Alpha-Iduronidase Enzyme Activity (Mucopolysaccharidosis Type I)

Indications for Ordering

Confirm diagnosis in individuals with clinical and/or biochemical evidence of mucopolysaccharidosis type I, also known as MPS I (Hurler, Hurler-Scheie, Scheie syndromes)

Test Description

Enzyme activity measured by quantitative fluorometry

Tests to Consider

Screening

Mucopolysaccharides Screen – Electrophoresis and Quantitation, Urine 0081352

- Recommended initial test to screen for all mucopolysaccharidosis types, including MPS I

Diagnosis

Alpha-Iduronidase Enzyme Activity in Leukocytes 2011415

- Recommended for excluding MPS I following abnormal screen
- Recommended for confirming MPS I in patients with a consistent clinical phenotype and/or a positive family history

Monitoring

Mucopolysaccharides, Quantitative, Urine 0081357

Mucopolysaccharidosis Type 1, Total HS and NRE (Sensi-Pro) Quantitative, Urine 2007488

Mucopolysaccharidosis Type 1, Total HS and NRE (Sensi-Pro) Quantitative, Serum or Plasma 2007599

- Monitors glycosaminoglycan (GAG) levels in patients with a confirmed MPS I diagnosis

Disease Overview

Incidence

- MPS I – ~1/70,000
  - Subtypes
    - Hurler syndrome – ~1/100,000
    - Hurler-Scheie syndrome – ~1/300,000
    - Scheie syndrome – ~1/million

Symptoms

- MPS I subtypes
  - Hurler syndrome – most severe
  - Hurler-Scheie syndrome – moderately severe
  - Scheie syndrome – least severe (intellect, life span, and stature can be normal)
- Overlap of clinical symptoms among MPS I subtypes
  - No biochemical differences have been identified
- Symptoms and severity vary widely
  - Coarse facial features
  - Organomegaly
  - Progressive skeletal dysplasia (dysostosis multiplex)
  - Gibbus
  - Short stature
  - Cardiomyopathy
  - Corneal clouding
  - Hearing loss
  - Progressive intellectual disability

Pathophysiology

- GAGs – degraded in lysosomes by a series of enzymes
- Alpha-iduronidase enzyme
  - One of several enzymes responsible for the degradation of the GAGs dermatan and heparan sulfate
  - Deficiency of alpha-iduronidase
    - Leads to incomplete degradation and accumulation of heparan and dermatan sulfate in connective tissue
    - Causes MPS I

Genetics

Gene – *IDUA*

Inheritance – autosomal recessive

Genotype/phenotype correlation

Hurler syndrome

- Associated with more severe, nonsense variants
  - Profound alpha-iduronidase deficiency

Hurler-Scheie and Scheie syndromes

- Variants are often milder (eg, single base-pair substitutions)
  - Some residual enzyme function is retained

Test Interpretation

Results

Alpha-iduronidase enzyme activity in leukocytes

- Extremely low/undetectable enzyme activity is consistent with MPS I (Hurler, Hurler-Scheie, Scheie)

Limitations

- Cannot differentiate between Hurler, Hurler-Scheie, and Scheie syndromes
  - Categorization depends on clinical and/or molecular genetic findings
- Cannot predict carrier status for MPS I
- Does not evaluate enzyme deficiencies in other MPS types
- Pseudodeficiency has been shown for this enzyme due to specific gene variants affecting the exogenous substrate, but not endogenous substrates
  - Individuals with pseudodeficiency are not affected with MPS I

References

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