Tay Sachs Disease

Synonyms of Tay Sachs Disease

- Amaurotic Familial Idiocy
- Amaurotic Familial Infantile Idiocy
- Cerebromacular Degeneration
- GM2 Gangliosidosis, Type 1
- Hexoaminidase Alpha-Subunit Deficiency (Variant B)
- Infantile Cerebral Ganglioside
- Infantile Sipoidosis GM-2 Gangliosideos (Type S)
- Lipidosis, ganglioside, infantile
- Sphingolipidosis, Tay-Sachs

General Discussion

Tay-Sachs disease is a rare, neurodegenerative disorder in which deficiency of an enzyme (hexosaminidase A) results in excessive accumulation of certain fats (lipids) known as gangliosides in the brain and nerve cells. This abnormal accumulation of gangliosides leads to progressive dysfunction of the central nervous system. This disorder is categorized as a lysosomal storage disease. Lysosomes are the major digestive units in cells. Enzymes within lysosomes break down or "digest" nutrients, including certain complex carbohydrates and fats.

Symptoms associated with Tay-Sachs disease may include an exaggerated startle response to sudden noises, listlessness, loss of previously acquired skills (i.e., psychomotor regression), and severely diminished muscle tone (hypotonia). With disease progression, affected infants and children may develop cherry-red spots within the middle layer of the eyes, gradual loss of vision, and deafness, increasing muscle stiffness and restricted movements (spasticity), eventual paralysis, uncontrolled electrical disturbances in the brain (seizures), and deterioration of cognitive processes (dementia). The classical form of Tay-Sachs disease occurs during infancy; an adult form (late-onset Tay-Sachs disease) may occur anytime from adolescence to the mid 30's.

Tay-Sachs disease is inherited as an autosomal recessive trait. The disorder results from changes (mutations) of a gene known as the HEXA gene, which regulates production of the hexosaminidase A enzyme. The HEXA gene has been mapped to the long arm (q) of chromosome 15 (15q23-q24).

Signs & Symptoms

Two main forms of Tay-Sachs disease exist: the classic or infantile form and the late-onset or adult form. In individuals with infantile Tay-Sachs disease, symptoms typically first appear between three and five months of age. In individuals with the late-onset form, symptoms may become apparent anytime from adolescence through the mid 30s.

Infantile Tay-Sachs Disease The infantile form of Tay-Sachs disease is characterized by an almost complete lack of hexosaminidase A enzyme activity. The disorder often progresses rapidly, resulting in significant mental and physical
deterioration.

Initial symptoms associated with Tay-Sachs disease include an exaggerated startle response to sudden noises (acoustic stimuli), decreased eye contact, listlessness, and irritability.

As affected infants age, they may experience slow growth, muscle weakness, diminished muscle tone (hypotonia), and diminished mental functioning. Affected infants may also exhibit gradual loss of vision, involuntary muscle spasms that result in slow, stiff movements (spasticity), and the loss of previously acquired skills (i.e., psychomotor regression) such as crawling or sitting up.

A characteristic symptom of Tay-Sachs disease is the development of cherry red spots in the eyes. This condition occurs when the macular cells of the eye deteriorate, exposing the underlying choroid. The choroid is the middle layer of the eye that consists of blood vessels that supply blood to the retina. This characteristic finding occurs in approximately 90 percent of individuals with Tay-Sachs disease.

As affected infants age, more serious complications may develop, including seizures; inability to swallow; deafness; confusion, disorientation, and/or deterioration of intellectual abilities (dementia); paralysis; and continued loss of vision, potentially resulting in blindness. Eventually, infants may become unresponsive to their environment and surroundings. By three to five years of age, life-threatening complications may occur.

Late-Onset Tay-Sachs Disease The symptoms associated with late-onset Tay-Sachs disease vary greatly from case to case. Individuals with this form of Tay-Sachs disease will not have all of the symptoms listed below. The disorder progresses much slower than the infantile form of Tay-Sachs disease.

Initial symptoms associated with late-onset Tay-Sachs disease may include clumsiness, mood alterations, and muscle weakness. As affected individuals age, they may exhibit tremors, muscle twitching (fasculations), slurred speech, an inability to coordinate voluntary movements (ataxia), and a condition known as dystonia. Dystonia is a group of disorders characterized by involuntary muscle contractions that may force certain body parts into unusual, and sometimes painful, movements and positions.

As late-onset Tay-Sachs disease progresses, affected individuals may experience problems with walking, running, and other similar activities. In severe cases, affected individuals may eventually need assistive devices such as braces or a wheelchair.

