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My46 Trait Profile

von Willebrand disease

von Willebrand disease is the most common inherited bleeding disorder. It is caused by mutations in the VWF gene which makes the protein called von Willebrand factor.

Characteristics of von Willebrand disease

Williams syndrome is a multi-system genetic disorder with both medical and developmental features. A hallmark medical feature of Williams syndrome is blood vessel stenosis or narrowing. Although narrowing may occur anywhere, supravalvar aortic stenosis (SVAS), a narrowing above the aortic valve in the heart, is the most common site of narrowing. Other medical problems often seen in Williams syndrome vary by age, but may include elevated calcium (hypercalcemia), feeding difficulties, constipation, reflux, diabetes, and contractures. Though the majority of individuals with this condition have mild to moderate intellectual disability, affected individuals often have a unique pattern of relative strengths and weaknesses. For instance, most individuals with Williams syndrome have a friendly, social personality with relatively strong language skills. Visual-spatial tasks (i.e., activities that require understanding of spatial relations among objects; e.g., reading a map, and driving), however, tend to be rather difficult for most individuals with Williams syndrome. Behavioral problems such as attention deficit hyperactivity disorder (ADHD) and anxiety are also very common in this condition. Individuals with Williams syndrome have a characteristic facial appearance; in children, these include a round upturned nose, wide mouth, small widely spaced teeth, stellate irises (a star pattern in the colored part of the eye visible in light colored eyes), and puffiness around the eyes.

Diagnosis/Testing

Diagnosis of VWD is often made by specific blood tests to evaluate multiple blood clotting factors. These blood tests help to diagnose and determine which type of VWD is present. These clotting factors can fluctuate however making diagnosis difficult in some instances. Diagnosis can also be made by genetic testing for a change or mutation in a gene called VWF. This gene makes the von Willebrand factor protein. This protein helps to form blood clots. Some mutations in the VWF gene cause less von Willebrand factor protein to be made while other mutations cause the von Willebrand factor protein to not work properly. In type 1 VWD, little von Willebrand factor protein is made. In type 2 VWD, von Willebrand factor protein is present, however it does not function properly. In type 3 VWD, von Willebrand factor protein is entirely absent. Not all individuals with VWD have an identified mutation in the VWF gene.

Management/Surveillance

The type of medicine used to treat VWD depends on the severity of VWD. Some individuals with VWD can be treated with DDAVP (also called desmopressin), a hormone that stimulates the release of von Willebrand factor. Other affected individuals must receive IV (intravenous) von Willebrand factor replacement products. When possible, aspirin and aspiring-containing products should be avoided in individuals with VWD.

Mode of inheritance

VWD may be inherited in one of two patterns of inheritance: autosomal dominant and autosomal recessive.
Autosomal dominant inheritance:

Type 1 and most of type 2 are inherited in an autosomal dominant pattern. This means inheriting one mutation is

enough for an individual to be affected. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child.

Autosomal recessive inheritance:

Type 3 is inherited in an autosomal recessive pattern. This means that an individual has to inherit two mutations (i.e., one from each parent) to be affected with VWD type 3. If both parents are carriers of a mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with VWD type 3.

Risk to family members

The risk to family members depends on the pattern of inheritance:

Autosomal dominant inheritance:

The risk to family members depends on whether or not the individual with VWD type 1 or type 2 has a parent affected with VWD type 1 or type 2. If a parent also has the condition, the risk of having a child with VWD is 50% with each pregnancy. If a parent does not have VWD, the risk of other siblings being affected is very low.

Autosomal recessive inheritance:

Parents of a child with VWD type 3 are carriers of VWD. If a sibling of a child with VWD type 3 is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of VWD.

Special considerations

None

Resources

Genetics Home Reference: Von Willebrand disease
http://ghr.nlm.nih.gov/condition/von-willebrand-disease
National Hemophilia Foundation
http://www.hemophilia.org
World Federation of Hemophilia
http://www.wfh.org
Canadian Hemophilia Society
http://www.hemophilia.ca
Haemophilia Society
http://www.haemophilia.org.uk

References

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Goodeve A, James P. (Updated 13 October 2011). von Willebrand Disease. In: GeneReviews at GeneTests Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2013. Available at http://www.ncbi.nlm.nih.gov/books/NBK7014/. Accessed [05/03/2013].

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