Argininosuccinic aciduria

Description

Argininosuccinic aciduria is an inherited disorder that causes ammonia to accumulate in the blood. Ammonia, which is formed when proteins are broken down in the body, is toxic if the levels become too high. The nervous system is especially sensitive to the effects of excess ammonia.

Argininosuccinic aciduria usually becomes evident in the first few days of life. An infant with argininosuccinic aciduria may be lacking in energy (lethargic) or unwilling to eat, and have a poorly controlled breathing rate or body temperature. Some babies with this disorder experience seizures or unusual body movements, or go into a coma. Complications from argininosuccinic aciduria may include developmental delay and intellectual disability. Progressive liver damage, high blood pressure (hypertension), skin lesions, and brittle hair may also be seen.

Occasionally, individuals may inherit a mild form of the disorder. These individuals can have an accumulation of ammonia in the bloodstream only during periods of illness or other stress, or mild intellectual disability or learning disabilities with no evidence of elevated ammonia levels.

Frequency

Argininosuccinic aciduria occurs in approximately 1 in 70,000 to 218,000 newborns. Most cases of this condition are detected shortly after birth by newborn screening.

Causes

Mutations in the *ASL* gene cause argininosuccinic aciduria. This condition belongs to a class of genetic diseases called urea cycle disorders because they are caused by problems with a process in the body called the urea cycle. The urea cycle is a sequence of reactions that occurs in liver cells. This cycle breaks down excess nitrogen, which is made when protein is used by the body, to make a compound called urea. Urea is removed from the body in urine. Breaking down excess nitrogen and excreting it as urea prevents it from accumulating in the body as ammonia.

The *ASL* gene provides instructions for making an enzyme called argininosuccinate lyase, which is needed for the fourth step of the urea cycle. The specific role of the argininosuccinate lyase enzyme is to start the reaction in which the amino acid arginine,

a building block of proteins, is produced from argininosuccinate, the molecule that carries the waste nitrogen collected earlier in the urea cycle. The arginine is later broken down into urea, which is excreted, and ornithine, which restarts the urea cycle.

In people with argininosuccinic aciduria, argininosuccinate lyase is dysfunctional or missing. As a result, the urea cycle cannot proceed normally, arginine is not produced, and nitrogen is not broken down efficiently. The excess nitrogen accumulates in the blood in the form of ammonia. This buildup of ammonia damages the brain and other tissues and causes neurological problems and other signs and symptoms of argininosuccinic aciduria. It is unclear how a lack of arginine contributes to the features of this condition.

Learn more about the gene associated with Argininosuccinic aciduria

- ASL

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

- Argininosuccinate lyase deficiency
- Argininosuccinic acidemia
- Argininosuccinicaciduria
- Argininosuccinyl-CoA lyase deficiency
- Arginosuccinase deficiency
- ASA
- ASAuria
- ASL deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Argininosuccinate lyase deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268547/)

Genetic and Rare Diseases Information Center

- Argininosuccinic aciduria (https://rarediseases.info.nih.gov/diseases/5843/index)

Patient Support and Advocacy Resources

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

Clinical Trials

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

Catalog of Genes and Diseases from OMIM

- ARGININOSUCCINIC ACIDURIA (https://omim.org/entry/207900)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28argininosuccinic+aciduria%5BTIAB%5D%29+OR+%28argininosuccinate+lyase+deficiency%5BTIAB%5D%29+OR+%28asl+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2160+days%22%5Bdp%5D)

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- National Organization for Rare Disorders (NORD) (https://rarediseases.org/rare-diseases/argininosuccinic-aciduria/)
- National Urea Cycle Disorders Foundation (http://www.nucdf.org/)
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Last updated March 1, 2020