Leydig cell hypoplasia

Description

Leydig cell hypoplasia is a condition that affects male sexual development. It is characterized by underdevelopment (hypoplasia) of Leydig cells in the testes. Leydig cells secrete male sex hormones (androgens) that are important for normal male sexual development before birth and during puberty.

In Leydig cell hypoplasia, affected individuals with a typical male chromosomal pattern (46,XY) may have a range of genital abnormalities. Affected males may have a small penis (micropenis), the opening of the urethra on the underside of the penis (hypospadias), or a scrotum divided into two lobes (bifid scrotum). Because of these abnormalities, the external genitalia may not look clearly male or clearly female.

In more severe cases of Leydig cell hypoplasia, people with a typical male chromosomal pattern (46,XY) have female external genitalia. They have small testes that are undescended, which means they are abnormally located in the pelvis, abdomen, or groin. People with this form of the disorder do not develop secondary sex characteristics, such as increased body hair, at puberty. Some researchers refer to this form of Leydig cell hypoplasia as type 1 and designate less severe cases as type 2.

Frequency

Leydig cell hypoplasia is a rare disorder; its prevalence is unknown.

Causes

Mutations in the *LHCGR* gene cause Leydig cell hypoplasia. The *LHCGR* gene provides instructions for making a protein called the luteinizing hormone/chorionic gonadotropin receptor. Receptor proteins have specific sites into which certain other proteins, called ligands, fit like keys into locks. Together, ligands and their receptors trigger signals that affect cell development and function.

The protein produced from the *LHCGR* gene acts as a receptor for two ligands: luteinizing hormone and a similar hormone called chorionic gonadotropin. The receptor allows the body to respond appropriately to these hormones. In males, chorionic gonadotropin stimulates the development of cells in the testes called Leydig cells, and luteinizing hormone triggers these cells to produce androgens. Androgens, including testosterone, are the hormones that control male sexual development and reproduction.

In females, luteinizing hormone triggers the release of egg cells from the ovary (ovulation). Chorionic gonadotropin is produced during pregnancy and helps maintain conditions necessary for the pregnancy to continue.

The *LHCGR* gene mutations that cause Leydig cell hypoplasia disrupt luteinizing hormone/chorionic gonadotropin receptor function, impeding the body's ability to react to these hormones. In males, the mutations result in poorly developed or absent Leydig cells and impaired production of testosterone. A lack of testosterone interferes with the development of male reproductive organs before birth and the changes that appear at puberty. Mutations that prevent the production of any functional receptor protein cause the more severe features of Leydig cell hypoplasia, and mutations that allow some receptor protein function cause milder signs and symptoms.

Learn more about the gene associated with Leydig cell hypoplasia

- LHCGR

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Only people who have mutations in both copies of the *LHCGR* gene and are genetically male (with one X and one Y chromosome in each cell) have the characteristic signs of Leydig cell hypoplasia. Although people who are genetically female (with two X chromosomes in each cell) may inherit mutations in both copies of the *LHCGR* gene, they do not have Leydig cell hypoplasia because they do not have Leydig cells. They have normal female genitalia and normal breast and pubic hair development, but they may begin menstruation later than usual (after age 16) and have irregular menstrual periods. *LHCGR* gene mutations in females also prevent ovulation, leading to inability to have children (infertility).

Other Names for This Condition

- 46,XY disorder of sex development due to LH defects
- LCH
- Leydig cell agenesis
- LH resistance due to LH receptor deactivation
- Male hypergonadotropic hypogonadism due to LHCGR defect

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Leydig cell agenesis (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0266432/)

Genetic and Rare Diseases Information Center

- Leydig cell hypoplasia (https://rarediseases.info.nih.gov/diseases/3244/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- LEYDIG CELL HYPOPLASIA, TYPE I (https://omim.org/entry/238320)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28leydig+cell+hypoplasia%5BTIAB%5D%29+OR+%28leydig+cell+agenesis%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3240+days%22%5Bdp%5D)

References

- Kossack N, Simoni M, Richter-Unruh A, Themmen AP, Gromoll J. Mutations in anovel, cryptic exon of the luteinizing hormone/chorionic gonadotropin receptorgene cause male pseudohermaphroditism. PLoS Med. 2008 Apr 22;5(4):e88. doi:10.1371/journal.pmed.0050088. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18433292) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2323302/)
- Qiao J, Han B, Liu BL, Chen X, Ru Y, Cheng KX, Chen FG, Zhao SX, Liang J, LuYL, Tang JF, Wu YX, Wu WL, Chen JL, Chen MD, Song HD. A splice site mutationcombined with a novel missense mutation of LHCGR cause malepseudohermaphroditism. Hum Mutat. 2009 Sep;30(9):E855-65. doi:10.1002/humu.21072. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19551906)
- Themmen AP, Verhoef-Post M. LH receptor defects. Semin Reprod Med. 2002Aug; 20(3):199-204. doi: 10.1055/s-2002-35384. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12428200)
- Wu SM, Chan WY. Male pseudohermaphroditism due to inactivating luteinizinghormone receptor mutations. Arch Med Res. 1999 Nov-Dec;30(6):495-500. doi:10.1016/s0188-4409(99)00074-0. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10714363)

- Wu SM, Leschek EW, Rennert OM, Chan WY. Luteinizing hormone receptor mutationsin disorders of sexual development and cancer. Front Biosci. 2000 Mar1;5: D343-52. doi: 10.2741/wu. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10704433)

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