International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Von Willebr and Disease Type 3 Presenting with Gastrointestinal Bleeding: A Case Report

I Gusti Lanang Rama Dwi Suputra

Intern of Internal Medicine Division, Sanjiwani Regional Hospital, Gianyar, Bali, Indonesia
Email: *lramasuputra[at]gmail.com*

Abstract: ***Von Willebrand disease (VWD) causes bleeding due to pro - VWF deficiency. VWD type 3 is the most severe form of this bleeding disease mainly because pro - VWF is nearly completely deficient. It is an inherited autosomal recessive trait, either homozygous or heterozygous gene mutations that affect the blood clotting factors. We present a case of a 25 - years old female diagnosed with VWDtype 3and admitted tothe hospital with complaints of melena. Blood investigations revealed low hemoglobin, and esophagogastroduodenoscopy showed gastritis erosive. This disorder cannot be cured, but the patient must be closely monitored to avoid mortality. Symptomatic treatment can be provided, such as tranexamic acid, desmopressin, factor VWF or VIII concentrate to control bleeding.***

Keywords: Von Willebrand disease, VWF, melena

1. Introduction

Von Willebrand disease is a bleeding illness characterized by pro - Von Willebrand factor (VWF) deficiency. [1] The von Willebrand factor is a glycoprotein involved in the process of clotting blood. It's made by endothelium and megakaryocytes. After the translation and transcription processes, pro - VWF is covalently bonded in the endoplasmic reticulum to create dimers, which then form massive dimers in the Golgi complex and secretory granules. The pro - von Willebrand factor propeptide is cleaved and released into the vessel lumen. It helps platelets adhere and bind to endothelial components following vascular damage by carrying factor VIII. [1, 2]

VWD could be inherited or acquired. It is the most prevalent hereditary bleeding condition, first identified by Erik von Willebrand in 1926. VWD is an autosomal (dominant and recessive) bleeding disorder. [1]VWD affects 1% of the unselected population, although statistically significant disease prevalence is around 125 per million, with severe illness affecting up to five per million. Both genders are equally represented. Acquired von Willebrand disease may present for 1%–5% of all cases. It's more common in certain populations. For instance, 20% of malignancies and 100% of high flow states like extracorporeal membrane oxygenation (ECMO) and metallic heart valves have it. [3, 4]

Three main VWD kinds exist. Type 1 is quantitative pro - VWF deficiency caused by genetic defects in the VWF gene on chromosome 12. It causes mild bleeding. Type 2 VWD is rare and characterized by qualitative pro - VWF molecular deficiencies. Type 3 VWD is uncommon and causes significant bleeding owing to VWF and pseudo - von Willebrand deficiency. Type 1 VWD presents 85% of VWD cases. Type 3 is the rarest, affecting 1 in 1 million people. [3, 5]VWD is diagnosed based on complaints of bleeding, familial history, and laboratory tests. Common characteristics bleeding features mucosal bleeding symptoms include easy bruising, epistaxis, gingival bleeding, surgical bleeding, and severe menstrual bleeding. Heavy menstrual bleeding is the most typical first appearance. Gastrointestinal (GI) bleeding, albeit rarer than epistaxis or menorrhagia, is more harmful. It is the most prevalent reason VWD patients need hospitalization during a bleeding episode. Patients with type 2A, 2B, and type 3 are particularly susceptible to experiencing GI bleeding and joint bleeds. [6, 7]

In VWD, GI bleeding is a major cause of death. [8] It is a challenging symptom to treat and is characterized by a high rate of recurrence. GI bleeding in VWD is poorly understood. Angiodysplastic lesions represent the prevailing etiology of recurrent gastrointestinal bleeding in individuals affected by VWD, and followed by ulcer duodenum or gaster, gastritis erosive, diverticulitis, or duodenitis. [6, 9]We report a 25 years old female with upper gastrointestinal bleeding in Von Willbrend Disease.

2. Case

A25 - year - old female was admitted to the hospital with melena since a day ago. She had a history of the same complaint in five months ago. Other complaints were epigastric pain, nausea, fatigue and weakness. She experienced spontaneous gum bleeding, easy bruising, and persistent bleeding after trauma since 3 years old. The patient's parents were cousins, and this pair of parents had a boy who died when he was 2years old due to a bleeding disorder. She had no history oflong - term use of the non - steroidal anti - inflammatory drug (NSAID) and chronic diseases. She was a housewife. She used to like drinking coffee and staying up late.

