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Von Willebrand disease: A case report

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***Abstract*---**An hereditary bleeding illness is Von Willebrand Disease (vWD). Along with normal or declining factor VIII levels, von Willebrand factor (vWF) levels also fall. Clinical signs include bleeding that looks "platelet-like" and bleeds resemble factor VIII insufficiency. Life-threatening bleeding might result from the strategic position of the bleed, the volume of blood lost, or complications brought on by the significant blood loss. Treatment modalities include desmopressin (DDAVP) and replacement of vWF. The aim of this report is to make health professionals aware of this possibility that could be in operating on bleeding patients.

***Keywords*---**Von Willebrand Disease, bleeding patients, blood loss.

Introduction

An hereditary bleeding problem is Von Willebrand disease. Prevalence in laboratory data is around 1%, but prevalence among clinically symptomatic persons is around 0.1% of population. vWF purposes as major adhesion molecule that ropes the platelet to the exposed sub-endothelium. Another purpose of vWF is to bind factor VIII and thereby extend its half-life in circulation.[1] The symptoms of vWD are mostly platelet-like, excluding in more severe vWD when the factor VIII is low enough to produce symptoms similar to those found in factor VIII deficiency (Hemophilia A).[2] Bleeding symptoms are very infrequent in

infancy and usually evident later in childhood with excessive bruising and epistaxis. Menorrhagia is a common manifestation of vWD. Although the inheritance of vWD is autosomal, many factors moderate both vWF levels and bleeding symptoms.[3] These include blood type, thyroid hormone status, race, stress, exercise, and hormonal (both endogenous and exogenous) influences.

Case report

We discuss the case of a 40-year-old man who complained of easy, nontraumatic bruising on both of his thighs and legs when he visited the haematology clinic. He is born to non-consanguineous marriage with 4 cousins who have history of epistaxis and nose bleeding. His left hip, both arms, and lower left quadrant of his abdomen all bore injuries from a recent fall. He had no family history of bleeding, clotting, or easy bruising, but there was a substantial link with Type 2B vWD. He denied having any bleeding gums, nosebleeds, stools, or urine. Over the previous six months, he had experienced an inexplicable decrease of appetite and weight loss. His medical history includes occasional use of inhaled albuterol. He has never before had surgery. He consumes three cans of beer every week, along with a pint of vodka every night and a pack of cigarettes each day. He is wed and engaged in sexual activity. Lung cancer afflicted his maternal grandmother.

With the exception of a few bruises on both thighs, the physical examination was normal. His inexplicable weight loss was the reason for the computed tomography (CT) scans of the chest, abdomen, and pelvis, which were unremarkable. Except for haemoglobin levels of 6.2 g/dL and a platelet count of 18,000/mm, the complete blood count, comprehensive metabolic panel, factor VIII, prothrombin time and partial thromboplastin time, D-Dimer, and antithrombin activity were all within normal ranges. Ristocetin induced platelet aggregometry:- response present with normal and low dose ristocetin. His von Willebrand factor activity was determined from the reports to be 43.7% (the reference range is 40%–163%), while the antigen was normal at 65 g/dl (the reference range is 61.3–157.8 g/dl), and the ratio of vWF:RCo is less than 0.5. (normal ratio is more than 0.7). A further test conducted after a week confirmed the initial results, with the antigen activity and factor activity being less than 19% and 37%, respectively. His von Willebrand factor multimer assay results were unusual. VIIIC (with 128.5%).

Discussion

In the current case study, a significant family history of Type 2B VWD was found along with pseudo-thrombocytopenia and platelet clumping on smear. 1%–2% of people have Von Willebrand disease. Megakaryocytes and endothelial cells both generate the glycoprotein known as von Willebrand factor. In their secretory granules, it is kept as multimers. A metalloproteinase called ADAMTS13 controls the size of the multimers. VWF's main job is to act as a factor VIII carrier molecule and facilitate the platelets' adhesion to the injured endothelium. [3].

70% of instances of von Willebrand disease type 1 are caused by a partial lack of the factor [4]. The clinical manifestation of this type is mild post-operative bleeding after tooth extraction, which is a common finding. This autosomal dominant variant has reduced vWF antigen and cofactor, but the multimers are

normal. Factor VIII is proportionately reduced but not as much as vWF [5]. In this type, the ratio of vWF activity to antigen is not reduced and is nearly 1. Type 2A, also an autosomal dominant, is due to the abnormal synthesis, defective packaging before its release, or the defect in the cleavage site of ADAMTS13 resulting in the loss of multimers. There is a reduced binding of platelets. In type 2B, due to the functional mutations in specific domains of vWF, there is increased binding of vWF-platelets through GP1B alpha which results in rapid clearance of these aggregates from the circulation. In addition to reducing the amounts of multimers and vWF, it also sometimes lowers platelet count [6]. Type 2N, an autosomal recessive variety, is attributed to a reduced binding affinity of vWF to FVIII. vWD type 3, autosomal recessive, is a rare entity and is characterized by complete absence of vWF [4].

The current instance is an autosomal dominant variant of type 2b with diminished high molecular weight multimers. It results from a missense mutation in the A3 domain of the vWF gene, which codes for the GPIb receptor on platelets, or from a deficiency in the A1 domain. These defects lead to incresed binding between platelets and vWF, resulting in decreased platelet count [7]. Less than 0.7 is the vWF activity to antigen ratio. (Normal ratio: >0.7) [6].

Factor VIII activity and the von Willebrand factor antigen are tested in laboratories. The subtype of vWD must be determined because different treatments apply to different subtypes. Desmopressin should be tried before utilising blood products for blood types 1, 2, A, M, and N, but not for blood types 2B and 3 [8]. Desmopressin is known to produce thrombocytopenia in type 2B and in case of type 3 when vWF is totally missing, desmopressin is of no value. Hence in these two categories vWF concentrate is the therapy of choice. For acute bleeding, desmopressin or tranexamic acid may be taken, and if accessible, vWF concentrate can be attempted [9].

To maintain hemostasis, >50% of Factor VIII and vWF levels are generally sufficient. Plasma-derived factor concentrated should be considered for prophylaxis for major surgical interventions, major bleeding manifestations, and where desmopressin is not effective or contraindicated. If factor concentrates are not available, cryoprecipitate can be used, with taking consideration of risk factors of TTIs, fluid overload, and increased thrombotic effect.

Conclusion

In this scenario, the von Willebrand factor has a type 2B vWD, which is characterised by a lower-than-0.7 ratio between the factor and the antigen. Despite the fact that the vWF are generated as multimers, there is a poor adherence of the factor to platelets in this type. If vWD is identified in an individual, screening of additional family members is required. All family members should undergo genetic testing in these situations. There are many different types of treatments available. Therefore, if identified early, this category of illnesses does not pose a danger to life.

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