Transcobalamin Deficiency

Subjects: Genetics & Heredity

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genetic conditions

1. Introduction

Transcobalamin deficiency is a disorder that impairs the transport of cobalamin (also known as vitamin B12) within the body. Cobalamin is obtained from the diet; this vitamin is found in animal products such as meat, eggs, and shellfish. An inability to transport cobalamin within the body results in cells that lack cobalamin, which they need for many functions including cell growth and division (proliferation) and DNA production. The absence of cobalamin leads to impaired growth, a shortage of blood cells, and many other signs and symptoms that usually become apparent within the first weeks or months of life.

The first signs of transcobalamin deficiency are typically a failure to gain weight and grow at the expected rate (failure to thrive), vomiting, diarrhea, and open sores (ulcers) on the mucous membranes such as the lining inside the mouth. Neurological function is impaired in affected individuals, and they can experience progressive stiffness and weakness in their legs (paraparesis), muscle twitches (myoclonus), or intellectual disability.

People with transcobalamin deficiency often develop a blood disorder called megaloblastic anemia. Megaloblastic anemia results in a shortage of red blood cells, and the remaining red blood cells are abnormally large. Individuals with transcobalamin deficiency may also have a shortage of white blood cells (neutropenia), which can lead to reduced immune system function. Decreased cellular cobalamin can lead to a buildup of certain compounds in the body, resulting in metabolic conditions known as methylmalonic aciduria or homocystinuria.

2. Frequency

The prevalence of transcobalamin deficiency is unknown. At least 45 affected individuals have been described in the medical literature.

3. Causes

Mutations in the *TCN2* gene cause transcobalamin deficiency. The *TCN2* gene provides instructions for making a protein called transcobalamin. This protein attaches (binds) to cobalamin and transports the vitamin to cells throughout the body. Within cells, cobalamin helps certain enzymes carry out chemical reactions. Cobalamin plays a role in the processes that produce the building blocks of DNA (nucleotides) and break down various compounds such as fatty acids; these processes are needed for cell proliferation and the production of cellular energy.

Most *TCN2* gene mutations that cause transcobalamin deficiency lead to a complete or near-complete lack (deficiency) of transcobalamin. Other *TCN2* gene mutations result in a transcobalamin protein that cannot transport cobalamin to cells. The resulting lack of cobalamin within cells interferes with the functioning of certain enzymes, which impacts many cell activities. As a result, a wide range of signs and symptoms can develop including impaired growth, blood cell shortages, and neurological problems.

3.1 The gene associated with Transcobalamin deficiency

- TCN2

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

- TC deficiency
- TC II deficiency
- TCN2 deficiency
- transcobalamin II deficiency

References

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