GAUCHER DISEASE

WHAT IS GAUCHER DISEASE?

Gaucher disease is an inherited disorder that affects many tissues and organs and shows significant variation among individuals. It is classified as a lysosomal storage disorder (LSD). Lysosomes are cell organelles that digest and recycle various molecules. Disorders that result in the accumulation of molecules within the lysosomes, including Gaucher disease, are identified as LSDs.

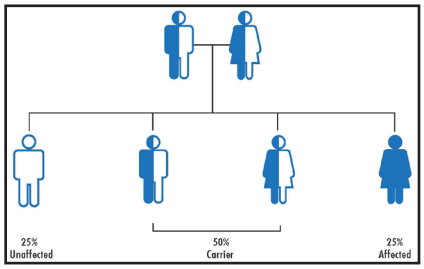
There are several types of Gaucher disease classified according to features and severity.

THE CAUSE

Gaucher disease is caused by mutations in the GBA gene. The normal function of this gene is to produce an enzyme, beta-glucocerebrosidase, which breaks down a fatty molecule called glucocerebroside into glucose and a simpler fat called ceramide. A gene mutation results in reduced quantity or complete absence of beta-glucocerebrosidase, which causes the accumulation of glucocerebroside within the lysosomes.

INHERITANCE PATTERN

Gaucher disease is an inherited autosomal recessive (AR) condition. In order to be affected, the individual would have had to inherit one mutation in the gene from each parent. Each parent is referred to as a carrier and does not show symptoms of the condition.



When two carrier parents of an AR condition have children, there is a 25% chance of having an affected child with each pregnancy.

Gaucher disease affects 1 in 50,000 to 100,000 births. Gaucher disease type 1 is the most common genetic disorder in those of Ashkenazi Jewish ancestry, occurring in approximately 1 in 450 births.

PATIENT CARE

DIAGNOSIS

1. Enzymatic testing to measure beta-glucocerebrosidase activity levels in peripheral blood leukocytes or other nucleated cells.
2. DNA mutation analysis of the GBA gene.

MANAGEMENT

The management team should include multidisciplinary care at a Comprehensive Gaucher Center to include gastroenterology, genetics, hematology, oncology, orthopedics, and neurology.

TREATMENT

Enzyme replacement therapy (ERT) is the standard of care for Gaucher disease. Therapies include Cerezyme, manufactured by Sanofi Genzyme, which was approved by the FDA in 1994. Additional sources are VPRIV from Shire Pharmaceuticals and Elelyso from Protalix Biotherapeutics.

In those for whom ERT is not an option, a drug that blocks the formation of glucocerebroside can be used. These include Cerdelga, manufactured by Sanofi Genzyme, and Miglustat and Zavesca, manufactured by Actelion.

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WHAT ARE THE SYMPTOMS?

For patients with severe Gaucher disease, the most commonly seen symptoms include:

- Anemia
- Fatigue
- Hepatosplenomegaly
- Thrombocytopenia

Gaucher Disease, Type 1 is also called non-neuronopathic because the CNS is usually unaffected. Symptoms can appear anytime from childhood to adulthood and may be mild to severe. Primary symptoms include hepatosplenomegaly, anemia, thrombocytopenia and bone abnormalities.

Gaucher Disease, Types 2 and 3 are called neuronopathic due to effects in the CNS. Type 2 usually occurs in infancy with life-threatening symptoms. Type 3 progresses more slowly than Type 2.

The Perinatal-Lethal Form of Gaucher Disease is the most severe. Significant issues begin prior to birth or in the newborn period and may include hydrops fetalis, ichthyosis, and hepatosplenomegaly. These patients survive for only a few days following birth.

RESOURCES

Gene Reviews: Gaucher
ncbi.nlm.nih.gov/books/NBK1269/

Genetics Home Reference
ghr.nlm.nih.gov/condition/gaucher-disease#resources

National Organization of Rare Diseases (NORD)
https://rarediseases.org

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