State of CT
Genetics Newborn Screening Program
Health Care Provider Fact Sheet

Propionic Acidemia (PA)

Introduction

Propionic acidemia is an autosomal recessive disorder of branched-chain amino acid metabolism in which a defective enzyme, propionyl-coenzyme A (CoA) carboxylase, results in an accumulation of propionic acid. In the United States, PA occurs in 1:50-100,000 live births. Although the disease generally is quite rare, the incidence has been reported as high as 1:2000-1:5000 births in areas of the world such as Saudi Arabia.

Many affected infants initially present in the first month of life, often with failure to thrive due to feeding intolerance and vomiting. Also, somnolence often is a part of the history, so that poor feeding may be erroneously attributed to central nervous system disorders. Other infants have a fulminant initial presentation, with rapidly developing ketoacidosis, dehydration, shock, and a precedent history of lethargy, poor feeding, and rapid breathing that only extends over 1-2 days. Occasionally, an older infant or young child may have a lifelong history of episodic lethargy, anorexia, vomiting, and acidosis that has responded to short hospital stays with intravenous glucose and bicarbonate administration.

In patients who previously have been diagnosed with propionic acidemia, the acute onset of movement disorders caused by basal ganglia infarction may be a presenting feature. Dystonia, rigidity, choreoathetosis, and dementia in a child with a prior diagnosis of propionic acidemia suggest a basal ganglia infarction. While most children suffer neurologic damage during a metabolic crisis, rare cases without an identifiable precipitating factor have been reported. The metabolic crisis may result from changes in feeding or may be secondary to an infection.

Diagnosis

Newborn screening—Tandem mass spectrometry: C3
Confirmation—a second sample may be requested or follow up testing will be done at the Metabolic Treatment Center at Yale or UCONN Genetics.
Urinary organic acids are the definitive clinical diagnostic study. Most frequently, it demonstrates large increases in beta-hydroxy propionic acid, lactic acid, and methylcitrate excretion.

Situations that risk metabolic decompensation

- Frequent episodes of decompensation can be devastating to the central nervous system. Any source of catabolic stress, such as vomiting, diarrhea, febrile illness, and decreased oral intake can lead to decompensation, which requires prompt and aggressive intervention.

Monitoring

- Clinical observation is the most important tool for monitoring patients with PA. It is important for the primary care provider and the Metabolic Treatment Center to develop an on-going collaborative relationship in caring for these patients.
- Carefully assess infants presenting with unexplained vomiting for signs of ketoacidosis; urinalysis is particularly important in this regard since neonates normally do not excrete large quantities of ketones.

- Central nervous system depression, signifying either severe acidosis or hyperammonemia, may be apparent on examination.
- Any infant with an inborn error also can be affected by other disorders. Suspicion of sepsis based upon the typical nonspecific signs must not eliminate the possibility of underlying disease, such as propionic acidemia, from the differential.

Treatment

- The use of specific metabolic foods (formulas) deficient in isoleucine, valine, threonine, and methionine is a critical part of management as it provides the essential amino acids in an otherwise protein-deficient diet. Adequate calories to inhibit catabolism are supplied as carbohydrate and fat, and appropriate protein must be supplied to support anabolism. The Metabolic Treatment Center will determine the patient's diet prescription.
- Use of adjunctive compounds to dispose of toxic metabolites and to increase activity of deficient enzymes and hemodialysis may be used during acute decompensation.
- Long-term outcome can be excellent, however, appropriate management does not guarantee a good outcome, as individuals affected with an OA are medically fragile.
- In propionic acidemia, liver transplantation alone ameliorates the disease, but does not completely eliminate the disorder because the kidney also makes propionic acid.
- The parents usually have an emergency protocol with them. This protocol, provided by the Metabolic Treatment Center, contains basic information about the disorder, necessary diagnostic investigations and guidelines for treatment.
- Infants and children with PA should have regularly scheduled visits at the Metabolic Treatment Center.

Illness

- Any illness can potentially lead to metabolic decompensation
- Prevention and/or early intervention is of particular importance
- Consult with the Metabolic Treatment Center within 24 hours of the onset of the illness

Immunization

- Immunizations must be kept current.

Surgical/surgical procedures

- Discuss any plans for surgical and dental procedures with the Metabolic Treatment Center.
- Any procedure requiring anesthesia should be done at a hospital with a metabolic service.

Growth and development

- It is crucial to closely monitor all growth, development, and biochemical parameters on a regular basis.
- The child should be referred to an early intervention program and developmental progress closely monitored by both the metabolic team and the primary care provider.

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