Gaucher Disease

Last Literature Review: April 2019 Last Update: August 2023

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.

Featured ARUP Testing

Gaucher Disease (GBA) Sequencing 3001648

Method: Polymerase Chain Reaction/Sequencing

Carrier screening or diagnostic testing for GD in individuals of non-Ashkenazi Jewish descent

Gaucher Disease (GBA), 8 Variants 0051438

Method: Polymerase Chain Reaction (PCR), Fluorescence Monitoring

Carrier screening or diagnostic testing for GD in individuals of Ashkenazi Jewish descent

Disease Overview

Prevalence

- Approximately 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

Test Methodology

- *GBA s*equencing: 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
  - Targeted variants: c.115+1G>A; c.84dupG, p.L29Afs; c.1226A>G, p.N409S; c.1263_1317del55; c.1297G>T, p.V433L; c.1342G>C, p.D448H; c.1448T>C, p.L483P; and c.1604G>A, p.R535H

Test Sensitivity and Specificity

Clinical Sensitivity

Sequencing: Approximately 99%[3]

Targeted variants: 90% in individuals of Ashkenazi Jewish descent; 55% in other ethnicities[3]

Analytic Sensitivity and Specificity

Approximately 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

1. Meikle PJ, Hopwood JJ, Clague AE, et al. Prevalence of lysosomal storage disorders. *JAMA*. 1999;281(3):249-254.

2. Biegstraaten M, van Schaik IN, Aerts JMFG, et al. 'Non-neuronopathic' Gaucher disease reconsidered. Prevalence of neurological manifestations in a Dutch cohort of type I Gaucher disease patients and a systematic review of the literature. *J Inherit Metab Dis*. 2008;31(3):337-349.

3. Pastores GM, Hughes DA. Gaucher disease. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews, University of Washington; 1993-2020. [Last Update: Jun 2018; Accessed: May 2020]

Related Information

Ashkenazi Jewish Genetic Diseases

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