



My46 Trait Profile

Acute intermittent porphyria

Other Names: Acute Hepatic Porphyria, Hydroxymethylbilane Synthase (HMBS, HMB-Synthase) Deficiency, Porphobilinogen Deaminase (PBGD) Deficiency, Uroporphyrinogen I Synthase Deficiency

Acute Intermittent Porphyria belongs to a group of conditions called porphyrias. It is mainly characterized by attacks of pain (especially in the abdomen, arms, legs, and back), muscle weakness, and mental symptoms. It is caused by mutations in the HMBS gene which makes the porphobilinogen deaminase enzyme.

Characteristics of Acute intermittent porphyria

The porphyrias are a group of disorders caused by deficiencies of specific enzymes in the pathway to make heme. Heme is an essential part of hemoglobin and many other hemoproteins in the body. Acute Intermittent Porphyria (AIP) is the most common of the acute (hepatic) porphyrias; the other acute porphyrias are Hereditary Coproporphyria and Variegate Porphyria. Acute porphyria symptoms are mostly from effects on the nervous system

Acute attacks usually lasts for days or weeks and almost always start with severe pain in the abdomen but sometimes in the chest, back, or thighs, and are often accompanied by nausea, vomiting, and constipation. Increased heart rate, elevated blood pressure, confusion, convulsions, muscular weakness, and paralysis may occur due to the effects of the disease on the nervous system. Acute attacks are often provoked by drugs (such as barbiturates, sulfonamide antibiotics, anti-seizure medications, rifampin, metoclopramide), alcohol, ovulation in women, reduced food intake, as well as infections, surgery, and stressful situations. Many people with AIP never develop symptoms; this is referred to as “latent” AIP.

Diagnosis/Testing

Most individuals with AIP have a change or mutation in the HMBS gene. This gene makes the porphobilinogen deaminase enzyme (also known as hydroxymethylbilane synthase). This enzyme, along with other enzymes, in a cascade of events, is responsible for making heme, an important part of hemoglobin. If the enzyme is not made or not made properly, certain chemicals in the cascade back up and are excreted in the urine. In AIP, these chemicals are porphobilinogen (PBG), aminolevulinic acid (ALA), and porphyrins. The screening test for AIP is the measurement of PBG, ALA, and total porphyrins in a urine sample collected at the time of an acute attack prior to any treatment and without exposure to any light. The finding of a substantial increase of porphobilinogen (PBG) in urine establishes that one of the three acute porphyrias is present. Genetic testing for a mutation in the HMBS gene can confirm a diagnosis of AIP.

Management/Surveillance

The prognosis of AIP is usually good if the disease is recognized early and prompt treatment is initiated. Although symptoms usually resolve after an attack, repair of nerve damage and associated muscle weakness may require several months or longer.

During an acute attack, individuals with AIP often require hospitalization for medical management. During treatment of an attack, attention should be given to sodium (salt) and water balance. Medications that can worsen symptoms should be avoided.

Acute attacks may be treated with glucose loading or intravenous hemin (e.g., Panhematin®) both of which lower the production of heme pathway intermediates by the liver.

Mode of inheritance

AIP is inherited in an autosomal dominant pattern. This means inheriting one HMBS mutation is enough for an individual to be affected. However, many individuals with AIP may never exhibit symptoms, particularly if triggering factors (e.g., certain drugs and alcohol) are avoided. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected individual.

Risk to family members

The risk to family members depends on whether or not the individual with AIP has a parent with AIP. If a parent has a HMBS mutation, the risk of having a child with AIP is 50% with each pregnancy. If a parent does not have a HMBS mutation, the risk of other siblings being affected is very low.

Special considerations

None

Resources

The American Porphyria Foundation

<http://www.porphyrifoundation.com>

The Porphyrias Consortium

<http://rarediseasesnetwork.epi.usf.edu/porphyrias/index.htm>

The European Porphyria Initiative

<http://www.porphyrria-europe.org>

The Drug Database for Acute Porphyrias

<http://www.drugs-porphyrria.com>

Genetics Home Reference: Porphyria

<http://ghr.nlm.nih.gov/condition/porphyria>

References

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