TRNT1 Deficiency

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TRNT1 deficiency is a condition that affects many body systems. Its signs and symptoms can involve blood cells, the immune system, the eyes, and the nervous system. The severity of the signs and symptoms vary widely.

Keywords: genetic conditions

1. Introduction

A common feature of TRNT1 deficiency is a blood condition called sideroblastic anemia, which is characterized by a shortage of red blood cells (anemia). In TRNT1 deficiency, the red blood cells that are present are unusually small (erythrocytic microcytosis). In addition, developing red blood cells in the bone marrow (erythroblasts) can have an abnormal buildup of iron that appears as a ring of blue staining in the cell after treatment in the lab with certain dyes. These abnormal cells are called ring sideroblasts.

Many people with TRNT1 deficiency have an immune system disorder (immunodeficiency) that can lead to recurrent bacterial infections. Repeated infections can cause life-threatening damage to internal organs. The immunodeficiency is characterized by low numbers of immune system cells called B cells, which normally help fight infections by producing immune proteins called antibodies (or immunoglobulins). These proteins target foreign invaders such as bacteria and viruses and mark them for destruction. In many individuals with TRNT1 deficiency, the amount of immunoglobulins is also low (hypogammaglobulinemia).

In addition, many individuals with TRNT1 deficiency have recurrent fevers that are not caused by an infection. These fever episodes are often one of the earliest recognized symptoms of TRNT1 deficiency, usually beginning in infancy. The fever episodes are typically accompanied by poor feeding, vomiting, and diarrhea, and can lead to hospitalization. In many affected individuals, the episodes occur regularly, arising approximately every 2 to 4 weeks and lasting 5 to 7 days, although the frequency can decrease with age.

Eye abnormalities, often involving the light-sensing tissue at the back of the eye (the retina), can occur in people with TRNT1 deficiency. Some of these individuals have a condition called retinitis pigmentosa, in which the light-sensing cells of the retina gradually deteriorate. Eye problems in TRNT1 deficiency can lead to vision loss.

Neurological problems are also frequent in TRNT1 deficiency. Many affected individuals have delayed development of speech and motor skills, such as sitting, standing, and walking, and some have low muscle tone (hypotonia).

Features that occur less commonly in people with TRNT1 deficiency include hearing loss caused by abnormalities of the inner ear (sensorineural hearing loss), recurrent seizures (epilepsy), and problems with the kidneys or heart.

TRNT1 deficiency encompasses what was first thought to be two separate disorders, a severe disorder called sideroblastic anemia with B-cell immunodeficiency, periodic fevers, and developmental delay (SIFD) and a milder disorder called retinitis pigmentosa with erythrocytic microcytosis (RPEM), each named for its most common features. SIFD begins in infancy, and affected individuals usually do not survive past childhood. RPEM, on the other hand, is recognized in early adulthood, and the microcytosis usually does not cause any health problems. However, it has since been recognized that some individuals have a combination of features that fall between these two ends of the severity spectrum. All of these cases are now considered part of TRNT1 deficiency.

2. Frequency

TRNT1 deficiency is a rare condition; its prevalence is unknown. Approximately 20 affected individuals have been described in the medical literature.

3. Causes

TRNT1 deficiency is caused by mutations in the *TRNT1* gene, which provides instructions for making a protein involved in the production (synthesis) of other proteins. During protein synthesis, a molecule called transfer RNA (tRNA) helps assemble protein building blocks (amino acids) into a chain that forms the protein. Each tRNA carries a specific amino acid to the growing chain. The TRNT1 protein modifies tRNAs, which allows the correct amino acid to be attached to each tRNA.

TRNT1 gene mutations lead to a shortage (deficiency) of functional TRNT1 protein. As a result, modification of tRNA molecules is impaired. Without the modification, tRNAs are thought to be less able to participate in protein synthesis. Researchers suspect that protein synthesis in cellular structures called mitochondria, which are the energy-producing centers of cells, is most strongly affected. The resulting decrease in energy production may damage cells in many body systems, leading to the varied signs and symptoms of TRNT1 deficiency. Researchers believe that mutations that cause a greater impairment of TRNT1 function lead to more severe signs and symptoms.

3.1Learn more about the gene associated with TRNT1 deficiency

- TRNT1

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

- retinitis pigmentosa with erythrocytic microcytosis
- RPEM
- sideroblastic anemia with B-cell immunodeficiency, periodic fevers, and developmental delay
- SIFD
- TRNT1 enzyme deficiency
- TRNT1-related immunodeficiency
- TRNT1-related immunodeficiency+

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