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The diagnosis and management of porphyria cutanea tarda (PCT)

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Abstract

The porphyrias are a group of disorders in which excessive quantities of porphyrins or their precursors are produced. They are due to abnormalities in the control of the porphyrin-haem metabolic pathway. The porphyrias are classified into acute and chronic. The acute porphyrias are acute intermittent porphyria (AIP), porphyria variegata (PV) and hereditary coproporphyria (HCP). The chronic porphyrias are porphyria cutanea tarda (PCT), erythropoietic protoporphyria (EPP) and congenital erythropoietic porphyria (CEP). They are further classified as hepatic or erythropoietic, depending on the major site of abnormal metabolism. This article is about PCT, which is more common in South Africa than the other porphyrias and is classified as chronic and hepatic.

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Introduction

PCT is the most common type of porphyria seen in South Africa. Due to the HIV epidemic we now see many cases of PCT. The disease may be acquired (sporadic or type I) or inherited (familial or type II) as an autosomal dominant trait.

Aetiology and pathogenesis

The fundamental abnormality in PCT is a reduction or deficiency of the hepatic enzyme uro-porphyrinogen decarboxylase. About 80% of cases of PCT are sporadic (type I), while the familial type accounts for 20% of cases.[1]

Sporadic (type I) PCT is often precipitated by environmental factors such as alcohol, oestrogens, iron overload, polyhalogenated hydrocarbons, hepatitis C virus and HIV. Other factors include renal failure, dialysis, diabetes mellitus and lupus erythematosus. In the South African population hepatitis C was found to be a relatively rare cause of PCT.[2] Recent evidence suggests that there may be a genetic basis for at least some cases of sporadic PCT because only a small proportion of people exposed to these agents develop PCT.

The use of oestrogens in oral contraceptives and hormone replacement therapy has resulted in an increase in PCT in women. Infection with hepatitis C virus (HCV) and/or HIV has been found to precipitate PCT in susceptible individuals.

It seems that HCV-induced hepatocellular damage can provoke manifestations of the latent enzyme defect.[1] HIV also seems to cause a direct hepatic damage, leading to PCT. Furthermore, HIV causes abnormality in endogenous steroid metabolism, leading to increased oestrogen levels, with subsequent alteration in prophyrin metabolism. O'Connor et al have demonstrated that porphyrin excretion commonly is abnormal in patients who have established HIV infection, and some of his HIV-positive patients had porphyrin excretion that was characteristic of PCT without clinical evidence of PCT.[3] The combination of HCV and HIV seems to be more potent than either virus alone in causing abnormalities in porphyrin metabolism.[4]

Clinical features

Patients are severely photosensitive with increased skin fragility. This results in blisters on friction areas and sun-exposed areas such as the face and the dorsa and palms of hands (see Figures 1 and 2). Lesions heal with atrophic depigmented scars. In areas with longstanding abnormality scleroderma-like changes are seen. Photo-onycholysis may occur. The face shows a prematurely aged appearance with the skin wrinkled and scarred. Hypertrichosis occurs on the sides of the forehead and temporal areas. Unlike patients with PV, patients with PCT do not have acute attacks of abdominal pains and neurological abnormalities.

Diagnosis

For most dermatologists PCT is a clinical diagnosis, but laboratory tests have to be done to confirm the diagnosis. Biopsy of an intact blister shows a cell-poor subepidermal blister with intact dermal papillae forming the floor of the blister; in histopathological terms this is called festooning. There is a minimal dermal inflammatory infiltrate (see Figure 3).

