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First Case of Von Willebrand Disease in Niger

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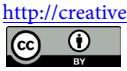

Abstract

Von Willebrand's disease was first described in 1926 by Erik Von Willebrand. It is a genetic, constitutional defect of hemostasis that is different from hemophilia. It is classified among the rare diseases whose clinical manifestations are dominated by a hemorrhagic profile, which varies from patient to patient. It is an easily diagnosed disease based on a quantitative and qualitative bioassay of VWF. Treatment is multidisciplinary and is based on well-structured prevention. We report the first case of von Willebrand disease in Niger, diagnosed in the Hematology Department of Niamey's National Hospital.

Keywords

Willebrand Disease, Onco, Hematology, Niamey, Niger

1. Introduction

Von WILLEBRAND's disease (VWD) is a constitutional, hemorrhagic, mostly autosomal dominant, genetic disease. It results from a quantitative and/or qualitative deficit in Willebrand factor (VWF). It is caused by a genetic defect in the concentration, structure or function of VWF, whether the molecular defect is located on the VWF gene or on another modulator gene [1]. It presents a great clinical and biological heterogeneity. Symptomatic forms are rare. It affects less than 10,000 patients in France. There are three main categories: type 1 corresponds to a partial quantitative deficit in VWF, type 2 to a qualitative deficit affecting either the interaction of VWF with the platelets and/or the sub endothelium, or the interaction of VWF with the factor VIII, type 3 (recessive form) with an almost total deficit [2] [3] [4]. Treatment depends on the type. It is a

rare disease, one of the 2500 rare pathologies listed [5]. We report the first case of Von Willebrand's disease in Niger, diagnosed in the Hematology Department of Niamey's National Hospital.

2. Case Report

The patient is a 23-year-old single female seen on hematology OPD for chronic anemia since the age of 5. The bleeding profile was marked by epistaxis, gingivorrhagia and prolonged bleeding from superficial wounds at the age of 7 years. At the age of 13, she started having menorrhagia of functional origin, which motivated the patient to seek medical help before being referred to hematology OPD for exploration. She was hospitalized and transfused several times for bleeding and chronic anemia. The clinical examination revealed a conscious patient, moderately colored conjunctiva and mucous membrane in good general condition (WHO 1) with a BMI of 22 kg/m^2, arterial blood pressure (BP) measured at 110/70mmHg, normal temperature (T˚: 37˚C), patches of bruising and history of menorrhagia. No subconjunctival hemorrhage, no headache. A Complete Blood Count (CBC), WBC: 5600/mm^3, Hb: 7.8 g/dl, Mean Blood Volume (MCV): 54.3 fl and normal platelet count at 335,000/mm^3. Normal Erythrocyte Sedimentation rate (ESR) at 19 mm at the first hour, low serum ferritin at 1 µg/L (20 - 300 µg/L). B positive blood grouping and plasma βHCG at 0.5 IU/l. A routine coagulation workup was performed which was normal (APTT: 37.9 seconds (Normal range: 25 - 43) and PT percentage: 100%). Coagulation Factor V (FV) assay was 80% normal (N: 62 to 150), factor VIII (FVIII) 82% normal (N: 50 to 150), factor IX (FIX) normal at 94% (N: 55 to 160), immunoassay of Willebrand factor decreased at 39% (N: 50 to 160) and the functional dosage of von Willebrand factor is also decreased at 21% (N: 50 to 160). VWF ratio: RCo/VWF Ag: 0.54.

Based on clinical data, hemorrhagic and laboratory profiles, the diagnosis is that of von Willebrand disease associated with iron deficiency. According to the adapted classification of von Willebrand's disease (**Table 1**) [6], our patient suffered from type 1 von Willebrand disease. A preventive program of estrogen-progestogen for menorrhagia, iron supplementation and the possible use of

Table 1. Classification of von Willebrand disease (adapted in 2006).

Type	Description
1	Partial quantitative deficit in VWF
2	Qualitative deficit in VW
2A	Interaction failure of VWF with platelets and subendothelium linked to the absence of high MW multimers
2B	Increased affinity of VWF for platelet GPIb
2M	Interaction failure of VWF with platelets and subendothelium unrelated to a high PM multimeric abnormalit
2N	Significant decrease in VWF affinity for FVIII
3	Almost total deficit in VWF

Fresh Frozen Plasma (FFP) given the unavailability of von Willebrand Factor, was established.

