Von Willebrand Disease

Subjects: Genetics & Heredity
Contributor: Bruce Ren

Von Willebrand disease is a bleeding disorder that slows the blood clotting process, causing prolonged bleeding after an injury.

Keywords: genetic conditions

1. Introduction

Von Willebrand disease is a bleeding disorder that slows the blood clotting process, causing prolonged bleeding after an injury. People with this condition often experience easy bruising, long-lasting nosebleeds, and excessive bleeding or oozing following an injury, surgery, or dental work. Mild forms of von Willebrand disease may become apparent only when abnormal bleeding occurs following surgery or a serious injury. Women with this condition typically have heavy or prolonged bleeding during menstruation (menorrhagia), and some may also experience reproductive tract bleeding during pregnancy and childbirth. In severe cases of von Willebrand disease, heavy bleeding occurs after minor trauma or even in the absence of injury (spontaneous bleeding). Symptoms of von Willebrand disease may change over time. Increased age, pregnancy, exercise, and stress may cause bleeding symptoms to become less frequent.

Von Willebrand disease is divided into three types, with type 2 being further divided into four subtypes. Type 1 is the mildest and most common of the three types, accounting for 75 percent of affected individuals. Type 3 is the most severe and rarest form of the condition. The four subtypes of type 2 von Willebrand disease are intermediate in severity. Another form of the disorder, acquired von Willebrand syndrome, is not caused by inherited gene mutations. Acquired von Willebrand syndrome is typically seen along with other disorders, such as diseases that affect bone marrow or immune cell function. This rare form of the condition is characterized by abnormal bleeding into the skin and other soft tissues, usually beginning in adulthood.

2. Frequency

Von Willebrand disease is estimated to affect 1 in 100 to 10,000 individuals. Because people with mild signs and symptoms may not come to medical attention, it is thought that this condition is underdiagnosed. Most researchers agree that von Willebrand disease is the most common genetic bleeding disorder.

3. Causes

Mutations in the *VWF* gene cause von Willebrand disease. The *VWF* gene provides instructions for making a blood clotting protein called von Willebrand factor, which is essential for the formation of blood clots. After an injury, clots protect the body by sealing off damaged blood vessels and preventing further blood loss. Von Willebrand factor acts as a glue to hold blood clots together and prevents the breakdown of other blood clotting proteins. If von Willebrand factor does not function normally or too little of the protein is available, blood clots cannot form properly. Abnormally slow blood clotting causes the prolonged bleeding episodes seen in von Willebrand disease.

The three types of von Willebrand disease are based upon the amount of von Willebrand factor that is produced. Mutations in the *VWF* gene that reduce the amount of von Willebrand factor cause type 1 von Willebrand disease. People with type 1 have varying amounts of von Willebrand factor in their bloodstream. Some people with a mild case of type 1 never experience a prolonged bleeding episode. Mutations that disrupt the function of von Willebrand factor cause the four subtypes of type 2 von Willebrand disease. People with type 2 von Willebrand disease have bleeding episodes of varying severity depending on the extent of von Willebrand factor dysfunction, but the bleeding episodes are typically similar to those seen in type 1. Mutations that result in an abnormally short, nonfunctional von Willebrand factor generally cause type 3 von Willebrand disease. Because there is no functional protein, people with type 3 von Willebrand disease usually have severe bleeding episodes.

3.1 The gene associated with Von Willebrand disease

- VWF

4. Inheritance

Von Willebrand disease can have different inheritance patterns.

Most cases of type 1 and type 2 von Willebrand disease are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Type 3, some cases of type 2, and a small number of type 1 cases of von Willebrand disease are inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they do not show signs and symptoms of the condition.

5. Other Names for This Condition

- angiohemophilia
- vascular pseudohemophilia
- von Willebrand disorder
- von Willebrand's factor deficiency

References

1. Federici AB, Mannucci PM. Management of inherited von Willebrand disease in2007. Ann Med. 2007;39(5):346-58. Review.
2. James AH, Jamison MG. Bleeding events and other complications during pregnancyand childbirth in women with von Willebrand disease. J Thromb Haemost. 2007Jun;5(6):1165-9.
3. Kessler CM. Diagnosis and treatment of von Willebrand disease: newperspectives and nuances. Haemophilia. 2007 Dec;13 Suppl 5:3-14. doi:10.1111/j.1365-2516.2007.01581.x. Review. Erratum in: Haemophilia. 2008May;14(3):669.
4. Nichols WL, Hultin MB, James AH, Manco-Johnson MJ, Montgomery RR, Ortel TL,Rick ME, Sadler JE, Weinstein M, Yawn BP. von Willebrand disease (VWD):evidence-based diagnosis and management guidelines, the National Heart, Lung, andBlood Institute (NHLBI) Expert Panel report (USA). Haemophilia. 2008Mar;14(2):171-232. doi: 10.1111/j.1365-2516.2007.01643.x.
5. Nichols WL, Rick ME, Ortel TL, Montgomery RR, Sadler JE, Yawn BP, James AH,Hultin MB, Manco-Johnson MJ, Weinstein M. Clinical and laboratory diagnosis ofvon Willebrand disease: a synopsis of the 2008 NHLBI/NIH guidelines. Am JHematol. 2009 Jun;84(6):366-70. doi: 10.1002/ajh.21405.
6. Peake I, Goodeve A. Type 1 von Willebrand disease. J Thromb Haemost. 2007Jul;5 Suppl 1:7-11. Review.
7. Pruthi RK. A practical approach to genetic testing for von Willebrand disease.Mayo Clin Proc. 2006 May;81(5):679-91. Review.
8. Wilde JT. Von Willebrand disease. Clin Med (Lond). 2007 Dec;7(6):629-32.Review.
