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
  o 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
  o Individuals with pseudodeficiency are not affected with MPS I

References