Gaucher Disease

Gaucher disease (GD) is a lysosomal storage disease most often affecting individuals of Ashkenazi Jewish (AJ) descent. GD type 1 is the most common form with symptoms ranging from mild to severe. Symptoms include hepatosplenomegaly, anemia, thrombocytopenia, lung disease, and bone abnormalities. Symptoms of type 1 can appear anytime from childhood to adulthood. GD types 2 and 3 are neuronopathic forms differentiated mainly by disease progression and involve the central nervous system with life-threatening problems that typically appear in early infancy. Symptoms of types 2 and 3 also include eye abnormalities, seizures, and damage to the brain. Testing is used for prepregnancy carrier screening or for diagnostic testing in individuals suspected of having GD.

Disease Overview

Prevalence

- ~1 in 57,000 to 1 in 75,000 \(^1,2\) in general population
- GD type 1 estimated at 1 in 855 in individuals of AJ descent \(^3\)

Age of Onset

- Type 1: childhood/adulthood
- Type 2: typically before age 2, with death by age 2-4
- Type 3: typically in childhood, but survival into third or fourth decade

Symptoms

GD affects lysosomal storage and has extreme symptom variability, ranging from perinatal lethality to asymptomatic individuals.

- Type 1
  - Represents 95% of GD; characterized by non-neuronopathic symptoms including bone disease, hepatosplenomegaly, lung disease, and anemia \(^3\)
- Type 2 (acute neuronopathic)
  - Primary central nervous system (CNS) involvement with rapidly progressive course
- Type 3 (subacute/chronic)
  - Primary CNS involvement with slowly progressive course

Genetics

Gene

GBA

Inheritance

Autosomal recessive

Penetrance

Variable

Tests to Consider

Gaucher Disease (GBA) Sequencing
Method: Polymerase Chain Reaction/Sequencing

Gaucher Disease (GBA), 8 Variants 0051438
Method: Polymerase Chain Reaction/Fluorescence Monitoring

Gaucher Disease (GBA), Enzyme Activity in Leukocytes 2014459
Method: Quantitative Fluorometry

Ashkenazi Jewish Diseases, 16 Genes 0051415
Method: Polymerase Chain Reaction/Fluorescence Monitoring

1, 2

3
Test Methodology

- **GBA sequencing:** Long range PCR followed by bidirectional sequencing of all coding regions and intron-exon boundaries of the GBA gene
- **GBA 8 Variants:** Polymerase chain reaction (PCR) and fluorescence monitoring

Test Sensitivity and Specificity

**Clinical Sensitivity**

Sequencing: ~99%³

Targeted variants: 90% in individuals of Ashkenazi Jewish descent; 55% in other ethnicities³

**Analytical Sensitivity and Specificity**

~99%

Limitations

- Diagnostic errors can occur due to rare sequence variations.
- Regulatory region variants, deep intronic variants, large deletions/duplications/insertions, gene conversion events and complex gene rearrangements may not be detected.

References


Related Information

**Ashkenazi Jewish Genetic Diseases**