Fabry Disease: Globotriaosylceramide (Gb3) Quantification, Urine

Test Code: BGBCU
Turnaround time: 7 days - 10 days
CPT Codes: 82542 x1, 82570 x1

Condition Description

Fabry disease, the only X-linked sphingolipidosis, is associated with severe multiorgan dysfunction. Its incidence has been estimated from 1 in 40,000 to 60,000 live births for males. Heterozygous females can be symptomatic. Although clinical onset often occurs in childhood, disease presentation may be subtle, leading to delayed diagnosis or misdiagnosis. The primary defect is a deficiency of the lysosomal enzyme, alpha-galactosidase A which releases galactose from ceramide trihexoside (globotriaosylceramide, Gb3) and related glycosphingolipids (especially galabiosylceramide, Gb2), due to mutations in the GLA gene. This results in progressive accumulation of Gb3 in vascular endothelial cells, epithelial and smooth muscle cells, leading to ischemia and infarction especially in the kidney, heart and brain. Large amounts of Gb3 are excreted by untreated male hemizygotes (except patients with a renal graft and those with a cardiac variant), and smaller but still significant amounts by heterozygote females, symptomatic or not. At present, urinary Gb3 quantification also provides additional diagnostic information for manifesting female carriers of Fabry disease, as well as patients with multiple glycolipid storage conditions. Measurement of Gb3 has also been used by some groups to monitor enzyme replacement therapy and disease progression.\(^1,2\)


References:
\(^1\) Rozenfeld et al. Clinica Chimica Acta 403 (2009) 194–197
\(^2\) M.J. van Breemen et. al. Biochim Biophys Acta. 2011. 1812(1):70-6

Genes

GLA

Indications

This test is indicated for:

- Males who have clinical symptoms of Fabry disease
- Females, both symptomatic and asymptomatic, who may be carriers of Fabry disease
- Males and females on enzyme replacement therapy (ERT) for Fabry disease

Methodology

LC-MS/MS

Detection

- Fabry patients not on treatment may have elevated Gb3 levels.
- Fabry patients on treatment have significantly lower to normal Gb3 levels.
- Mildly elevated Gb3 levels may also be caused by other renal diseases or injury to the urinary tract.
- This assay may be affected by urine that is stored at room temperature for a prolonged period of time.

Reference Range

<1 year old: 0-149 ug/mmol Cr
1-4 years old: 0.0-17 ug/mmol Cr
>4 years old: 0.0-8.0 ug/mmol Cr

Specimen Requirements

Additional Specimen Collection/Handling Instructions Required for this Test

Urine that has been stored at room temperature and received more than 24 hours from the date of collection may be rejected at the discretion of the Laboratory Director.

Type: Urine

Specimen Requirements:

In a clean container without preservatives: 1-8 ml.

First void preferred but random accepted.

Specimen Collection and Shipping: For fresh sample, ship at room temperature for receipt at EGL within 24 hours of collection. For frozen sample, ship on dry ice with overnight delivery.
Special Instructions

Clinical information is required for complete interpretation.

Related Tests

Biochemical:

- Fabry Disease: Alpha-Galactosidase A Enzyme Activity (LB)

Molecular:

- Fabry Disease: GLA Full Gene Sequencing (DG)
- Fabry Disease: GLA Gene Deletion/Duplication (KX)