Prolidase deficiency

Description

Prolidase deficiency is a disorder that causes a wide variety of symptoms. The disorder typically becomes apparent during infancy. Affected individuals may have enlargement of the spleen (splenomegaly); in some cases, both the spleen and liver are enlarged (hepatosplenomegaly). Diarrhea, vomiting, and dehydration may also occur. People with prolidase deficiency are susceptible to severe infections of the skin or ears, or potentially life-threatening respiratory tract infections. Some individuals with prolidase deficiency have chronic lung disease.

Characteristic facial features in people with prolidase deficiency include prominent eyes that are widely spaced (hypertelorism), a high forehead, a flat bridge of the nose, and a very small lower jaw and chin (micrognathia). Affected children may experience delayed development, and about 75 percent of people with prolidase deficiency have intellectual disability that may range from mild to severe.

People with prolidase deficiency often develop skin lesions, especially on their hands, feet, lower legs, and face. The severity of the skin involvement, which usually begins during childhood, may range from a mild rash to severe skin ulcers. Skin ulcers, especially on the legs, may not heal completely, resulting in complications including infection and amputation.

The severity of symptoms in prolidase deficiency varies greatly among affected individuals. Some people with this disorder do not have any symptoms. In these individuals the condition can be detected by laboratory tests such as newborn screening tests or tests offered to relatives of affected individuals.

Frequency

Prolidase deficiency is a rare disorder. Approximately 70 individuals with this disorder have been documented in the medical literature, and researchers have estimated that the condition occurs in approximately 1 in 1 million to 1 in 2 million newborns. It is more common in certain areas in northern Israel, both among members of a religious minority called the Druze and in nearby Arab Moslem populations.

Causes

Prolidase deficiency is caused by mutations in the *PEPD* gene. This gene provides instructions for making the enzyme prolidase, also called peptidase D. Prolidase helps divide certain dipeptides, which are molecules composed of two protein building blocks (amino acids). Specifically, prolidase divides dipeptides containing the amino acids proline or hydroxyproline. By freeing these amino acids, prolidase helps make them available for use in producing proteins that the body needs.

Prolidase is also involved in the final step of the breakdown of some proteins obtained through the diet and proteins that are no longer needed in the body. Prolidase is particularly important in the breakdown of collagens, a family of proteins that are rich in proline and hydroxyproline. Collagens are an important part of the extracellular matrix, which is the lattice of proteins and other molecules outside the cell. The extracellular matrix strengthens and supports connective tissues, such as skin, bone, cartilage, tendons, and ligaments. Collagen breakdown occurs during the maintenance (remodeling) of the extracellular matrix.

PEPD gene mutations that cause prolidase deficiency result in the loss of prolidase enzyme activity. It is not well understood how the absence of prolidase activity causes the various signs and symptoms of prolidase deficiency. Researchers have suggested that accumulation of dipeptides that have not been broken down may lead to cell death. When cells die, their contents are released into the surrounding tissue, which could cause inflammation and lead to the skin problems seen in prolidase deficiency. Impaired collagen breakdown during remodeling of the extracellular matrix may also contribute to the skin problems. The intellectual disability that occurs in prolidase deficiency might result from problems in processing neuropeptides, which are brain signaling proteins that are rich in proline. It is unclear how absence of prolidase activity results in the other features of prolidase deficiency.

Learn more about the gene associated with Prolidase deficiency

- PEPD

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

- Hyperimidodipeptiduria
- Imidodipeptidase deficiency
- PD
- Peptidase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Prolidase deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268532/)

Genetic and Rare Diseases Information Center

- Prolidase deficiency (https://rarediseases.info.nih.gov/diseases/7473/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Prolidase deficiency%22)

Catalog of Genes and Diseases from OMIM

- PROLIDASE DEFICIENCY (https://omim.org/entry/170100)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28prolidase+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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