Porphyria Cutanea Tarda (PCT)

OVERVIEW

Currently, in the USA, PCT has a prevalence of approximately 5 case for every 100,000 people. PCT develops when the activity of the uroporphyrinogen decarboxylase (UROD) enzyme becomes severely deficient (less than 20% of normal activity) in the liver. In most cases of PCT, patients do not have inherited UROD gene mutations and are said to have sporadic (or Type I) PCT (s-PCT). A UROD inhibitor generated only in the liver accounts for the severely deficient enzyme activity in s-PCT. Approximately 20 percent of cases have familial (or Type II) PCT (f-PCT). Such individuals have inherited a UROD gene mutation from one parent, which has reduced the amount of UROD in all tissues. However, to develop PCT symptoms, other factors must be present to further reduce the UROD level in the liver to less than 20% of normal.

Excess iron, excess use of alcohol, use of oral estrogens, chronic hepatitis C, smoking, HIV infections, and mutations of the HFE gene (associated with the hemochromatosis) where excess iron accumulates in the liver have all shown to play a role in development of PCT. Other susceptibility factors may exist but have yet to be identified.

SYMPTOMS

In PCT the skin blisters develop on sun-exposed areas of the body, such as the hands, feet and face. The skin in these areas may blister or peel after minor trauma. Increased hair growth, as well as darkening and thickening of the skin may also occur. Neurological and abdominal symptoms are not characteristic of PCT.

LONG TERM COMPLICATIONS

Liver function abnormalities are common, but are usually mild. PCT is often associated with hepatitis C infection, which also can cause these liver complications. However, liver tests are generally abnormal even in PCT patients without hepatitis C infection. Progression to cirrhosis and even liver cancer occurs in some patients.

TREATMENT & PROGNOSIS

Treatment seems to be equally effective in f-PCT and s-PCT. The most widely recommended treatment is a schedule of repeated phlebotomies (removal of blood), with the aim of reducing iron in the liver. The target of this treatment is a serum ferritin near the lower limit of normal [serum ferritin ~ 25-75 ng/mL], without development of anemia. Another treatment approach is a low dose regimen of the drug hydroxychloroquine, typically, 100 mg HCQ twice per week. This drug mobilizes porphyrins from the liver. There is some risk of liver injury when PCT is treated with hydroxychloroquine, but this adverse effect is minimized by treating with a low-dose regimen. Relapses that occur after the initial treatment can be treated successfully using the same approach as for initial treatment. Chronic HCQ therapy has potential adverse effects, especially development of retinopathy; thus, baseline and at least annual and detailed eye examinations are recommended.

UNITED PORPHYRIAS ASSOCIATION
Advancing Awareness, Research & Therapies

Porphyria Cutanea Tarda (PCT)

continued

TREATMENT & PROGNOSIS

PCT caused by hepatitis C can be treated with one of the antiviral regimens to remove that specific risk factor. Patients with marked iron overload should be treated by phlebotomy rather than hydroxychloroquine, to correct both the PCT and the underlying iron overload.

PCT is often more severe and difficult to treat in patients with end-stage renal disease. Iron supplements should be stopped and erythropoietin administered to support small volume phlebotomies to reduce the serum ferritin level. Hydroxychloroquine is less effective in this setting.

MANAGEMENT

PREVENTION

Factors that tend to activate the disease (i. e., susceptibility factors above) should be removed. Sun protective clothing and avoidance may be necessary while someone is having active symptoms.

FAMILY TESTING & COUNSELING

Most cases of PCT are sporadic and will have no UROD mutations detected, for those with familial PCT the inheritance is autosomal dominant. With each pregnancy someone with f-PCT has a 50% chance of passing on the mutated UROD gene, however the penetrance is very low and if it is inherited it is unlikely symptoms will develop.

References

1. Singal AK. Porphyria Cutanea Tarda: Recent Update. 2019
2. Singal et al. Low-dose hydroxychloroquine is as effective as phlebotomy in treatment of patients with porphyria cutanea tarda. 2012