In some cases, affected individuals may experience mental deterioration, memory problems, and behavioral changes including short attention spans and personality changes. In approximately 40 percent of cases, psychotic episodes (e.g., loss of contact with reality) and depression may be present.

**Causes**

Tay-Sachs disease is inherited as an autosomal recessive trait. Human traits, including the classic genetic diseases, are the product of the interaction of two genes for that condition, one received from the father and one from the mother.

In recessive disorders, the condition does not appear unless a person inherits the same defective gene for the same trait from each parent. If an individual receives one normal gene and one gene for the disease, the person will be a carrier for the disease but usually will not show symptoms. The risk of transmitting the disease to the children of a couple, both of whom are carriers for a recessive disorder, is 25 percent. Fifty percent of their children risk being carriers of the disease but generally will not show symptoms of the disorder. Twenty-five percent of their children may receive both normal genes, one from each parent, and will be genetically normal (for that particular trait). The risk is the same for each pregnancy.

Researchers have determined that the gene for Tay-Sachs disease is located on the long arm (q) of chromosome 15 (15q23-q24). Chromosomes are found in the nucleus of all body cells. They carry the genetic characteristics of
Pairs of human chromosomes are numbered from 1 through 22, with an unequal 23rd pair of X and Y chromosomes for males and two X chromosomes for females. Each chromosome has a short arm designated as “p” and a long arm identified by the letter “q”. Chromosomes are further subdivided into bands that are numbered.

The gene responsible for Tay-Sachs disease, known as the HEXA gene, regulates the production of the enzyme hexosaminidase A. More than 80 different mutations of the HEXA gene have been identified in individuals with the disease. Inheriting two mutated copies of the HEXA gene (homozygotes) causes deficiency of the hexosaminidase A enzyme, which is necessary to breakdown fatty substance (lipid) known as GM2-ganglioside within cells of the body. Failure to breakdown GM2-ganglioside results in its abnormal accumulation in brain and nerve cells eventually resulting in the progressive deterioration of the central nervous system.

In infantile Tay-Sachs disease, there is an almost complete lack of hexosaminidase A. In late-onset Tay-Sachs disease, there is deficiency of hexosaminidase A enzyme activity. Because there is some enzyme activity, the disorder is less severe and progresses much slower than infantile Tay-Sachs disease. The exact amount of enzyme activity in late-onset Tay-Sach disease varies greatly from case to case. Consequently, the age of onset, severity, specific symptoms, and rate of progression of late-onset Tay-Sachs disease also vary greatly from case to case.

Affected Populations

Tay-Sachs disease affects males and females in equal numbers. Tay-Sachs disease occurs with greater frequency among Ashkenazic Jews of Eastern or Central European descent. Approximately one in 25-30 Ashkenazi Jews carries the gene for Tay-Sachs disease. In addition, one in 300 individuals of non-Jewish heritage is a carrier. In the Jewish population, about one in 3,900 live births is affected. The disease has also been reported in some individuals of Italian, Irish Catholic, and non-Jewish French Canadian descent, especially those living in the Cajun community of Louisiana and the southeastern Quebec. In the general population, approximately one in 112,000 live births is affected by Tay-Sachs disease.

Fewer than 100 cases of late-onset Tay-Sachs disease have been reported in the medical literature. However, rare disorders like late-onset Tay-Sachs disease often go unrecognized. These disorders are under-diagnosed, making it difficult to determine the true frequency of such disorders in the general population.

The prevalence of late-onset Tay-Sachs disease has been estimated at one in 67,000 in the Jewish population of the United States and one in 14,000 in Israel.

Related Disorders

Symptoms of the following disorders can be similar to those of Tay-Sachs disease. Comparisons may be useful for a differential diagnosis:

Sandhoff disease is a rare inherited lipid storage disorder resulting in the progressive deterioration of the central nervous system (neurodegenerative disorder). A deficiency of the enzymes hexosaminidase A and B results in the accumulation of certain fats (lipids) in the brain and other organs of the body. Symptoms in infants may include feeding problems, general weakness, and an exaggerated startle reflex in response to sudden loud noise. Motor delays and mental impairment are progressive. Sandhoff disease is a severe form of Tay-Sachs disease and is not limited to any particular ethnic group. Sandhoff disease is inherited as an autosomal recessive trait. (For more information on this disorder, choose “Sandhoff” as your search term in the Rare Disease Database.)

