Holocarboxylase Synthetase Deficiency

Subjects: Genetics & Heredity

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Holocarboxylase synthetase deficiency is an inherited disorder in which the body is unable to use the vitamin biotin effectively. This disorder is classified as a multiple carboxylase deficiency, which is a group of disorders characterized by impaired activity of certain enzymes that depend on biotin.

genetic conditions

1. Introduction

The signs and symptoms of holocarboxylase synthetase deficiency typically appear within the first few months of life, but the age of onset varies. Affected infants often have difficulty feeding, breathing problems, a skin rash, hair loss (alopecia), and a lack of energy (lethargy). Immediate treatment and lifelong management with biotin supplements may prevent many of these complications. If left untreated, the disorder can lead to delayed development, seizures, and coma. These medical problems may be life-threatening in some cases.

2. Frequency

The exact incidence of this condition is unknown, but it is estimated to affect 1 in 87,000 people.

3. Causes

Mutations in the *HLCS* gene cause holocarboxylase synthetase deficiency. The *HLCS* gene provides instructions for making an enzyme called holocarboxylase synthetase. This enzyme is important for the effective use of biotin, a B vitamin found in foods such as liver, egg yolks, and milk. Holocarboxylase synthetase attaches biotin to certain enzymes that are essential for the normal production and breakdown of proteins, fats, and carbohydrates in the body. Mutations in the *HLCS* gene reduce the enzyme's ability to attach biotin to these enzymes, preventing them from processing nutrients properly and disrupting many cellular functions. These defects lead to the serious medical problems associated with holocarboxylase synthetase deficiency.

3.1. The gene associated with Holocarboxylase synthetase deficiency

- HLCS

4. 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.

5. Other Names for This Condition

- Biotin-(propionyl-CoA-carboxylase) ligase deficiency
- Biotin-(propionyl-coenzyme A-carboxylase) ligase deficiency
- early-onset biotin-responsive multiple carboxylase deficiency
- early-onset combined carboxylase deficiency
- HLCS deficiency
- infantile multiple carboxylase deficiency

References

1. Bandaralage SP, Farnaghi S, Dulhunty JM, Kothari A. Antenatal and postnatalradiologic diagnosis of holocarboxylase synthetase deficiency: a systematicreview. Pediatr Radiol. 2016 Mar;46(3):357-64. doi: 10.1007/s00247-015-3492-8.
2. Baumgartner MR. Vitamin-responsive disorders: cobalamin, folate, biotin,vitamins B1 and E. Handb Clin Neurol. 2013;113:1799-810. doi:10.1016/B978-0-444-59565-2.00049-6. Review.
3. León-Del-Río A, Valadez-Graham V, Gravel RA. Holocarboxylase Synthetase: AMoonlighting Transcriptional Coregulator of Gene Expression and a CytosolicRegulator of Biotin Utilization. Annu Rev Nutr. 2017 Aug 21;37:207-223. doi:10.1146/annurev-nutr-042617-104653.
4. Morrone A, Malvagia S, Donati MA, Funghini S, Ciani F, Pela I, Boneh A, PetersH, Pasquini E, Zammarchi E. Clinical findings and biochemical and molecularanalysis of four patients with holocarboxylase synthetase deficiency. Am J MedGenet. 2002 Jul 22;111(1):10-8.
5. Tang NL, Hui J, Yong CK, Wong LT, Applegarth DA, Vallance HD, Law LK, Fung SL,Mak TW, Sung YM, Cheung KL, Fok TF. A genomic approach to mutation analysis ofholocarboxylase synthetase gene in three Chinese patients with late-onsetholocarboxylase synthetase deficiency. Clin Biochem. 2003 Mar;36(2):145-9.