GM2 activator deficiency

Description

GM2 activator deficiency (sometimes called GM2 gangliosidosis, AB variant) is a rare inherited disorder that causes progressive brain injury.

Most individuals with GM2 activator deficiency have the acute infantile form of the disease. Signs and symptoms of acute infantile GM2 activator deficiency typically appear between the ages of 4 and 12 months, when development slows and the muscles used for movement weaken. Infants with acute infantile GM2 activator deficiency stop achieving normal developmental milestones and eventually lose previously acquired skills such as turning over, sitting, and crawling. These infants also develop an exaggerated startle reaction to loud noises. Over time, infants with acute infantile GM2 activator deficiency typically experience seizures, vision loss, and intellectual disabilites. They eventually become unable to respond to their environment. An eye abnormality called a cherry-red spot, which can be identified with an eye examination, is characteristic of the infantile form of this disorder. Infants with acute infantile GM2 activator deficiency may survive into early childhood.

Some people with GM2 activator deficiency may develop milder and more variable signs and symptoms later in life. Due to the rarity of this condition, the full spectrum of the late-onset presentation has not been clearly defined.

Frequency

GM2 activator deficiency is extremely rare; fewer than 30 cases have been reported worldwide.

Causes

Variants (also called mutations) in the *GM2A* gene cause GM2 activator deficiency. The *GM2A* gene provides instructions for making a protein called the ganglioside GM2 activator. This protein is required for the normal function of an enzyme called beta-hexosaminidase A. Beta-hexosaminidase A and the ganglioside GM2 activator protein work together in lysosomes, which are compartments in the cell that digest and recycle different types of molecules. Within lysosomes, the activator protein binds to a fatty substance called GM2 ganglioside and presents it to beta-hexosaminidase A to be broken down.

Variants in the *GM2A* gene disrupt the activity of the ganglioside GM2 activator, which prevents beta-hexosaminidase A from breaking down GM2 ganglioside. As a result, this substance accumulates in the body, particularly in the central nervous system. Over time, damage caused by the buildup of GM2 ganglioside leads to the typical signs and symptoms of GM2 activator deficiency.

Because GM2 activator deficiency 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 activator deficiency

- GM2A

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell must have a variant to cause the disorder. 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

- GM2 gangliosidosis, AB variant
- 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/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22GM2 activator deficiency%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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