Acute intermittent porphyria (AIP)

Genetics

-HMBS (11q23.3)

-AD; only 1% de novo; low penetrance

Clinical findings/Dysmorphic features

-Onset after puberty

-Life-threatening acute neurovisceral (neuronal system connected to internal organs) attacks

-Abdominal pain, muscle weakness, neuropathy, hysteria, anxiety, hepatocellular carcinoma

-No cutaneous findings

-More likely to present in women

Etiology

-5 in 10,000 (but penetrance is only ~1%)

Pathogenesis

-Partial deficiency of porphobilinogen deaminase (PBGD, encoded by HMBS): 3rd enzyme in heme biosynthetic pathway

-Toxic delta-aminolevulinic acid (ALA) and PBG accumulation

-Induction of hepatic ALA synthase activity

Genetic testing/diagnosis

-Increased urine ALA and porphobilinogen (PBG) during acute attack

-HMBS gene sequencing (>98%)

Others

-Urine may be reddish-brown or red; color is enhanced by exposure to air and light

-Mechanism of acute attacks not clear --> PBG buildup may have toxic effects on neurons