Generalized Gangliosidoses

National Institute of Neurological Disorders and Stroke (NINDS)

Source

National Institute of Neurological Disorders and Stroke (NINDS). Generalized Gangliosidoses Information Page.

The gangliosidoses are a group of inherited metabolic diseases caused by a deficiency of the different proteins needed to break down fatty substances called lipids. Excess buildup of these fatty materials (oils, waxes, steroids, and other compounds) can cause permanent damage in the cells and tissues in the brain and nervous systems, particularly in nerve cells. There are two distinct groups of the gangliosidoses, which affect males and females equally.

The GM1 gangliosidoses are caused by a deficiency of the enzyme beta-galactosidase and has 3 clinical subtypes:

- Early infantile GM1 gangliosidosis (the most severe subtype, with onset shortly after birth) has symptoms that may include nerve function degeneration, seizures, liver and spleen enlargement, coarsening of facial features, skeletal irregularities, joint stiffness, distended abdomen, muscle weakness, exaggerated startle response, and problems with gait. About half of affected persons develop cherry-red spots in the eye. Children may be deaf and blind by age 1.
- Onset of late infantile GM1 gangliosidosis typically between ages 1 and 3 years. Signs include an inability to control movement, seizures, dementia, and difficulties with speech.
- Adult GM1 gangliosidosis strikes between ages 3 and 30, with symptoms that include the wasting away of muscles, cloudiness in the corneas, and dystonia (sustained moscle contractions that case twisting and repetitive movements or abnormal postures). Non-cancerous skin blemishes may develop on the lower part of the trunk of the body. Adult GM1 is usually less severe and progresses more slowly than other forms of the disorder.

The GM2 gangliosidoses include Tay-Sachs disease and its more severe form, called Sandhoff disease, both of which result from a deficiency of the enzyme beta-

hexosaminidase. Symptoms begin by age 6 months and include progressive mental deterioration, cherry-red spots in the retina, marked startle reflex, and seizures. Children with Tay-Sachs may also have dementia, progressive loss of hearing, some paralysis, and difficulty in swallowing that may require a feeding tube. A rarer form of the disorder, which occurs in individuals in their twenties and early thirties, is characterized by an unsteady gait and progressive neurological deterioration. Additional signs of Sandhoff disease include weakness in nerve signaling that causes muscles to contract, early blindness, spasticity, muscle contractions, an abnormally enlarged head, and an enlarged liver and spleen.