MAYO CLINIC LABORATORIES

Newborn Screening Act Sheet

Fabry Disease: Decreased Alpha-Galactosidase A

Differential Diagnosis: Fabry disease; pseudodeficiency of alpha-galactosidase

Condition Description: Fabry disease is an X-linked lysosomal storage disorder resulting from deficient activity of the enzyme alpha-galactosidase A (alpha-Gal A) and the subsequent deposition of glycosylsphingolipids in tissues throughout the body, in particular, the kidney, heart, and brain. There is wide variability in severity and age of onset in both males and females.

You should take the following actions:

- Contact family to inform them of the newborn screening result and ascertain clinical status.
- Consult with genetic or metabolic specialist.
- Evaluate the newborn. Infants with Fabry disease are typically asymptomatic. A thorough family history may indicate other relatives with symptoms suggestive of Fabry disease.
- Initiate timely confirmatory/diagnostic testing and management, as recommended by specialist.
- Provide family with basic information about Fabry disease.

Diagnostic Evaluation: Confirmatory alpha-galactosidase enzyme assay in males. When male patients have low enzyme activity, *GLA* gene analysis and other laboratory studies may be required in consultation with the pediatric metabolic specialist. Because female heterozygotes are known to have variability in alpha-galactosidase levels, *GLA* gene analysis should be the primary diagnostic test for females with abnormal newborn screening as they may be missed by confirmatory enzyme testing alone. At risk family members should be offered familial mutation testing if a *GLA* mutation is found.

Clinical Expectations: Severity and onset of symptoms are variable. The classic form of Fabry disease occurs in males with <1% alpha-Gal A activity. Symptoms usually appear in childhood or adolescence and can include acroparesthesias, gastrointestinal issues, multiple angiokeratomas, reduced or absent sweating, corneal opacity, and proteinuria. Males with residual alpha-Gal A activity may present with either a renal or cardiac form of Fabry disease with onset of symptoms later in life. Pseudodeficiency alleles may also be detected by newborn screening. Females with Fabry disease can have clinical presentations ranging from asymptomatic to severely affected. Fabry disease is caused by mutations in the *GLA* gene and has an estimated incidence varying from 1 in 3,000 infants detected via newborn screening to 1 in 10,000 males diagnosed after onset of symptoms. Treatment with enzyme replacement therapy (ERT) is available for both males and females with Fabry disease. ERT administration is highly complicated and should only be given under the guidance of a specialist with expertise in lysosomal storage disorders.

Additional Information

Genetics Home Reference

Genetic Testing Registry

Baby's First Test

Mayo Clinic Laboratories Testing

AGABS / Alpha-Galactosidase, Blood Spot

AGA / Alpha-Galactosidase, Leukocytes

FABRZ / Fabry Disease, Full Gene Analysis