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My46 Trait Profile

von Hippel Lindau syndrome

Other Names: von Hippel Lindau disease

von Hippel Lindau syndrome is a rare genetic condition in which individuals have a higher chance to have certain cancerous and noncancerous tumors. It is caused by mutations in the VHL gene which makes the von hippel lindau protein.

Characteristics of von Hippel Lindau syndrome

Individuals with von Hippel Lindau syndrome (VHL) have a higher chance to have certain cancerous (malignant) and noncancerous (benign) tumors. The tumors most frequently appear during young adulthood but can occur at any point during an affected individuals lifetime. The most common tumors are hemangioblastomas (tumors of the blood vessels) in the brain, spinal cord, and retina (back of the eye). These tumors are usually benign, but can be life-threatening. Hemangioblastomas in the brain and spinal cord may cause pain, headaches, vomiting, weakness and ataxia (an unsteady gait). The tumors in the retina are often the first tumor identified in individuals with VHL. These tumors can lead to vision loss. Other tumors include pheochromocytomas (tumors on the adrenal gland an organ that sits on top of the kidney), pancreatic neuroendocrine tumors (tumors that may affect certain hormones), pancreatic cysts, endolymphatic sac tumors (growths that develop in the inner ear and can cause hearing loss) and epididymal papillary cystadenomas (growths in the testicles). Renal cell carcinomas or kidney cancer can occur in about 70% of individuals with VHL. Kidney cancer is the most common cause of death in individuals with VHL.

The signs and symptoms of the tumors are highly variable within families as well as between other unrelated, affected individuals. Individuals with VHL usually have normal intellectual abilities.

Diagnosis/Testing

Most individuals with VHL (90-100%) have a change or mutation in a gene called VHL. This is the only gene known to cause VHL. The VHL gene is a tumor suppressor gene which means that it keeps cells from growing too fast. Mutations in the VHL gene do not allow the VHL protein to work normally and as a result, cells may grow uncontrollably. This uncontrolled growth is what can cause the tumors and cysts in affected individuals.

Sometimes, individuals with certain VHL mutations are more likely to have specific physical aspects of the condition. This is called genotype/phenotype correlation. For example, in VHL type 1, affected individuals may be more likely to have retinal and brain/spinal cord tumors and less likely to have pheochromocytomas. These individuals often have mutations in the VHL gene that cause the VHL protein to not be made at all. Individuals with VHL type 2 have a higher risk of pheochromocytomas as well as the retinal and brain/spinal cord tumors. Many of these individuals have mis-spellings or missense mutations in the VHL gene.

Almost all individuals who have a VHL mutation show signs of the condition by the age of 65.

Management/Surveillance

Management of VHL includes treatment of the brain and spinal hemangioblastomas when they are large or causing health problems. Other surgeries may be required to treat the retinal tumors, endolymphatic sac tumors, pancreatic cysts, or kidney tumors as well as pheochromocytomas. Some individuals may require kidney transplant.

Individuals who have VHL or are at risk to have the condition and have not had genetic testing should follow specific surveillance recommendations with their healthcare provider. These vary depending upon an individuals age and include annual vision and hearing evaluations, blood pressure monitoring, and MRI of the ear canal, abdomen, brain and total spine at varying intervals.

It is very important that an individual with VHL be followed closely by his or her healthcare provider. It is known that early detection and treatment of tumors may reduce or prevent problems such as hearing or vision loss, neurologic symptoms, and the need for kidney transplant. Individuals with VHL should avoid tobacco products (cigarette smoking, chewing tobacco, etc.) as these are considered risk factors for kidney cancer.

Mode of inheritance

VHL is inherited in an autosomal dominant pattern. This means inheriting one VHL mutation is enough for an individual to be affected and show signs of VHL. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child. Most of the time (approximately 80%), the condition is inherited from an affected parent.

Risk to family members

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

Special considerations

None

Resources

von Hippel Lindau Family Alliance
http://www.vhl.org/
Genetics Home Reference: von Hippel Lindau syndrome
http://ghr.nlm.nih.gov/condition/von-hippel-lindau-syndrome

References

Bader, HR. et al. (2012)."Systemic VHL gene functions and VHL disease." FEBS Letters 586: 1562-1569.
Frantzen C, Links TP, Giles RH. (Updated 21 June 2012). Von Hippel-Lindau 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/NBK1463/. Accessed [04/05/2013].
Richard, S. et al. (2013)."Von Hippel-Lindau: how a rare disease illuminates cancer biology." Seminars in Cancer Biology 23(1): 26-37.

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