On physical examination, she appeared sick and pale. She was not icteric, and there were no signs of hepatic failure. Her vitals were normal. There was no organomegaly and joint swelling or hemarthosis. She had no active bleeding on admission. Laboratory investigations revealed hemoglobin (Hb) level at 6.7 g/dL with mean corpuscular volume (MCV) 78.7 fL andMean Corpuscular Hemoglobin Concentration (MCHC) 22.00 fL, platelet count was 205 x 103 uL, bleeding time (BT) was 11 minutes, clotting time (CT) was 14 minutes. The result of Von Willebrand factor:

Ag assay was very low at <2% (normal value 72% - 167%), and the ristocetin cofactor activity test (VWF: RCo) was <4% (normal value 63 - 200%). Elective esophagogastroduodenoscopy (EGD) showed gastritis erosive. A peripheral blood smear was found an anisopoikilocytosis bichromaticanemia (microcytes, elliptocytes, teardrops, target cells, pencil cells, fragmentocytes), suspected iron deficiency anemia. The patient was diagnosed with Von Willebrand disease type 3 and gastritis erosive with severe anemia. She was treated with transfusion - packed red cell (PRC), bolus omeprazole80mg and continued with drip 8mg/hour, antacids, sulcrafatsyr, and tranexamic acid. Bone marrow could not be done. Seven days following hospitalization, the patient had normal hemoglobin and no complaints of bleeding or gastritis. The patient was discharged with the recommendation of a sedentary lifestyle. The patient was recommended to visit a more sophisticated hospital to evaluate other causes of GI bleeding in VWF and bone marrow test.

3. Discussion

Von Willebrand disease is a complicated genetic condition that a lack of either the quality or quantity of VWF in the circulatory system may cause. VWF is an essential hemostatic protein generated by endothelial cells and megakaryocytes. VWF promotes normal hemostasis by binding platelets to exposed collagen in endothelial damage. VWF protects FVIII from plasma proteases and helps form the fibrin clot. Platelet, collagen, and FVIII binding are VWF's three functions. VWD is caused by VWF gene mutations on 12p13.3. [1, 2] VWD symptoms differ by disease subtype, residual VWF activity, and demographic parameters such as age and gender. Most cases are discovered after evaluating severe bleeding issues such as recurring and excessive bruising, continual bleeding from minor skin damage, and long - lasting bleeding from mucosal surfaces such as epistaxis, dental extractions, and menstruation. [3, 5] Our patient had a history of spontaneous gum bleeding, easy bruising, and persistent bleeding after mild trauma from childhood. She also had history of prolong bleeding after dental extraction. Postoperative or post - dental extraction bleeding occurs in 60%–80% of VWD patients. [4]

Gastrointestinal bleeding is a widely recognized and severe complication that could be a risk in VWD to an individual's life. A study by a National Inpatient Sample (NIS) [9], revealed that the most common cause of GI bleeding in VWD was angiodysplasia, 36.5%, which was significantly more common than in non - VWD, 9.5% (*p - value*<0.0001). It is most common in elderly patients with type 2 or 3 VWD. By contrast, the next most common causes of GI bleeding in VWD were ulcer disease, 10.8%; diverticulitis, 9.7%; and gastritis or duodenitis, 8.9%, each less common than in non - VWD (*p value*<0.01). The most common ulcer type was gastric ulcer. [9] The presenting patient had a history of melena with epigastric pain and nausea. She was quite pale, with several bruises on her limbs and no active bleeding upon arrival.

VWD is diagnosed based on family history, bleeding symptoms, abnormal VWF, factor VIII, or lab tests. [2] Most patients have a bleeding family history. Our patient's family had a brother who passed away from a bleeding disorder at 2 years of age. VWD screening tests are unreliable, although severe bleeding may cause anemia. Thrombocytopenia may occur in Type 2B VWD or platelet - type pseudo - VWD. [2, 10] Our patient showed normal platelets and low hemoglobin. Although its low sensitivity and specificity, platelet function investigation has been used to screen for VWD. Bleeding time is also unreliable for VWD diagnosis. [2, 5] Our patient's bleeding and clotting times were 11 and 14 minutes, respectively. Unfortunately, no test can properly diagnose VWD. Therefore, a panel of testing is frequently necessary. These include VWF: Ag, which evaluates the total quantity of VWF protein, and VWF activity, which assesses functional VWF using the ristocetin cofactor activity test (VWF: RCo). [2, 3] Our patient exhibited VWF: Ag <2% anda low level of VWF: RCo, confirming type 3 of VWD. The result of elective EGD showed gastritis erosive without active bleeding.

