A Review on Tay-Sachs Disease

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Abstract:

Tay-Sachs disease (TSD) is a fatal genetic disorder that causes progressive destruction of the nervous system. It also affects the mental and physical abilities of that being around six month of age. TSD most commonly occurs in children that causes the slow destruction of the central nervous system. It occurs when more quantities of cell membrane components called gangliosides, accumulate in the brain’s nerve cells. This occurs due to the absence of an important enzyme called Hexosaminidase-A (HEX-A).

1. Introduction:

Tay - Sachs disease¹⁻² is an autosomal recessive disease caused by a deficiency of β-Hexosaminidase A, the lysosomal enzyme that normally degrades GM2 ganglioside. As a result, GM2 ganglioside accumulates in the lysosomes of nerve cells. Tay-Sachs disease commonly refers to the classic infantile form of GM2 ganglioside (also called type 1 GM2 gangliosidosis), wherein β-hexosaminidase A is virtually absent, juvenile and late-onset forms also occur when there is residual enzymatic activity³⁻⁸. The Hex-A gene provides instructions for making a subunit of an enzyme called beta-Hexosaminidase A (Beta-Hex A) which plays a critical role in the brain and spinal cord. This enzyme is found in lysosomes (organelles that break down toxic substances). Within lysosomes, Beta-Hex A forms a part of a complex that breaks down GM2 ganglioside⁴. TSD occurs when harmful quantities of gangliosides (Component of cell membrane) accumulate in the brain’s nerve cells. TSD has high incidence among Ashkenazi Jews⁵, Cajuns and French Canadians. European and Russian (Ashkenazi) Jews are at high risk for developing Tay-Sachs. 1 out of every 3,600 babies born to Ashkenazi Jewish couples has the
disease. 1 in 27 are carriers in the US. Irish Americans are at moderate risk, with 1 in 50 being carriers. French Canadians and the Pennsylvanian Dutch are also mentionable ethnicities that are at higher risks for Tay-Sachs, whereas in the general population 1 in 250 people are carriers.

High prevalence of GM2 gangliosidosis (12 cases of Tay-Sachs disease (infantile, 9; late, 3) has been reported in children with neurological disorders from the southern region of India, consanguinity is more common. Higher incidence of Tay-Sachs disease was observed in the SC community of Gujarat. The mutation p.E462V was found in six unrelated families from Gujarat indicating a founder mutation in HEXA gene.

History:

A British ophthalmologist, Warren Tay in 1881 described a patient with a cherry-red spot on the retina of the eye and a New York neurologist, Bernard Sachs gave the first description of the cellular changes in this disease. So it is named after these two physicians as Tay-Sachs disease.

Types:

The form is determined by the age of the individual when symptoms appear.

1. Classic Infantile Tay-Sachs symptoms appear around 6 months of age. It may be noticed in reduction in vision and the baby does not show normal startle responses. Children gradually regress, loss of coordination, inability to swallow and difficulty breathing, losing skills one by one, unable to crawl, turn over, sit or reach out.

2. Juvenile Tay-Sachs: Symptoms typically appear between ages 2 and 5, but can occur anytime during childhood. Lack of coordination or clumsiness and muscle weakness, exhibit slurred speech, swallowing difficulties and muscle cramps, losing their ability to walk, eat on their own and communicate, prone to respiratory infections and often experience recurrent bouts of pneumonia. Many have seizures.

3. Late Onset Tay-Sachs: Symptoms typically appear in adolescence or early adulthood, but can appear later include clumsiness and muscle weakness in the legs, mental health symptoms.

Symptoms:

Begin not before 6 months of age. Child shows loss of motor skills, loss of mental functions. The child becomes blind caused by lipid-laden ganglion cells which show “cherry-red” spot on eye, deaf, paralyzed, mentally retarded and non-responsive.

Clinical Importance:

Affected infants lose motor skills such as turning over, sitting and crawling. They also develop an exaggerated startle reaction to loud noises. As disease progress the children with TSD experience seizures, vision and hearing loss, intellectual disability and paralysis. An eye abnormality called Cherry-Red spot can also be identified using an eye examination.

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. Hexosaminidase A is reduced in people with Tay-Sachs disease, and absent or nearly absent in the infantile form.
Blood tests can determine whether individuals are carriers for Tay-Sachs disease. In some instances, 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).

**Treatment:**

Treatment is directed toward the specific symptoms that are apparent in each individual. Treatment may require the coordinated efforts of a team of specialists. Paediatricians, neurologists, 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. Genetic counselling may be of benefit for affected individuals and their families. Psychosocial support is recommended for the entire family.

Research is ongoing to develop enzyme replacement therapy (ERT) for Tay-Sachs disease. Enzyme replacement therapy involves replacing a missing enzyme in individuals who are deficient or lack a particular enzyme. Synthetic versions of missing enzymes have been developed and used to treat individuals with other lysosomal storage diseases including Hurler syndrome, Fabry syndrome, and Gaucher disease. However, ERT has not proven successful in people with Tay-Sachs disease. One issue is the inability to find a way for the replacement enzyme to cross the blood-brain barrier.

**Prognosis:**

Usually death of the child occurs by the age of 5. On the rare cases of Late onset of TSD, the children’s death occurs as soon as they reach their Teens. Hence provision of symptomatic care ensures the easy living of the children diagnosed with TSD.

**2. Conclusions:**

TSD is an autosomal recessive neurodegenerative disorder caused by the deficiency of the lysosomal enzyme β-hexosaminidase A (HexA), which result in the accumulation of GM2 gangliosides mainly in neurons. There is no effective treatment approved to treat TSD. Though, various methods have been investigated to restore the function of β-hexosaminidase A. Gene therapies to restore enzymes in patients could offer treatment for these diseases but more studies and research are needed as they currently have multiple limitations. Concentration to the importance of conducting research on this disease in order to provide timely treatment and achieve good prognosis for patients is considered necessary.
limitations. Gathering existing information on the pathology allows emphasizing the importance of conducting research on this disease in order to provide timely treatment and achieve good prognosis for patients.

3. Bibliography:
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