Porphyria Cutanea Tarda (PCT)

The porphyrias are metabolic disorders caused by defective heme synthesis, leading to an accumulation of heme precursors. Porphyria Cutanea Tarda (PCT) is the most common porphyria, and can be classified as either sporadic or genetically inherited. PCT is caused by deficient activity of uroporphyrinogen decarboxylase (UROD) in the heme synthesis pathway, leading to accumulation of uroporphyrin. Patients present with photosensitivity, blistering skin lesions and tea-colored urine. It is diagnosed by the detection of elevated urine and serum uroporphyrins. Treatment includes sunlight avoidance, phlebotomy and low-dose hydroxychloroquine.



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Pathophysiology

Inhibited Uroporphyrinogen Decarboxylase (UROD)

Inhibiting-chains on Euro-poor-fairy and Dog in Cardboard-box with lace

PCT is caused by deficient activity of the enzyme uroporphyrinogen decarboxylase (UROD) in the heme synthesis pathway. UROD catalyzes the decarboxylation of uroporphyrinogen to coproporphyrinogen. Deficient UROD activity leads to the accumulation of uroporphyrin, which appears in the plasma and is excreted mostly in urine.

Most Common Porphyria

#1 Foam-finger and Poor-fairy

PCT is the most common porphyria, and can be classified as either acquired or genetically inherited. The acquired type is more common and accounts for approximately 80% of cases. The inherited type accounts for about 20% of cases. PCT is generally a disease of adults and it usually presents in mid or late life.

20% Autosomal Dominant

(20) Dollar-bill and Domino

Approximately 20% of PCT is inherited via an autosomal dominant pattern. Since there is low penetrance, often there are no relatives with PCT.

80% Sporadic Type

Eating (80) Sporadic-spear

The sporadic, or acquired type accounts for 80% of PCT cases. In this form of porphyria, patients do not have a UROD mutation, which is inherited, but rather they have deficient function.

Hepatitis C Association

Happy-tie-liver Cat

There is a strong association with Hepatitis C Virus (HCV) and PCT, although the exact mechanism is unknown. HCV increases oxidative stress in hepatocytes and also increases iron absorption by dysregulating hepcidin. Iron overload is a common feature in patients with PCT, which explains why phlebotomy is often part of the treatment regimen. Other risk factors that increase susceptibility for PCT include alcohol usage, smoking, HIV, exogenous estrogen and HFE mutation (the hemochromatosis gene). HFE mutations are common in PCT, even in the absence of hereditary hemochromatosis.

Signs & Symptoms

Photosensitivity

Photo-camera causing Sensitive-crying

PCT presents with many cutaneous manifestations including blistering skin lesions due to photosensitivity. Sun-exposed skin may show scarring, bullae, along with hyper- and hypopigmented skin lesions.

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Blistering of Skin

Blisters

PCT is characterized by fluid filled vesicles on sun-exposed areas, friable skin and wounds that heal slowly. This is because increased mechanical fragility of the skin leads to blistering or superficial erosions from miniscule amounts of skin trauma. These blisters can then become infected.

Tea Colored Urine

Tea

The excess uroporphyrin spills out of the liver and eventually into urine, giving rise to the characteristic tea-colored urine. Examination of the urine with a UV light (Wood's lamp) may reveal pink fluorescence, due to excessive porphyrins present.

Diagnosis

Increased Uroporphyrins (Urinary & Serum)

Up-arrow Euro-poor-fairy with Urinal and Syrup

If PCT is suspected, it is important to measure the serum and urine for increased uroporphyrins. Normal levels of total porphyrins in plasma or urine rule out a diagnosis of PCT.

Treatment

Avoid Sunlight

Avoid-sign Sunlight

Patients with PCT have blistering skin lesions due to photosensitivity. Therefore, they must avoid sun exposure until treatment is initiated and plasma porphyrin levels have normalized.

Phlebotomy

Flea-bottom

Increased hepatic iron deposition (iron overload) is common in PCT patients. Therefore, repeated phlebotomy to reduce hepatic iron content is a highly effective treatment for PCT.

Hydroxychloroquine (Low Dose)

Hydra-color-queen

Treatment regimens often include hydroxychloroquine because it forms complexes with porphyrins to enhance excretion. A low dose regimen is preferred. The choice between treatment with phlebotomy and/or hydroxychloroquine depends on the degree of iron overload, and often, hydroxychloroquine is used when phlebotomy cannot be completed.

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