Aspartylglucosaminuria

Subjects: Genetics & Heredity

Contributor: Catherine Yang

Aspartylglucosaminuria is a condition that causes a progressive decline in mental functioning.

genetic conditions

1. Introduction

Infants with aspartylglucosaminuria appear healthy at birth, and development is typically normal throughout early childhood. The first sign of this condition, evident around the age of 2 or 3, is usually delayed speech. Mild intellectual disability then becomes apparent, and learning occurs at a slowed pace. Intellectual disability progressively worsens 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 may develop seizures or problems with movement.

People with this condition 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. Children with this condition may be tall for their age, but lack of a growth spurt in puberty typically causes adults to be short. Affected children also tend to have frequent upper respiratory infections. Individuals with aspartylglucosaminuria usually survive into mid-adulthood.

2. Frequency

Aspartylglucosaminuria is estimated to affect 1 in 18,500 people in Finland. This condition is less common outside of Finland, but the incidence is unknown.

3. Causes

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 complexes of sugar molecules (oligosaccharides) attached to certain proteins (glycoproteins).

AGA gene mutations result in the absence or shortage 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 destruction of the cell. 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.

3.1. The gene associated with Aspartylglucosaminuria

- AGA

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

- AGA deficiency
- aspartylglucosamidase deficiency
- Aspartylglucosaminidase deficiency
- aspartylglycosaminuria
- glycosylasparaginase deficiency

References

1. Aronson NN Jr. Aspartylglycosaminuria: biochemistry and molecular biology.Biochim Biophys Acta. 1999 Oct 8;1455(2-3):139-54. Review.
2. Arvio MA, Peippo MM, Arvio PJ, Kääriäinen HA. Dysmorphic facial features inaspartylglucosaminuria patients and carriers. Clin Dysmorphol. 2004Jan;13(1):11-5.
3. Saarela J, Laine M, Oinonen C, von Schantz C, Jalanko A, Rouvinen J, Peltonen L. Molecular pathogenesis of a disease: structural consequences ofaspartylglucosaminuria mutations. Hum Mol Genet. 2001 Apr 15;10(9):983-95.