission, the patient underwent a dental implant procedure. Given history of VWD, he was provided with prophylactic intranasal desmopressin (DDAVP) prior to the procedure; however, post-procedure he still experienced significant blood loss from the surgical site the following days. On the morning of admission, the patient was found unconscious on his bathroom floor by his wife. He spontaneously regained consciousness, but while en route to the ED, he experienced a second syncopal episode.

At the ED, the patient reported symptoms of generalized fatigue, lightheadedness, and nausea. He was afebrile, tachycardic with heart rates in the 140s, blood pressure at 133/80mmHg, respiratory rate of 20 breaths/min, and 100% SpO2 saturation on room air. On physical examination, he was anxious and appeared weak. He had decreased skin turgor, pale conjunctiva, decreased capillary refill time, and slow gingival bleeding from the dental procedure site.

Initial lab values included: white blood cell count of 29.75 k/µL, hemoglobin 10.7 g/dL, hematocrit 30.7%, platelet count 47k/µL, and activated prothrombin time (aPTT) of 36.6 seconds. One month prior, his CBC values were all within normal limits.

Electrocardiography showed sinus tachycardia with heart rate of 140s, blood pressure at 133/80mmHg, respiratory rate of 20 breaths/min, and 100% SpO2 saturation on room air. On physical examination, he was anxious and appeared weak. He had decreased skin turgor, pale conjunctiva, decreased capillary refill time, and slow gingival bleeding from the dental procedure site.

Discussion

Primary hemostasis – including platelet aggregation and platelet plug formation - is a coordinated effort by multiple molecular structures including Von Willebrand factor (VWF). VWF is a large glycoprotein produced by endothelial cells and stored in endothelial Weibel-Palade bodies and platelets to be released during events of endothelial injury. VWF serves three major functions: 1. facilitate platelet adhesion by connecting platelet molecules’ GpIIb/IIIa receptors to collagen of the exposed subendothelial tissue 2. encourage platelet aggregation and 3. act as Factor VIII’s carrier for fibrin formation.1

First described by Dr. Erik von Willebrand in 1924 while investigating a hematologic disorder in a Finnish family, VWD is now recognized as three major types – all associated with either insufficient levels of or dysfunctional VWF. Type I has reduced levels of VWF and is the most common of the VWD types.1 Type II has defective VWF and is further divided into the following subtypes: Type IIA – reduced VWF, Type IIB – excessive platelet clumping activity, Type IIM – decreased VWF activity, and Type IIN – error in VWF’s factor VIII transport. Type III is exceptionally rare with a severe deficiency of VWF that is undetectable.1

The most common hereditary bleeding disorder, VWD affects 1% of the population, but most individuals with the disease will not require medical intervention. Patients often first present for medical attention during episodes of excessive bleeding such as prolonged epistaxis, heavy menstrual bleeding, or easy bruising. Gastrointestinal bleeds are more common in Type IIA and hemarthroses in Type III.2 Accompanying symptoms are manifestations of anemia such as tachycardia, fatigue, hypovolemia, pale conjunctiva, and a source of bleed as is highlighted in our case.

Common lab values in patients with VWD Type IIA include normal hemoglobin, normal platelet count, and mildly elevated aPTT. During an active bleeding event, this patient had low hemoglobin, high white blood cell count, low platelets, and an elevated aPTT. His leukocytosis was most likely reactive in setting of several days of blood loss and physiologic stress - a reflection of the bone marrow’s increased metabolism to replace blood cell lines. Interestingly, low platelet counts are typically seen only in VWD Type IIB, especially after administration of DDAVP. However, Castaman et al. have reported a case of DDAVP-induced thrombocytopenia in VWD type I, suggesting the possibility that DDAVP may induce...
thrombocytopenia in all types of VWD. This patient’s thrombocytopenia, was likely due to prolonged blood loss with possible contribution from the pre-procedural DDAVP.

Prevention strategies and treatment address increasing endogenous and exogenous VWF and promotion of bleeding cessation. Ideally, shortly after a diagnosis of VWD has been made, patients should undergo a DDAVP trial at their baseline health. Physiologically, DDVAP serves to release endogenous VWF from storage reserves, thus increasing VWF during expected bleeding challenges such as surgery. Completion of the DDAVP trial ensures that patients are responsive to this treatment.

Minor bleeding is defined as blood loss that results in less than 2 g/dL hemoglobin drop or less than 2 units of red blood cell transfusion. In minor bleeding situations, DDAVP as well as tranexamic acid are standard treatments. Tranexamic acid inhibits plasminogen activation to plasmin, thus effectively preventing fibrin degradation. Other adjunct treatments that should be considered include intravenous fluids, pressure application to bleeding site, and blood transfusion. Additionally, VWF concentrates can be administered to patients who do not achieve appropriate response after first line therapy.

Major bleeding is defined as blood loss that results in greater than 2 g/dL hemoglobin drop or greater than 2 units of red blood cell transfusion. In addition to aforementioned therapies, treatment may be escalated to Factor VIII transfusion, recombinant activated factor VII transfusion, platelet transfusion, Surgicel with topical thrombin, topical collagen, and/or fibrin sealant.

Conclusion

VWD has a wide spectrum of severity and multiple modes of pathophysiology with the ultimate downstream effect of insufficient VWF effect to provide primary hemostasis. By understanding the pathophysiology, medical providers may address this deficiency with an array of treatments to resuscitate patients and achieve hemostasis.

REFERENCES