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My46 Trait Profile

Sandhoff disease

Other Names: Hexosaminidase A and B deficiency, Type II GM2 gangliosidosis

Sandhoff disease is a genetic condition characterized by the body's inability to break down a fatty substance called GM2 ganglioside. As a result, the GM2 ganglioside builds up in the brain and spinal cord. It is caused by mutations in the HEXB gene which makes the hexosaminidase subunit B protein.

Characteristics of Sandhoff disease

Sandhoff disease is a neurodegenerative condition characterized by progressive deterioration, weakness, loss of movement and cognitive decline. Children with Sandhoff disease typically begin showing symptoms of the condition around three to six months of age. Sandhoff disease is caused by an inability to break down a fatty substance called GM2 ganglioside, allowing it to build up in the brain, and cause the physical and intellectual disabilities seen in the condition. With continual damage to the brain and spinal cord, blindness, seizures, loss of muscle tone, and eventual death result. Skeletal abnormalities and hepatosplenomegaly (i.e., enlarged liver and spleen) are also commonly seen in this condition. A child with Sandhoff disease usually does not live past the age of five or six.

Diagnosis/Testing

Sandhoff disease can be diagnosed by genetic testing for a change or mutation in a gene called HEXB. This gene encodes a protein that is part of the beta-hexosaminidase A and B enzymes. These enzymes play an important role in the brain and spinal cord and help to break down a fatty substance called GM2 ganglioside. Mutations in the HEXB gene result in deficiency of both the beta-hexosaminidase A and B enzymes, thus allowing GM2 ganglioside to build up in the brain and spinal cord, and cause the features seen in the condition.

Not all mutations in the HEXB gene cause classic Sandhoff disease. Certain mutations in this gene allow some beta-hexosaminidase A and B enzyme to be made, and thus are associated with juvenile, chronic, and adult-onset variations. Compared to classic Sandhoff disease, these forms are usually milder, symptoms usually appear in later childhood, adolescence or adulthood and include weakness, ataxia (i.e., loss of muscle coordination), and mental illness.

Management/Surveillance

Management of children with Sandhoff disease typically includes providing supportive care, adequate nutrition and hydration, and medication to control seizures.

Mode of inheritance

Sandhoff is inherited in an autosomal recessive pattern. This means that an individual has to inherit two HEXB mutations (i.e., one from each parent) to be affected with Sandhoff disease. If both parents are carriers of a HEXB mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with Sandhoff disease.

Risk to family members

Parents of a child with Sandhoff disease are carriers of Sandhoff disease. If a sibling of a child with Sandhoff disease is unaffected, he/she has a 2 in 3 (or 66%) chance of being a carrier of Sandhoff disease.

Special considerations

The clinical features of Sandhoff syndrome overlap with other genetic conditions such as Tay Sachs disease (see trait profile) and GM2 activator protein deficiency. While these conditions share similar features, individuals with Sandhoff disease typically also develop skeletal problems and hepatosplenomegaly.

Resources

National Tay-Sachs and Allied Diseases Association, Inc.
http://www.ntsad.org
Genetics Home Reference: Sandhoff disease
http://ghr.nlm.nih.gov/condition/sandhoff-disease

References

Bley, AE. et al. (2011)."Natural History of Infantile GM2." Pediatrics 128(5): e1233-e1241.
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