Familial exudative vitreoretinopathy

Description

Familial exudative vitreoretinopathy is a hereditary disorder that can cause vision loss that worsens over time. This condition affects the retina, the specialized light-sensitive tissue that lines the back of the eye. In people with this disorder, blood vessels do not fully develop at the outer edges (periphery) of the retina, which reduces the blood supply to this tissue. This prolonged reduction in blood supply (chronic ischemia) causes continued damage to the retina and can lead to worsening of the condition.

The signs and symptoms of familial exudative vitreoretinopathy vary widely, even within the same family. In many affected individuals, the retinal abnormalities never cause any vision problems. Other people with this condition develop abnormal vessels that leak. This causes chronic inflammation which, over time, can lead to fluid under the retina (exudate). A reduction in the retina's blood supply causes the retina to fold, tear, or separate from the back of the eye (retinal detachment). The resulting retinal damage can lead to vision loss and blindness. Other eye abnormalities are also possible, including eyes that do not look in the same direction (strabismus) and a visible whiteness (leukocoria) in the normally black pupil.

Some people with familial exudative vitreoretinopathy also have a condition known as osteoporosis-pseudoglioma syndrome, which is characterized by reduced bone density. People with this condition have weakened bones and an increased risk of fractures.

Frequency

The prevalence of familial exudative vitreoretinopathy is unknown. It is thought to be rare, although affected people with normal vision may never receive a diagnosis.

Causes

Variants (also called mutations) in the *FZD4*, *LRP5*, and *NDP* genes cause most cases of familial exudative vitreoretinopathy. These genes provide instructions for making proteins that participate in a chemical signaling pathway that affects the way cells and tissues develop. In particular, the proteins produced from the *FZD4*, *LRP5*, and *NDP* genes appear to play critical roles in the specialization of retinal cells and the formation of blood vessels in the retina and the inner ear. The LRP5 protein also helps regulate bone formation.

Variants in the *FZD4*, *LRP5*, or *NDP* gene disrupt chemical signaling during early development, which interferes with the formation of blood vessels at the periphery of the retina. The resulting abnormal blood supply to this tissue leads to retinal damage and vision loss in some people with familial exudative vitreoretinopathy.

The eye abnormalities associated with familial exudative vitreoretinopathy tend to be similar no matter which gene is altered. However, affected individuals with *LRP5* gene variants often have reduced bone mineral density in addition to vision loss. Variants in the other genes responsible for familial exudative vitreoretinopathy do not appear to affect bone density.

Variants in other genes each cause a small number of cases of familial exudative vitreoretinopathy. In other cases, the cause of familial exudative vitreoretinopathy is unknown.

Learn more about the genes associated with Familial exudative vitreoretinopathy

- CTNNB1
- FZD4
- LRP5
- NDP

Additional Information from NCBI Gene:

- KIF11
- TSPAN12
- ZNF408

Inheritance

Familial exudative vitreoretinopathy has different inheritance patterns depending on the gene involved. Most commonly, the condition results from variants in the *FZD4* or *LRP5* gene and has an autosomal dominant pattern of inheritance. Autosomal dominant inheritance means one copy of the altered gene in each cell is sufficient to cause the disorder. Most people with autosomal dominant familial exudative vitreoretinopathy inherit the altered gene from a parent, although the parent may not have any signs or symptoms associated with this disorder.

Familial exudative vitreoretinopathy caused by *LRP5* gene variants can also have an autosomal recessive pattern of inheritance. Autosomal recessive inheritance means both copies of the gene in each cell must have a variant to cause the disorder. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they typically do not show signs and symptoms of the condition.

When familial exudative vitreoretinopathy is caused by variants in the *NDP* gene, it has an X-linked recessive pattern of inheritance. The *NDP* gene is located on the X

chromosome, which is one of the two sex chromosomes. In people who have only one X chromosome (typical for males), one altered copy of the gene in each cell is sufficient to cause the condition. In people who have two X chromosomes (typical for females), a variant would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that both copies of a gene would be altered, people with one X chromosome are affected by X-linked recessive disorders much more frequently than those with two. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- FEVR

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Exudative vitreoretinopathy 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1851402/)
- Genetic Testing Registry: Exudative vitreoretinopathy 4 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1866176/)
- Genetic Testing Registry: Exudative vitreoretinopathy 5 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2750079/)
- Genetic Testing Registry: Exudative vitreoretinopathy 6 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4225316/)
- Genetic Testing Registry: Exudative vitreoretinopathy 2, X-linked (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1844579/)

Genetic and Rare Diseases Information Center

- Familial exudative vitreoretinopathy (https://rarediseases.info.nih.gov/diseases/1613/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Familial exudative vitreoretinopathy%22)

Catalog of Genes and Diseases from OMIM

- EXUDATIVE VITREORETINOPATHY 1; EVR1 (https://omim.org/entry/133780)
- EXUDATIVE VITREORETINOPATHY 2, X-LINKED; EVR2 (https://omim.org/entry/305390)
- EXUDATIVE VITREORETINOPATHY 4; EVR4 (https://omim.org/entry/601813)
- EXUDATIVE VITREORETINOPATHY 3; EVR3 (https://omim.org/entry/605750)
- EXUDATIVE VITREORETINOPATHY 6; EVR6 (https://omim.org/entry/616468)
- EXUDATIVE VITREORETINOPATHY 5; EVR5 (https://omim.org/entry/613310)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28familial+exudative+vitreoretinopathy%5BTIAB%5D%29+OR+%28fevr%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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