Leigh’s disease is a rare inherited neurometabolic disorder. It is characterized by the degeneration of the central nervous system (i.e., brain, spinal cord, and optic nerve). The symptoms of Leigh’s disease usually begin between the ages of three months and two years. Symptoms are associated with progressive neurological deterioration and may include loss of previously acquired motor skills, loss of appetite, vomiting, irritability, and/or seizure activity. As Leigh’s disease progresses, symptoms may also include generalized weakness, lack of muscle tone, and episodes
of lactic acidosis, which may lead to impairment of respiratory and kidney function. In most cases, Leigh’s disease is inherited as an autosomal recessive genetic trait. However, autosomal dominant, X-linked recessive, and mitochondrial inheritance have also been noted. There appear to be several different types of genetically determined enzyme defects that can cause Leigh’s disease. (For more information on this disorder, choose “Leigh’s” as your search term in the Rare Disease Database.)

The neuronal ceroid lipofuscinoses (NCL) are a group of progressive degenerative neurometabolic diseases. These diseases share certain similar symptoms and are distinguished in part by the age at which such symptoms appear. Two forms occur during infancy: Santavuori disease (infantile type) and Jansky-Bielschowsky disease (late infantile type). These disorders are characterized by a delay in the acquisition of skills that require the coordination of mental and muscular activity (psychomotor retardation). In addition, affected infants begin to lose previously acquired physical and mental abilities (developmental regression). Affected infants may then experience a variety of symptoms including episodes of uncontrolled electrical disturbances in the brain (seizures), impaired ability to coordinate voluntary movements (cerebellar ataxia), abnormally diminished muscle tone (hypotonia), and repeated, brief, shock-like muscle spasms of the arms, legs, or entire body (myoclonic seizures). Affected infants also experience progressive visual impairment due to deterioration of the nerves of the eyes (optic nerves) that transmit impulses from the retina to the brain (optic atrophy). Neurological impairment progresses and may result in an inability to move voluntarily (immobility), sudden involuntary muscle spasms (spasticity), and lack of response to stimuli in the environment. Life-threatening complications may develop by the end of the first decade. (For more information, choose the specific disorder name as your search term in the Rare Disease Database.)

Symptoms of the following disorders can be similar to those of late-onset Tay-Sachs disease. Comparisons may be useful for a differential diagnosis:

Kugelberg-Welander syndrome, also known as spinal muscular atrophy type III, is a rare inherited disorder. Major symptoms may include wasting and weakness in the muscles of the arms and legs, twitching, clumsiness in walking, and eventual loss of reflexes. Kugelberg-Welander syndrome is not apparent at birth; it usually appears during the first 10 to 20 years of life. (For more information on this disorder, choose “Kugelberg-Welander” as your search term in the Rare Disease Database.)

Amyotrophic lateral sclerosis (ALS) is characterized by slight muscle weakness, clumsy hand movements, and/or difficulty performing tasks that require delicate movements of the fingers and/or hands. Muscular weakness in the legs may cause tripping and falling. People with ALS may have difficulty swallowing (dysphagia), and speech may be slowed. Additional symptoms of this disorder include progressive weakness of the lips and impairment and/or loss of function of the tongue, mouth, and/or voice box (bulbar symptoms). Leg cramps may occur during the night, most frequently in the calf and/or thigh muscles. ALS may progress quickly or slowly, and gradually additional muscles become involved. Individuals with ALS may also exhibit uncontrolled twitching of muscles (fasciculations), stiffness in the legs, and/or coughing. As the ability to move becomes progressively impaired, people with this disease are at increased risk for respiratory failure. The exact cause of ALS is unknown. (For more information on this disorder, choose “Amyotrophic Lateral Sclerosis” as your search term in the Rare Disease Database.)

Diagnosis

The diagnosis of Tay-Sachs disease may be confirmed by a thorough clinical evaluation and specialized tests, such as blood tests that measure the levels of hexosaminidase A in the body.

In some cases, it is possible that a diagnosis of Tay-Sachs disease may be suspected before birth (prenatally) based upon specialized tests, such as amniocentesis and chorionic villus sampling (CVS). During amniocentesis, a sample of fluid that surrounds the developing fetus is removed, while CVS involves the removal of tissue samples from a portion of the placenta. These samples are studied to determine whether hexosaminidase A is present or, as in cases of Tay-Sachs disease, absent or present in greatly reduced levels.

Blood tests can determine whether individuals are carriers for Tay-Sachs disease (i.e., they have one copy of the
disease gene). Relatives of individuals with Tay-Sachs disease should be tested to determine whether they are carriers of the disease gene.

Quest Diagnostics Incorporated announced in July 2000 that it was voluntarily offering free retesting for certain individuals who received "non-carrier" results from Tay-Sachs testing performed between November 1992 and the end of 1998. Recent analysis of statistical data suggests that some people who received results in the low end of the non-carrier range should be retested. However, it is expected that approximately 99 percent of those retested will remain in the non-carrier category. People who received testing performed by MetPath, MetWest, Corning Clinical Laboratories, or Quest Diagnostics from 1992 through 1998 should speak to the doctor who ordered their original test or call toll-free (877) 806-8175 for information.

