GM2-gangliosidosis, AB variant

Description

GM2-gangliosidosis, AB variant is a rare inherited disorder that progressively destroys nerve cells (neurons) in the brain and spinal cord.

Signs and symptoms of the AB variant become apparent in infancy. Infants with this disorder typically appear normal until the age of 3 to 6 months, when their development slows and muscles used for movement weaken. Affected infants lose motor skills such as turning over, sitting, and crawling. They also develop an exaggerated startle reaction to loud noises. As the disease progresses, children with the AB variant experience seizures, vision and hearing loss, intellectual disability, and paralysis. An eye abnormality called a cherry-red spot, which can be identified with an eye examination, is characteristic of this disorder. Children with the AB variant usually live only into early childhood.

Frequency

The AB variant is extremely rare; only a few cases have been reported worldwide.

Causes

Mutations in the *GM2A* gene cause GM2-gangliosidosis, AB variant. The *GM2A* gene provides instructions for making a protein called the GM2 ganglioside activator. This protein is required for the normal function of an enzyme called beta-hexosaminidase A, which plays a critical role in the brain and spinal cord. Beta-hexosaminidase A and the GM2 ganglioside activator protein work together in lysosomes, which are structures in cells that break down toxic substances and act as recycling centers. Within lysosomes, the activator protein binds to a fatty substance called GM2 ganglioside and presents it to beta-hexosaminidase A to be broken down.

Mutations in the *GM2A* gene disrupt the activity of the GM2 ganglioside activator, which prevents beta-hexosaminidase A from breaking down GM2 ganglioside. As a result, this substance accumulates to toxic levels, particularly in neurons in the brain and spinal cord. Progressive damage caused by the buildup of GM2 ganglioside leads to the destruction of these neurons, which causes the signs and symptoms of the AB variant.

Because the AB variant impairs the function of a lysosomal enzyme and involves the buildup of GM2 ganglioside, this condition is sometimes referred to as a lysosomal

storage disorder or a GM2-gangliosidosis.

Learn more about the gene associated with GM2-gangliosidosis, AB variant

- GM2A

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

- AB variant
- Activator deficiency/GM2 gangliosidosis
- Activator-deficient Tay-Sachs disease
- GM2 activator deficiency disease
- GM2 gangliosidosis, type AB
- Hexosaminidase activator deficiency
- Tay-Sachs disease, AB variant

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Tay-Sachs disease, variant AB (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268275/)

Genetic and Rare Diseases Information Center

- GM2-gangliosidosis, B, B1, AB variant (https://rarediseases.info.nih.gov/diseases/2522/gm2-gangliosidosis-b-b1-ab-variant)

Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)
- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22GM2-gangliosidosis, A B variant%22)

Catalog of Genes and Diseases from OMIM

- GM2-GANGLIOSIDOSIS, AB VARIANT (https://omim.org/entry/272750)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28GM2+ganglioside%29+OR+%28GM2-gangliosidosis%29+OR+%28tay-sachs%5BTIAB%5D%29+OR+%28GM2A%5BTIAB%5D%29%29+AND+%28%28ab+variant%29+OR+%28variant+AB%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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