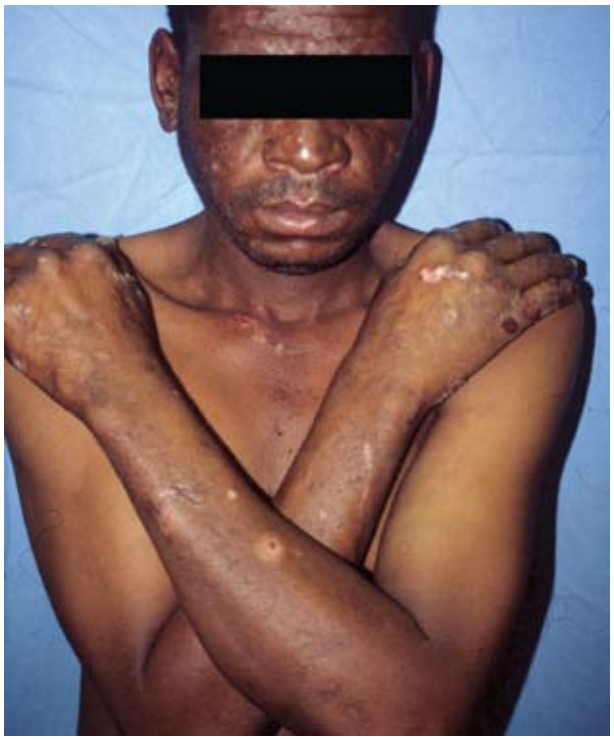

Figure 1: Lesions in photosensitive distribution

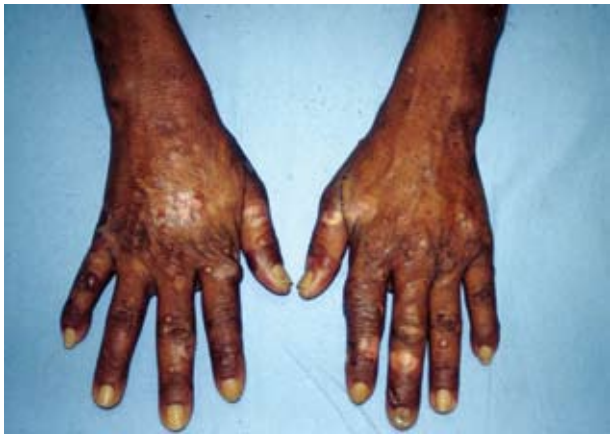

Figure 2: Blisters and erosions on dorsa of hands

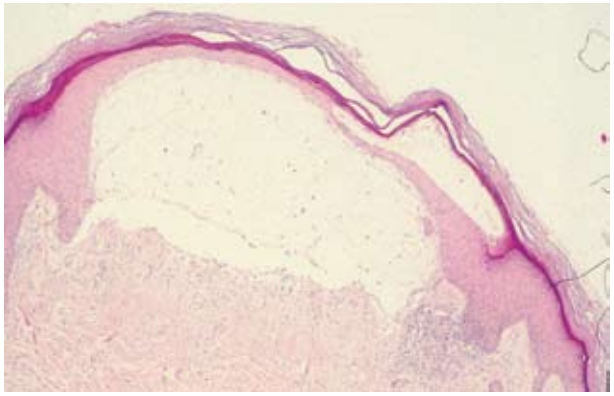

Figure 3: Cell-poor subepidermal blister with festooning

Biochemical tests are done to demonstrate the porphyrins in the blood, stool and urine specimens. There is increased uroporphyrin and 7-decarboxylate porphyrin in urine and plasma. In stools coproporphyrin and iso-coproporphyrin are increased. Once collected the samples should be immediately protected from sun exposure by wrapping them with brown paper and sending them to the laboratory quickly.

Other tests in PCT include liver and renal function tests, full blood count, serum iron studies, hepatitis B and C serology and HIV.

Pitfalls in diagnosis

- Skin fragility and erosions of sun-exposed areas may be misdiagnosed as photosensitive dermatitis.
- If blood, stool or urine samples for porphyrins are not immediately protected from sunlight the porphyrins become degraded and disappear and cannot be detected, thereby giving a false negative result.
- If biopsy is not done on an intact blister the typical histological features may not be demonstrable.

Management

The principles of management are as follows:

1) Treat or remove the precipitating factor/s.
2) Sun protection and avoidance – reduction of light exposure by wearing protective clothing such as hats and gloves greatly reduces skin damage.
3) Venesection – this should however be avoided in patients with low haemoglobin.
4) Treat blisters symptomatically.
5) Chloroquine 100 mg po three times weekly, which may be increased to 200 mg po three times weekly if necessary. This drug binds the porphyrins and assists in their excretion, thereby reducing the levels of porphyrins. Extreme care should be taken when commencing this treatment as chloroquine even in normal doses can induce acute hepatic necrosis in these patients. Patients should be told to report any right hypochondriac pain that may occur once they start this treatment. Liver function tests should also be done during follow-up.
6) Bone marrow stimulants such as erythropoietin may be helpful in cases with anaemia where venesection cannot be done. Erythropoietin stimulates erythropoiesis, which can mobilise tissue iron, thus decreasing the amount of free iron in circulation.
7) Interferon alpha used in progressive hepatitis C liver disease may improve the symptoms of PCT.[5]

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