X-linked hyper IgM syndrome

Description

X-linked hyper IgM syndrome is a condition that affects the immune system and occurs almost exclusively in males. People with this disorder have abnormal levels of proteins called antibodies or immunoglobulins. Antibodies help protect the body against infection by attaching to specific foreign particles and germs, marking them for destruction. There are several classes of antibodies, and each one has a different function in the immune system. Although the name of this condition implies that affected individuals always have high levels of immunoglobulin M (IgM), some people have normal levels of this antibody. People with X-linked hyper IgM syndrome have low levels of three other classes of antibodies: immunoglobulin G (IgG), immunoglobulin A (IgA), and immunoglobulin E (IgE). The lack of certain antibody classes makes it difficult for people with this disorder to fight off infections.

Individuals with X-linked hyper IgM syndrome begin to develop frequent infections in infancy and early childhood. Common infections include pneumonia, sinus infections (sinusitis), and ear infections (otitis). Infections often cause these children to have chronic diarrhea and they do not gain weight and grow at the expected rate (faltering weight). Some people with X-linked hyper IgM syndrome have low levels of white blood cells called neutrophils (neutropenia). Affected individuals may develop autoimmune disorders, neurologic complications from brain and spinal cord (central nervous system) infections, liver disease, and gastrointestinal tumors. They also have an increased risk of lymphoma, which is a cancer of immune system cells.

The severity of X-linked hyper IgM syndrome varies among affected individuals, even among members of the same family. Without treatment, this condition can result in death during childhood or adolescence.

Frequency

X-linked hyper IgM syndrome is estimated to occur in 2 per million newborn boys.

Causes

Variants (also known as mutations) in the *CD40LG* gene cause X-linked hyper IgM syndrome. This gene provides instructions for making a protein called CD40 ligand, which is found on the surface of immune system cells known as T cells. CD40 ligand

attaches like a key in a lock to its receptor protein, which is located on the surface of immune system cells called B cells. B cells are involved in the production of antibodies, and initially they are able to make only IgM antibodies. When CD40 ligand and its receptor protein are connected, they trigger a series of chemical signals that instruct the B cell to start making IgG, IgA, or IgE antibodies.

CD40 ligand is also necessary for T cells to interact with other cells of the immune system, and it plays a key role in the maturation (differentiation) of T cells, which allows them to carry out their specific functions.

Variants in the *CD40LG* gene lead to the production of an abnormal CD40 ligand or prevent production of this protein. If CD40 ligand does not attach to its receptor on B cells, these cells cannot produce IgG, IgA, or IgE antibodies. Variants in the *CD40LG* gene also impair the T cell's ability to mature and interact with other immune system cells. People with X-linked hyper IgM syndrome are prone to infections because they do not have a properly functioning immune system.

Learn more about the gene associated with X-linked hyper IgM syndrome

- CD40LG

Inheritance

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

Other Names for This Condition

- HIGM1
- Hyper-IgM syndrome 1
- Immunodeficiency with Hyper-IgM, type 1

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hyper-IgM syndrome type 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0398689/)

Genetic and Rare Diseases Information Center

- X-linked hyper-IgM syndrome (https://rarediseases.info.nih.gov/diseases/73/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22X-linked hyper IgM syndrome%22)

Catalog of Genes and Diseases from OMIM

- IMMUNODEFICIENCY WITH HYPER-IgM, TYPE 1; HIGM1 (https://omim.org/entry/308230)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28x-linked+hyper+igm+syndrome%5BTIAB%5D%29+OR+%28hyper-igm+syndrome+1%5BTIAB%5D%29+OR+%28higm1%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D)

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