Congenital leptin deficiency

Description

Congenital leptin deficiency is a condition that causes severe obesity beginning in the first few months of life. Affected individuals are of normal weight at birth, but they are constantly hungry and quickly gain weight. Without treatment, the extreme hunger continues and leads to chronic excessive eating (hyperphagia) and obesity. Beginning in early childhood, affected individuals develop abnormal eating behaviors such as fighting with other children over food, hoarding food, and eating in secret.

People with congenital leptin deficiency also have hypogonadotropic hypogonadism, which is a condition caused by reduced production of hormones that direct sexual development. Without treatment, affected individuals experience delayed puberty or do not go through puberty, and may be unable to conceive children (infertile).

Frequency

Congenital leptin deficiency is a rare disorder. Only a few dozen cases have been reported in the medical literature.

Causes

Congenital leptin deficiency is caused by mutations in the *LEP* gene. This gene provides instructions for making a hormone called leptin, which is involved in the regulation of body weight. Normally, the body's fat cells release leptin in proportion to their size. As fat accumulates in cells, more leptin is produced. This rise in leptin indicates that fat stores are increasing.

Leptin attaches (binds) to and activates a protein called the leptin receptor, fitting into the receptor like a key into a lock. The leptin receptor protein is found on the surface of cells in many organs and tissues of the body including a part of the brain called the hypothalamus. The hypothalamus controls hunger and thirst as well as other functions such as sleep, moods, and body temperature. It also regulates the release of many hormones that have functions throughout the body. In the hypothalamus, the binding of leptin to its receptor triggers a series of chemical signals that affect hunger and help produce a feeling of fullness (satiety).

LEP gene mutations that cause congenital leptin deficiency lead to an absence of leptin. As a result, the signaling that triggers feelings of satiety does not occur, leading to the

excessive hunger and weight gain associated with this disorder. Because hypogonadotropic hypogonadism occurs in congenital leptin deficiency, researchers suggest that leptin signaling is also involved in regulating the hormones that control sexual development. However, the specifics of this involvement and how it may be altered in congenital leptin deficiency are unknown.

Congenital leptin deficiency is a rare cause of obesity. Researchers are studying the factors involved in more common forms of obesity.

Learn more about the gene associated with Congenital leptin deficiency

- LEP

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.

Other Names for This Condition

- LEPD
- Leptin deficiency
- Obesity due to congenital leptin deficiency
- Obesity, morbid, due to leptin deficiency
- Obesity, morbid, nonsyndromic 1
- Obesity, severe, due to leptin deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Obesity due to congenital leptin deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3554224/)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Congenital leptin defici

ency%22)

Catalog of Genes and Diseases from OMIM

- LEPTIN DEFICIENCY OR DYSFUNCTION; LEPD (https://omim.org/entry/614962)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28congenital+leptin+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

References

- Bluher S, Shah S, Mantzoros CS. Leptin deficiency: clinical implications andopportunities for therapeutic interventions. J Investig Med. 2009Oct;57(7):784-8. doi: 10.2310/JIM.0b013e3181b9163d. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19730134)
- Dubern B, Clement K. Leptin and leptin receptor-related monogenic obesity. Biochimie. 2012 Oct;94(10):2111-5. doi: 10.1016/j.biochi.2012.05.010. Epub 2012May 22. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22627381)
- Farooqi IS, Jebb SA, Langmack G, Lawrence E, Cheetham CH, Prentice AM, HughesIA, McCamish MA, O'Rahilly S. Effects of recombinant leptin therapy in a childwith congenital leptin deficiency. N Engl J Med. 1999 Sep 16;341(12):879-84. doi:10.1056/NEJM199909163411204. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10486419)
- Farooqi IS, Matarese G, Lord GM, Keogh JM, Lawrence E, Agwu C, Sanna V, JebbSA, Perna F, Fontana S, Lechler RI, DePaoli AM, O'Rahilly S. Beneficial effectsof leptin on obesity, T cell hyporesponsiveness, and neuroendocrine/metabolicdysfunction of human congenital leptin deficiency. J Clin Invest. 2002Oct;110(8):1093-103. doi: 10.1172/JCI15693. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12393845) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC150795/)
- Fatima W, Shahid A, Imran M, Manzoor J, Hasnain S, Rana S, Mahmood S. Leptindeficiency and leptin gene mutations in obese children from Pakistan. Int JPediatr Obes. 2011 Oct;6(5-6):419-27. doi: 10.3109/17477166.2011.608431. Epub2011 Aug 19. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21854111)
- Gibson WT, Farooqi IS, Moreau M, DePaoli AM, Lawrence E, O'Rahilly S, TrussellRA. Congenital leptin deficiency due to homozygosity for the Delta133G mutation:report of another case and evaluation of response to four years of leptintherapy. J Clin Endocrinol Metab. 2004 Oct;89(10):4821-6. doi:10.1210/jc.2004-0376. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15472169)
- Montague CT, Farooqi IS, Whitehead JP, Soos MA, Rau H, Wareham NJ, Sewter CP,Digby JE, Mohammed SN, Hurst JA, Cheetham CH, Earley AR, Barnett AH,

Prins JB,O'Rahilly S. Congenital leptin deficiency is associated with severe early-onsetobesity in humans. Nature. 1997 Jun 26;387(6636):903-8. doi: 10.1038/43185. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/9202122)

- O'Rahilly S. Leptin: defining its role in humans by the clinical study ofgenetic disorders. Nutr Rev. 2002 Oct;60(10 Pt 2):S30-4; discussion S68-84, 85-7.doi: 10.1301/002966402320634904. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12403081)
- Ozata M, Ozdemir IC, Licinio J. Human leptin deficiency caused by a missensemutation: multiple endocrine defects, decreased sympathetic tone, and immunesystem dysfunction indicate new targets for leptin action, greater central thanperipheral resistance to the effects of leptin, and spontaneous correction ofleptin-mediated defects. J Clin Endocrinol Metab. 1999 Oct;84(10):3686-95. doi:10.1210/jcem.84.10.5999. Erratum In: J Clin Endocrinol Metab 2000 Jan;85(1):416. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10523015)
- Paz-Filho G, Wong ML, Licinio J. Ten years of leptin replacement therapy. ObesRev. 2011 May;12(5):e315-23. doi: 10.1111/j.1467-789X.2010.00840.x. Epub 2011 Mar17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21410864)
- Saeed S, Butt TA, Anwer M, Arslan M, Froguel P. High prevalence of leptin andmelanocortin-4 receptor gene mutations in children with severe obesity fromPakistani consanguineous families. Mol Genet Metab. 2012 May;106(1):121-6. doi:10.1016/j.ymgme.2012.03.001. Epub 2012 Mar 10. Erratum In: Mol Genet Metab. 2013Aug;109(4):404. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22463805)

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