**Standard Therapies**

**Treatment**

There is no specific treatment for Tay-Sachs disease. Treatment is directed toward the specific symptoms that are apparent in each individual. Treatment may require the coordinated efforts of a team of specialists. Pediatricians, speech pathologists, specialists who assess and treat hearing problems (audiologists), eye specialists, and other health care professionals may need to systematically and comprehensively plan an affected child's treatment.

Anticonvulsants may be used to treat seizures associated with some cases of Tay-Sachs disease, but may not be effective in all cases. Genetic counseling may be of benefit for affected individuals and their families. Additional treatment is symptomatic and supportive.

**Investigational Therapies**

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov. All studies receiving U.S. government funding, and some supported by private industry, are posted on this government website.

For information about clinical trials being conducted at the National Institutes of Health (NIH) in Bethesda, MD, contact the NIH Patient Recruitment Office:

Tollfree: (800) 411-1222
TTY: (866) 411-1010
Email: prpl@cc.nih.gov

For information about clinical trials sponsored by private sources, contact:

www.centerwatch.com

**Resources**

Please note that some of these organizations may provide information concerning certain conditions potentially associated with this disorder.

**NORD Member Organizations**

- **CLIMB (Children Living with Inherited Metabolic Diseases)**
  Climb Building
  176 Nantwich Road
  Crewe, CW2 6BG United Kingdom
  Phone: 4408452412173
Email: enquiries@climb.org.uk  
Website: http://www.CLIMB.org.uk  

- **National Tay-Sachs and Allied Diseases Association, Inc.**  
  2001 Beacon Street  
  204  
  Brookline, MA 02146-4227 USA  
  Phone: (617) 277-4463  
  Toll-free: (800) 906-8723  
  Email: info@ntsad.org  
  Website: http://www.NTSAD.org  

**Other Organizations**  

- **Canadian Society for Mucopolysaccharide and Related Diseases, Inc.**  
  #218-2055 Commercial Drive  
  Vancouver, BC V5N 0C7 Canada  
  Phone: (604) 924-5130  
  Toll-free: (800) 667-1846  
  Email: info@mpssociety.ca  
  Website: http://www.mpssociety.ca  

- **Genetic and Rare Diseases (GARD) Information Center**  
  PO Box 8126  
  Gaithersburg, MD 20898-8126  
  Phone: (301) 251-4925  
  Toll-free: (888) 205-2311  
  Website: http://rarediseases.info.nih.gov/GARD/  

- **Hide & Seek Foundation for Lysosomal Disease Research**  
  6475 East Pacific Coast Highway Suite 466  
  Long Beach, CA 90803  
  Phone: (877) 621-1122  
  Email: info@hideandseek.org  
  Website: http://www.hideandseek.org  

- **Instituto de Errores Innatos del Metabolismo**  
  Pontificia Universidad Javeriana Ed. Jesús Emilio Ramírez (53) Laboratorios 305A - 303  
  Bogota, Colombia  
  Phone: (571) 320-8320  
  Email: abarrera@javeriana.edu.co  
  Website: http://www.javeriana.edu.co/ieim/programas_ieim.htm  

- **Let Them Hear Foundation**  
  1900 University Avenue, Suite 101  
  East Palo Alto, CA 94303  
  Phone: (650) 462-3174  
  Email: info@letthemhear.org  
  Website: http://www.letthemhear.org  

- **March of Dimes**  
  1275 Mamaroneck Avenue
Tay Sachs Disease - NORD (National Organization for Rare Disorders)

White Plains, NY 10605
Phone: (914) 997-4488
Email: AskUs@marchofdimes.org or preguntas@nacersano.org
Website: http://www.marchofdimes.org and nacersano.org

- NIH/National Institute of Child Health and Human Development
  31 Center Dr
  Building 31, Room 2A32
  Bethesda, MD 20892
  Toll-free: (800) 370-2943
  Email: NICHDInformationResourceCenter@mail.nih.gov
  Website: http://www.nichd.nih.gov/

- NIH/National Institute of Neurological Disorders and Stroke
  P.O. Box 5801
  Bethesda, MD 20824
  Phone: (301) 496-5751
  Toll-free: (800) 352-9424
  Website: http://www.ninds.nih.gov/

References

TEXTBOOKS


JOURNAL ARTICLES


FROM THE INTERNET


Years Published

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