**Tay - Sachs disease**

Tay-Sachs disease (TSD) is a disorder of the nervous system that influences the functions of the brain and the neurons in the body. Genetic inheritance influences the pattern of occurrence of TSD that presents with a progressive loss of neurological functions such as hypotonia, listlessness, and startle reaction to noises (National Organization for Rare Disorders [NORD], 2017). TSD is a significant health challenge owing to its prevalence and medical impacts on the population. For instance, one in every 3,600 live births among Jewish individuals of the Ashkenazi descent have TSD, and the disease occurs equally in males and females at a prevalence rate of 1 in every 250-300 people in the general population (NORD, 2017).

**Etiology and Risk Factors**

TSD occurs as a result of consequential gene mutations since it is a genetic condition affecting the entire nervous system. Particularly, the autosomal recessive acquisition of the loss of function mutation of the gene *HEXA* that regulates the production of hexosaminidase A enzyme is the cause of TSD (Dersh, Iwamoto, & Argon, 2016). Individuals with mutations of both alleles of the *HEXA* gene will develop the manifestations of TSD following the failure to compensate for the lost genetic information. In this case, the body will have insufficient hexosaminidase A enzyme to break down GM2-gangliosides within the neuron cells (NORD, 2017).

Additionally, the risks for acquiring and developing the signs and symptoms of TSD depends on an individual’s age, gender, environmental, genetic, and lifestyle. Young children of either male or female gender from TSD carrier parents have 25% and 50% risks for developing TSD and being a carrier, respectively (NORD, 2017). Therefore, the risks are young age and parents with TSD or carriers while gender does not influence its occurrence. Even though the environment and lifestyle do not influence the pattern of inheritance of TSD, this disease has a high frequency among Ashkenazi Jews from Central and Eastern Europe (NORD, 2017). Therefore, the best preventive strategy would be screening couples during family counseling to avoid the risks to the children of both carrier parents.

**Pathophysiological Processes**

Patients with TSD develop neurological abnormalities following the damage that the disease causes to the brain and nerves. First, the cause of TSD is a loss of function mutation of the *HEXA* gene that codes for the regulatory protein of the hexosaminidase A enzyme (Dersh et al. 2016). This enzyme facilitates the breakdown of lipids known as GM2-gangliosides within the body cells; hence, its absence will lead to the excessive accumulation of the lipids in the nerve and brain cells (NORD, 2017). As a result of this mechanism, the conduction of nerve impulses around the body slows down causing a deterioration in the neurological functions of the body.

Moreover, changes at the cellular level include accumulation of gangliosides in the brain and spinal cord neurons leading to a progressive neurodegeneration as the cells lose their functions (Dersh et al. 2016). For instance, deficiency of hexosaminase A would result to the failure to metabolize gangliosides and their accumulation in cells of the nervous system. The body also attempts to overcome the abnormal accumulation of the ganglioside metabolites in the brain and spinal cord by cell death (Dersh et al. 2016). Nonetheless, the cell death further deteriorates neurological functions.

**Clinical Manifestations & Complications**

The important signs and symptoms for the inclusion of TSD as a differential diagnosis are specific to the age of onset of the disease. Overall, infantile TSD presents clinically with muscle twitching, myoclonic jerks, slow growth, hypotonia, poor mental functioning, and muscle weakness while the juvenile group may experience ataxia, behavioral problems, and visual loss (NORD, 2017). On the other hand, amyotrophy, dystonia, and mood alterations are significant clinical features of late-onset TSD.

However, patients with TSD can develop severe complications in the course of the illness. TSD, whilst left untreated, have common complications such as seizures, paralysis, hearing loss, visual impairment, bipolar episodes, hallucinations, depression, and mobility problems (NORD, 2017). The complications might make the child unresponsive to the environment while the motor challenges would require wheelchairs to promote patient mobility.

**Diagnostics**

Health care providers use laboratory and diagnostic tests to confirm the presence of TSD in patients with suggestive clinical manifestations. These tests include blood biochemical analysis and molecular genetic testing for the detection of changes in the hexosaminidase A enzyme and *HEXA* gene, respectively (NORD, 2017). The amount of the enzyme in blood samples would be a predictor of TSD that requires a confirmation by genetic testing. Prenatal screening using amniotic fluid is also possible since amniocentesis can assess the amount of hexosaminidase A the fetus produces (NORD, 2017).

The patient care team must interpret the diagnostic workups before treating TSD. Overall, the significant findings would include a reduction or absence of the enzyme hexosaminidase A and mutations of the *HEXA* gene (NORD, 2017). These results are also significant in amniocentesis since a reduction in the amount of hexosaminidase A enzyme below the normal limit would indicate that the fetus does not produce enough quantity of the enzyme to diffuse into the amniotic fluid.

In summary, TSD is a genetic disease with an autosomal recessive pattern of inheritance that affects the functions of the nervous system. The etiology of TSD is a loss of function mutation in the *HEXA* gene that regulates the hexosaminidase A enzyme; hence, having both carrier parents for this gene is the major risk factor. Additionally, the pathophysiological changes in TSD results from the accumulation of GM2-gangliosides in the cells of the brain and the spinal cord. The nervous system deteriorates in function as a result of the accumulation of the gangliosides and the patients present with neurological deficits such as ataxia, visual impairments, mental problems, and loss of hearing. Young patients can proceed to experience TSD complications such as seizures and paralysis. Therefore, health care teams must make a timely diagnosis using genetic testing for *HEXA* mutations and blood tests for hexosaminidase enzyme quantities.

**References**

Dersh, D., Iwamoto, Y., & Argon, Y. (2016). Tay-Sachs disease mutations in HEXA target the α chain of hexosaminidase A to endoplasmic reticulum-associated degradation. *Molecular Biology of the Cell*, *27*(24), 3813-3827. doi: https://doi.org/10.1091/mbc.e16-01-0012.

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