Management of VWD depends on the type of VWD. In general, Type 1VWD patients may be treated with desmopressin, which increases the amount of circulating VWF by release from storage. Treatment of Type 2 and 3 VWD requires VWF - containing concentrate or factor VIII, similar to hemophilia treatment. [1, 2]Due to limited resources, our patient was not treated with desmopressin or VWF concentrate. However, shewastreated with transfuse PRC for anemia, antacids to neutralize stomach acid, omeprazole asproton pump inhibitor (PPI) to reduce stomach acid for protecting the ulcer while it cures completely, sulcrafat for forming a barrier or coat over the gaster, and tranexamic acid to stop the bleeding. Seven days after the initial admission, the patientwas discharged with stable hemoglobin and no clinical evidence of bleeding. Shewas discharged with the recommendation fora sedentary lifestyle in combination with prophylactic therapy in minor surgery. Surgery and serious trauma therapy need certain VWF and FVIII monitoring. When feasible, adjuvant medication such as antifibrinolytics for oral surgery or hormonal treatment for menorrhagia should be explored for all VWD. [2, 10] Particularly for severe VWD or troublesome symptoms, and other treatments should be examined. Although uncommon to VWD, hormonal treatment for women with menorrhagia may help manage symptoms and improve quality of life. Nasal cauterization or packing may help treat epistaxis locally. Patients with iron - deficiency anemia additionally require iron treatment. [3, 11]

4. Conclusions

Von Willebrand disease is the most prevalent hereditary bleeding disorder, however, diagnosis may be challenging. This study reports a 25 years old female with type 3 VWD that seldom causes GI bleeding. Clinicians should carefully evaluate coagulation abnormalities, including VWD when screening patients with recurrent GI bleeding.

References

[1] Sabih A, Babiker H. *Von Willebrand Disease*. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan - . Available from: https: //www.ncbi. nlm. nih. gov/books/NBK459222/; 2022.
[2] Fogarty H, Doherty D, O'Donnell JS. New developments in von Willebrand disease. *Br J Haematol*.2020; 191 (3): 329 - 339. doi: 10.1111/bjh.16681
[3] Sharma R, Flood VH. Advances in the diagnosis and treatment of Von Willebrand disease. *Blood*.2017; 130 (22): 2386 - 2391. doi: 10.1182/blood - 2017 - 05 - 782029
[4] Du P, Bergamasco A, Moride Y, Truong Berthoz F, Özen G, Tzivelekis S. Von Willebrand Disease Epidemiology, Burden of Illness and Management: A Systematic Review. *J Blood Med*.2023; Volume 14: 189 - 208. doi: 10.2147/JBM. S389241
[5] Swami A, Kaur V. von Willebrand Disease: A Concise Review and Update for the Practicing Physician. *Clinical and Applied Thrombosis/Hemostasis*.2017; 23 (8): 900 - 910. doi: 10.1177/1076029616675969
[6] Chornenki NLJ, Ocran E, James PD. Special considerations in GI bleeding in VWD patients. *Hematology*.2022; 2022 (1): 624 - 630. doi: 10.1182/hematology.2022000390
[7] Tosetto A, Badiee Z, Baghaipour M, et al. Bleeding symptoms in patients diagnosed as type 3 von Willebrand disease: Results from 3WINTERS-IPS, an international and collaborative cross-sectional study. *Journal of Thrombosis and Haemostasis*.2020; 18 (9): 2145 - 2154. doi: 10.1111/jth.14886
[8] Brown R. Recombinant von Willebrand factor for severe gastrointestinal bleeding unresponsive to other treatments in a patient with type 2A von Willebrand disease. *Blood Coagulation & Fibrinolysis*.2017; 28 (7): 570 - 575. doi: 10.1097/MBC.0000000000000632
[9] Tsagianni A, Ragni M V., Comer DM, Yabes JG. Von Willebrand Disease and Gastrointestinal Bleeding: A National Inpatient Sample (NIS) Study. *Blood*.2018; 132 (Supplement 1): 1179 - 1179. doi: 10.1182/blood - 2018 - 99 - 111731
[10] Lillicrap D. von Willebrand disease: advances in pathogenetic understanding, diagnosis, and therapy. *Blood*.2013; 122 (23): 3735 - 3740. doi: 10.1182/blood - 2013 - 06 - 498303
[11] Federici AB, James P. Current Management of Patients with Severe von Willebrand Disease Type 3: A 2012 Update. *Acta Haematol*.2012; 128 (2): 88 - 99. doi: 10.1159/000338208