= Hereditary coproporphyria =

Hereditary coproporphyria (HCP) is a disorder of heme biosynthesis , classified as an acute hepatic porphyria . HCP is caused by a deficiency of the enzyme coproporphyrinogen oxidase , coded for by the CPOX gene , and is inherited in an autosomal dominant fashion , although homozygous individuals have been identified . Unlike acute intermittent porphyria , individuals with HCP can present with cutaneous findings similar to those found in porphyria cutanea tarda in addition to the acute attacks of abdominal pain , vomiting and neurological dysfunction characteristic of acute porphyrias . Like other porphyrias , attacks of HCP can be induced by certain drugs , environmental stressors or diet changes . Biochemical and molecular testing can be used to narrow down the diagnosis of a porphyria and identify the specific genetic defect . Overall , porphyrias are rare diseases . The combined incidence for all forms of the disease has been estimated at 1 : 20 @,@ 000 . The exact incidence of HCP is difficult to determine , due to its reduced penetrance .

= = Signs and symptoms = =

Clinically , patients affected with HCP present similarly to those with other acute porphyrias , such as acute intermittent porphyria (AIP) and variegate porphyria (VP) . Patients with HCP and VP can present with symptoms shared between the acute and cutaneous porphyrias . This includes the acute attacks of abdominal pain , nausea , vomiting , diarrhea , tachycardia , hypertension and seizures , as well as the cutaneous findings seen in porphyria cutanea tarda (PCT) , namely increased skin fragility , bullous lesions after exposure to sunlight and increased scarring .

Individuals with HCP may be asymptomatic in the absence of triggering factors . Common triggers include certain drugs , alcohol , hormonal changes , and dietary changes . Sunlight and other ultraviolet light can trigger the skin manifestations . Homozygous individuals for CPOX mutations can present with these findings at an earlier age than heterozygotes .

= = Genetics = =

HCP is caused by mutations in the CPOX gene , which codes for the enzyme coproporphyrinogen oxidase . This enzyme is responsible for the sixth step in the heme biosynthetic pathway , converting coproporphyrinogen III to protoporphyrinogen IX . The CPOX gene is located at 3q11.2 @-@ q12.1 , has 6 introns and 7 exons and produces an mRNA strand that is 2675 bases in length . It is inherited in an autosomal dominant fashion , meaning that a deficiency of 50 % of the normal enzyme activity is enough to cause symptoms . As reproductive fitness is not impacted , homozygous affected individuals have been reported . Along with other acute porphyrias HCP demonstrates reduced penetrance , meaning not all individuals who carry a disease @-@ causing mutation will express symptoms .

Individuals who are homozygous for a specific mutation (K404E) or compound heterozygous with a null allele in CPOX have a more severe erythropoietic porphyria , harderoporphyria , characterized by neonatal jaundice , hyperbilirubinemia , hepatosplenomegaly and skin lesions upon exposure to ultraviolet light . HCP is a rare disease , but the exact incidence is difficult to determine due to the reduced penetrance of the acute porphyrias . Overall , the incidence of all porphyrias is estimated at 1 : 20 @,@ 000 in the United States . The incidence of harderoporphyria is even lower , with less than 10 cases reported worldwide .

= = Diagnosis = =

The diagnosis of any porphyria is often delayed due to the rarity of the disease as well as the varied and non @-@ specific findings that patients present with . Bedside measurement of urine porphobilinogen is recommended as a screening test for patients suspected of having an acute porphyria . Elevated porphobilinogen is indicative of an acute porphyria , and additional testing can be done to narrow down the specific type .

The identification of a specific porphyria is based on the results of laboratory findings , including blood , urine and stool tests . HCP can be distinguished from most other acute porphyrias by the cutaneous findings . VP presents similarly , but can be distinguished based on urine and stool porphyrin analysis , typically done using high performance liquid chromatography with fluorescence detection . The results of biochemical testing for porphyrias are most informative when samples are collected during an acute attack . Typically , the distinguishing metabolite for HCP and VP is the presence of protoporphyrin in the plasma and feces of individuals affected with VP .

Elevated coproporphyrin is a common finding in urine , known as coproporphyrinuria as it is the predominant porphyrin species in urine . This is a non @-@ specific finding that is not necessarily due to an acute porphyria . Coproporphyrinuria can be caused by other stressors to the heme biosynthetic pathway , such as liver disease , lead poisoning and certain bone marrow disorders .

= = Treatment = =

There is no cure for HCP caused by the deficient activity of coproporphyrinogen oxidase . Treatment of the acute symptoms of HCP is the same as for other acute porphyrias . Intravenous hemin (as heme arginate or hematin) is the recommended therapy for acute attacks . Acute attacks can be severe enough to cause death if not treated quickly and correctly . Hospitalization is typically required for administration of hemin , and appropriate drug selection is key to avoid exacerbating symptoms with drugs that interact poorly with porphyrias . Proper drug selection is most difficult when it comes to treatment of the seizures that can accompany HCP , as most anti @-@ seizure medications can make the symptoms worse . Gabapentin and levetiracetam are two anti @-@ seizure drugs that are thought to be safe .

In patients where management of symptoms is difficult even with hemin , liver transplant is an option before the symptoms have progressed to advanced paralysis . Combined liver and kidney transplants are sometimes undertaken in patients with renal failure .

Long term treatment of acute porphyrias is centered on the avoidance of acute attacks by eliminating precipitating factors , such as drugs , dietary changes , and infections . Females often have attacks coincident with their menstrual cycle , which can be managed effectively with hormonal birth control . Because of the reduced penetrance of HCP , family members of a patient may carry the same mutation without ever presenting with symptoms . Molecular analysis of CPOX is the best way to identify these patients , as they will not express a biochemical phenotype on laboratory testing unless they are symptomatic . Identification of asymptomatic patients allows them to adjust their lifestyle to avoid common triggering factors .