Aspartylglucosaminuria

Description

Aspartylglucosaminuria is a condition that primarily affects mental functioning and movement. This conditions worsens over time. Infants with aspartylglucosaminuria appear healthy at birth, and development is typically normal throughout early childhood. Around the age of 2 or 3, affected children usually begin to have delayed speech, mild intellectual disability, and problems coordinating movements. Other features that develop in childhood include respiratory infections, a protrusion of organs through gaps in muscles (hernia), and a growth spurt resulting in a large head size (macrocephaly).

Intellectual disability and movement problems worsen in adolescence. Most people with this disorder lose much of the speech they have learned, and affected adults usually have only a few words in their vocabulary. Adults with aspartylglucosaminuria often have psychological disorders and may develop seizures.

People with aspartylglucosaminuria may also have bones that become progressively weak and prone to fracture (osteoporosis), an unusually large range of joint movement (hypermobility), and loose skin. Affected individuals tend to have a characteristic facial appearance that includes widely spaced eyes (ocular hypertelorism), small ears, and full lips. The nose is short and broad and the face is usually square-shaped. They often have poor oral health, including infections and gum disease (gingivitis). Children with this condition may be tall for their age, but lack of a growth spurt in puberty typically causes adults to be short with a small head size (microcephaly). Individuals with aspartylglucosaminuria usually survive into mid-adulthood.

Frequency

In Finland, it is estimated that 1 to 3 individuals are born with aspartylglucosaminuria each year. This condition is less common outside of Finland, but the incidence is unknown.

Causes

Variants (also known as mutations) in the *AGA* gene cause aspartylglucosaminuria. The *AGA* gene provides instructions for producing an enzyme called aspartylglucosaminidase. This enzyme is active in lysosomes, which are structures inside cells that act as recycling centers. Within lysosomes, the enzyme helps break

down complex chains of sugar molecules (oligosaccharides) attached to certain proteins (glycoproteins).

AGA gene variants result in a lack (deficiency) of the aspartylglucosaminidase enzyme in lysosomes, preventing the normal breakdown of glycoproteins. As a result, glycoproteins can build up within the lysosomes. Excess glycoproteins disrupt the normal functions of the cell and can result in cell death. A buildup of glycoproteins seems to particularly affect nerve cells in the brain; loss of these cells causes many of the signs and symptoms of aspartylglucosaminuria.

Learn more about the gene associated with Aspartylglucosaminuria

- AGA

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have variants. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- AGA deficiency
- Aspartylglucosamidase deficiency
- Aspartylglucosaminidase deficiency
- Aspartylglycosaminuria
- Glycosylasparaginase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Aspartylglucosaminuria (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268225/)

Genetic and Rare Diseases Information Center

- Aspartylglucosaminuria (https://rarediseases.info.nih.gov/diseases/5854/index)

Patient Support and Advocacy Resources

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

Clinical Trials

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

Catalog of Genes and Diseases from OMIM

- ASPARTYLGLUCOSAMINURIA; AGU (https://omim.org/entry/208400)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=(aspartylglucosaminuria%5BTIAB%5D)+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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