3. Discussion

Von Willebrand's disease is a genetic disease, described in 1926 by Erik Von Willebrand. It is considered a constitutional anomaly of hemostasis different from hemophilia. The common feature of all forms of the disease is the existence of a quantitative and/or qualitative deficit in VWF. VWF is synthesized by a gene located on the short arm of chromosome 12. It is exclusively expressed in two cell types: endothelial cells and megakaryocytes [7] [8]. VWF allows platelets to adhere to the damaged vascular wall through its binding sites for platelet GPIb and collagen. It also facilitates platelets aggregation thanks to its interaction with GPIIb/IIIa; this role of VWF is essential in hemorheological conditions where the shear rate is high, such as in the microcirculation [9]. It is probably the most common constitutional abnormality of hemostasis. Two large epidemiological studies conducted in a predominantly pediatric population with a history of bleeding and VWF deficiency determined a prevalence of 1% [10] [11]. In Niger, this is the first case diagnosed, due to a very limited technical platform and the high number of investigations required for diagnosis. Clinically it manifests mostly by current or past history of cutaneous, mucosal hemorrhage. Clinical manifestations are highly variable and depend on the type and severity of the disease [12]. It is common to find a history of excessive prolonged bleeding after a vulnerable act, and in women, menorrhagia could be the only clinical manifestation present [13], which is the case of our patient where the clinical manifestations were dominated by menorrhagia and cutaneous bleeding.

Laboratory examination should confirm the diagnosis and specify the type of VWF abnormality [14]. Routine screening tests, bleeding time (BT), platelet count, partial activated thromboplastin time (APTT) are necessary but insufficient. On the other hand, the assay of the Willebrand factor antigen, the assay of the Willebrand factor cofactor of ristocetin (VWF: RCo) and the measurement of the capacity of the Willebrand factor to bind to collagen (VWF: CB) are specific to the diagnosis [14].

The study of VWF: RCo/VWF: Ag, VWF: CB/VWF: Ag and FVIII/VWF: Ag ratios classically makes it possible to distinguish a quantitative anomaly from a qualitative anomaly. A lowered VWF: RCo/VWF: Ag ratio supports an abnormal VWF interaction with platelets, whether or not associated with the absence of high molecular weight (MW) multimer. A lowered VWF: CB/VWF: Ag ratio supports an abnormal VWF interaction with collagens or an absence of high PM multimer. The discriminative thresholds of 0.6 or 0.7 are still debated [14]. Our patient has a VWF: RCo/VWF: Ag ratio of 0.54 which concludes that VWF has an abnormal interaction with platelets. The classification is clinical to facilitate patients' management. The distinction between certain types and subtypes is still difficult, and it's mainly based on the patient's phenotype. According to the clas-

sification of the VWF subcommittee updated in 2006, it is possible to identify three categories: type 1 relates to a partial quantitative deficit of VWF and type 3 to a near-total deficit of VWF. Type 2 defines qualitative anomalies of VWF [6] [15]. This is how our patient is classified as type 1.

The treatment is mainly based on the prevention of hemorrhagic situations, and in case of hemorrhage by providing Willebrand factors concentrates. There are special situations including long-term prophylaxis (in some hemophiliacs or some rheumatological diseases) or some gynecological and obstetrical situations, which require multidisciplinary management. Due to our very limited technical platform, our patient benefited from estrogen-progestogens and FFP in an emergency situation.

4. Conclusion

Von Willebrand's disease is a rare disease with varying clinical manifestations. It remains easy to diagnose in a chronic hemorrhagic situation. In developing countries, diagnostic means are lacking even if the clinical manifestations are in favor of the disease. Its management remains preventive.

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Author Contribution

Djibrilla Almoustapha Amadou was largely contributed to the realization of this work, passing by the diagnosis of the therapeutic decision and the writing of the work.

Malam-Abdou Badé contributed to the patient, but also the development of the body of this work.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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