von Willebrand disease (VWD)

Clotting-Guide
vom Labor zur Diagnose

Description:

The von Willebrand factor (VWF) has a variety of physiological functions, and mutations in the Willebrand gene can cause very different phenotypes. The VWF molecule is very large and complex; it circulates in the form of multimers that are stretched by blood flow shear forces and then bind to platelets, endothelial cells and collagen as well as to factor VIII. This creates platelet aggregates that are important for primary hemostasis.

However, the stretched VWF is also specifically cleaved and regulated by ADAMTS13, which creates the typical multimeric pattern (triplett structure).

The different forms of VWD are shown in the table. The most common form (incidence 1:100-1:1000) is type 1, in which there is an absolute reduction in the amount of VWF molecules. It is characterized by mild bleeding (mucous membrane bleeding, hypermennorrhea, hematomas, postoperative bleeding). If VWF levels are very low, a bleeding pattern similar to hemophilia A can occur, with intestinal angiodysplasia, leading to chronic gastrointestinal bleeding.

The lower limit of normal VWF activity is not clearly defined; it depends on the blood group (blood group 0 has physiologically lower VWF levels). This makes it difficult to distinguish “low Willebrand syndrome” from mild type 1 VWD. Values below 30% are certainly pathological. Only a genetical analysis can then confirm the diagnosis. Since VWF is an acute-phase protein, measurements within 3 weeks of an infection or an acute event can produce falsely high values.

The other subtypes of VWD affect other qualities of VWF (multimerization, binding strengths, etc.) and can often not be diagnosed without genetic analysis.

Subtypes of von Willebrand disease (VWD):

Low-Willebrand syndrome:

- Quantitative reduction of VWF concentration
- VWF:Ag 30-50%; VWF:Act 30-50%; FVIII normal; VWF Akt/Ag >0.7
- Therapy: if necessary, desmopressin

VWD type 1:

- Quantitative reduction of VWF concentration
- VWF:Ag <30%; VWF:Akt <30%; FVIII normal; VWF Akt/Ag >0.7
- Therapy: if necessary, desmopressin or VWF concentrate

VWD type 2A:

- Reduction of large multimers, therefore reduced platelet adhesion
- VWF:Ag >30%; VWF:Akt <30%; FVIII normal; VWF Act/Ag <0.7
- Therapy: if necessary, desmopressin or VWF concentrate

VWD type 2B:

- Enhanced, spontaneous platelet binding
- VWF:Ag >30%; VWF:Akt <30%; FVIII normal; VWF Act/Ag <0.7
- Therapy: VWF concentrate

VWD Type 2 M:

- Decreased platelet or collagen binding
- VWF:Ag >30%; VWF:Akt <30%; FVIII normal; VWF Act/Ag <0.7
- Therapy: VWF concentrate

VWD Type 2 N:

- Decreased factor VIII binding
- VWF:Ag >30%; VWF:Akt >30%; FVIII <30%; FVIII/VWF:Ag <0.6
- Therapy: VWF concentrate

VWD type 3:

- Lack of VWF and FVIII activity
- VWF:Ag <5%; VWF:Akt <5%; FVIII <5%
- Therapy: VWF concentrate

Treatment options:

To treat von Willebrand disease types 1 and 2A, desmopressin (Minirin®, Octostim®, Nocutil®) can be used, which leads to an increase in Willebrand levels for 1-4 days. Desmopressin can be administered intravenously, subcutaneously or as a nasal spray (dose 0.4 µg/kg, maximum for 4 days); oral administration is ineffective. The other VWD subtypes must be treated intravenously with Willebrand-containing plasma preparations (Haemate®) or recombinant Willebrand concentrate (Veyvondi®). Additional treatment with tranexamic acid is helpful to reduce bleedinh, especially in the case of mucous membrane bleeding.

The information in the product information must be observed!

The management of severe von Willebrand disease is similar to hemophilia A and should take place in competence centers.

Surveillance:

Determination of the von Willebrand factor (VWF:Ag and VWF:Akt). Goal: depending on the indication for bleeding, trough level >50%.

For questions please contact a coagulation specialist.

References:

Thomas L, Laboratory and Diagnosis, 2023, Release 5: https://www.labor-und-diagnose.de/index.html
Parameter catalog of the Clinical Institute for Laboratory Medicine, Med.Univ.Wien and AKH Vienna: https://www.akhwien.at/default.aspx?pid=3982
List of services for clinical chemistry, Univ.Klinikum Ulm: https://www.uniklinik-ulm.de/zentrale-einrichtung-klinische-chemie/leistungskatalog.html