Acute Intermittent Porphyria (AIP)

Acute intermittent porphyria is caused by an autosomal-dominant mutation in porphobilinogen deaminase, a key enzyme in the heme synthesis pathway. When porphobilinogen deaminase is inhibited, serum porphobilinogen and Delta-ALA as well as urinary porphyrins build up. AIP attacks occur intermittently and are precipitated by cytochrome P450 inducers, alcohol and starvation. Symptoms may include severe abdominal pain, port wine-colored urine, polyneuropathy and CNS symptoms, as well as psychiatric disturbances. Treatment for AIP flares involves hemin and glucose; two inhibitors of the heme synthesis pathway. Patients should avoid known triggers of AIP flares to prevent symptoms.

PLAY PICMONIC

Pathophysiology

Autosomal Dominant

Domino

Acute intermittent porphyria is inherited in an autosomal-dominant pattern. Therefore, patients only need one mutated gene to inherit the disease.

Inhibited Porphobilinogen Deaminase

Inhibiting-chains on Poor-fairy-babies and Dog-ammo

In acute intermittent porphyria, patients inherit an inhibiting mutation in porphobilinogen deaminase, which converts porphobilinogen into hydroxymethylbilane. In contrast, uroporphyrinogen decarboxylase converts uroporphyrinogen III to coproporphyrinogen III, and is the enzyme mutated in porphyria cutanea tarda.

Increased Serum Porphobilinogen

Up-arrow Poor-fairy-babies

Because porphobilinogen deaminase is inhibited, serum porphobilinogen and delta-ALA build up, as they are synthesized upstream from porphobilinogen deaminase. Urinary porphyrins are also increased, as they spill from the blood to the urine.

Increased Serum Delta-ALA

Up-arrow Delta-Ala

Because porphobilinogen deaminase is inhibited, serum porphobilinogen and delta-ALA build up, as they are synthesized upstream from porphobilinogen deaminase. Urinary porphyrins are also increased, as they spill from the blood to the urine.

Increased Urinary Porphyrin Precursors

Up-arrow Urinal Poor-fairy

Because porphobilinogen deaminase is inhibited, serum porphobilinogen and delta-ALA build up, as they are synthesized upstream from porphobilinogen deaminase. Urinary delta-ALA and porphobilinogen are also increased, as they spill from the blood to the urine.

Signs & Symptoms

Precipitated By P450 Inducers

Pea-450 Inducer-rocket

Patients with acute intermittent porphyria have symptom flares precipitated by various triggers such as cytochrome P450 inducers, alcohol and starvation. Symptoms may include severe abdominal pain, port wine-colored urine, polyneuropathy and CNS symptoms and psychiatric disturbances.

Painful Abdomen

Pain-bolt in Abdomen

Colicky epigastric abdominal pain is typically the presenting sign of an AIP flare. It lasts for several days and is often associated with nausea, vomiting and constipation.

Polyneuropathy

Polly-nerve

During attacks, patients may experience polyneuropathy and other neurological symptoms; such as ascending weakness, seizures and cortical blindness.

Psychological Disturbances

Psycho in a straight-jacket

Patients may experience psychological disturbances such as depression during attacks. They are also at increased risk for certain psychiatric diseases such as bipolar disorder and schizophrenia.

Port Wine-Colored Urine

Port-wine

During flares, patients may have port wine-colored urine; initially the urine is colorless, but exposure to light causes the urine to change its color.

Treatment

Glucose and Hemin

Glue-bottle and Heme-man

Glucose and hemin are the mainstays of treatment for AIP attacks. Hemin is a heme-containing porphyrin that comes as an IV solution. Both glucose and hemin inhibit ALA synthase, which is the first step in the heme synthesis pathway. By administering these two inhibitors, porphyrins are unable to build up and cause the classic symptoms of an AIP attack.

Considerations

Avoid Triggers

Avoid-sign with Trigger

Acute intermittent porphyria is triggered by alcohol, starvation and cytochrome P450-inducing drugs including barbiturates, carbamazepine and rifampin. Therefore, patients should avoid these to prevent disease symptoms.