



## Milium cysts on hands; hypertrichosis on face

The patient's dermatologic symptoms and his history of a particular chronic condition pointed toward the diagnosis.

**A 55-YEAR-OLD MAN** with hypertension and untreated hepatitis C virus (HCV) was referred to the Dermatology Clinic after reporting a 2-year history of photosensitivity and intermittent episodes of blistering and scars on the dorsal side of his hands and feet. No alcohol consumption or drug use was reported.

Physical examination revealed small and shallow erosions on the dorsal aspect of the hands and feet (but no visible blisters) and milium cysts (**FIGURE 1A**). Additionally, hypertrichosis and hyperpigmentation were observed in the zygomatic areas (**FIGURE 1B**).

Complete blood count and kidney function test results were within normal ranges. Liver function tests showed slightly elevated levels of alanine aminotransferase (79 U/L; normal range, 0-41 U/L), aspartate aminotransferase (62 U/L; normal range, 0-40 U/L), and ferritin (121 ng/mL; normal range, 30-100 ng/mL). Serologies for syphilis, HIV, and hepatitis B virus were negative.

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

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**FIGURE 1**

### Telltale signs on hands and face



The patient had milium cysts, as well as small, shallow erosions, on the dorsal surface of both hands (**A**). Hypertrichosis and hyperpigmentation were visible around the patient's right eye (**B**).

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**Porphyria cutanea tarda has a global prevalence of 1 per 10,000 people.**

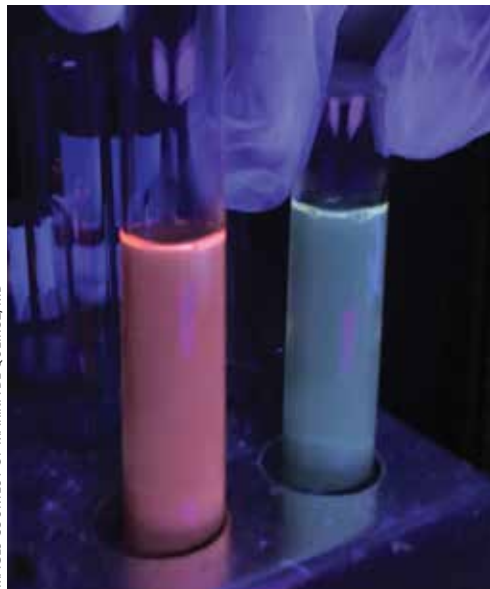
**Diagnosis: Porphyria cutanea tarda**

The clinical presentation, along with the elevated laboratory values, suggested that this might be a case of porphyria cutanea tarda (PCT). Therefore, a sample of the patient's urine was examined under Wood lamp and compared to a sample from a healthy control. In the sample of urine from our patient, a vivid red-pink fluorescence could be visualized under the lamp (FIGURE 2), confirming the diagnosis.

■ **The porphyrias** are a group of metabolic diseases that affect the heme biosynthesis. They can be classified into 1 of 3 groups, according to clinical features:

- **acute hepatic porphyrias**, with neurovisceral symptoms (eg, acute intermittent porphyria),
- **nonblistering cutaneous porphyrias**, with severe photosensitivity but without bullae formation (eg, erythropoietic protoporphyria), or
- **blistering cutaneous porphyrias** (eg, PCT, hepatoerythropoietic porphyria, and variegate porphyria).

**FIGURE 2**  
**Wood lamp confirmed the diagnosis**



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Under Wood lamp, the patient's urine sample yielded a vivid red-pink fluorescence. A healthy control sample is pictured at right.

PCT is the most common type of porphyria, with a global prevalence of 1 per 10,000 people.<sup>1,2</sup> It affects adults after the third or fourth decade of life.

■ **PCT involves dysfunction of the uroporphyrinogen decarboxylase enzyme (UROD)**, the fifth enzyme in heme biosynthesis, which catalyzes the conversion of uroporphyrinogen to coproporphyrinogen. This dysfunction causes the accumulation of porphyrinogens that are auto-oxidized to photosensitizing porphyrins.<sup>1-4</sup> PCT can be classified as "sporadic" or "familial" based on the absence or presence of UROD mutation. Approximately 80% of cases of PCT are sporadic.<sup>2</sup>

■ **In sporadic PCT**, triggers for UROD dysfunction include alcohol use, use of estrogens, hemochromatosis or iron overload, chronic HCV infection, and HIV infection.<sup>1-4</sup> HCV (which this patient had) is the most common infection associated with sporadic PCT, with a prevalence of about 50% among these patients.<sup>5</sup>

■ **Dermatologic manifestations of PCT** include photosensitivity, skin fragility, vesicles, bullae, erosions, and crusts observed in sun-exposed areas. A nonvirilizing type of hypertrichosis may appear prominently on the temples and the cheeks.<sup>2-4</sup> After blisters rupture, atrophy and scarring occur. Milia cysts can form on the dorsal side of the hands and fingers. Less common manifestations include pruritus, scarring alopecia, sclerodermatous changes, and periorbital purple-red suffusion.

■ **Hepatic involvement** is demonstrated with elevated serum transaminases and gamma-glutamyl transpeptidase. Hepatomegaly is common, and cirrhosis manifests in 30% to 40% of patients.<sup>2-5</sup> On liver biopsy, some degree of siderosis is found in 80% of patients with PCT, and most of them have increased levels of serum iron. The incidence of hepatocellular carcinoma in patients with PCT is greater than in patients with other liver diseases.<sup>2</sup>

**A Wood lamp can be a useful diagnostic first step**

Plasma or urine porphyrin lab tests are the gold standard for PCT diagnosis. These tests can be followed by more specific tests (eg, porphyrin fractionation) to exclude other forms of porphyria. However, if plasma or urine por-

phyrin testing is not readily available, a good first step is a Wood lamp exam, which can be performed on urine or stool. (Plasma or urine porphyrin testing may ultimately be necessary if there is doubt about the diagnosis following the Wood lamp screening.) Histopathologic examination does not confirm the diagnosis of PCT<sup>4</sup>; however, it can be helpful in differential diagnosis.

Wood lamp is a source of long-wave UV light (320 to 400 nm), visualized as a purple or violet light. When porphyrins are present in a urine sample, a red-pink fluorescence may be seen.<sup>3,4,6</sup> The Wood lamp examination should be performed in a completely dark room after the lamp has been warmed up for about 1 minute; time should be allowed for the clinician's vision to adapt to the dark.<sup>6</sup> There are no data regarding the sensitivity or specificity of the Wood lamp test in the diagnosis of PCT.

### These conditions also cause skin fragility and photosensitivity

The differential diagnosis for PCT includes diseases that also cause skin fragility, blistering, or photosensitivity, such as pseudoporphyria, bullous systemic lupus erythematosus (SLE), and epidermolysis bullosa acquisita (EBA).<sup>3</sup>

■ **In pseudoporphyria**, the clinical findings may be indistinguishable from PCT. Thus, the patient's history will be especially important; suspect pseudoporphyria if the patient has a history of chronic renal failure or use of a photosensitizing drug.<sup>1,3</sup>

■ **Bullous SLE** usually manifests with systemic involvement and widespread, tense bullae. Serologic investigation will demonstrate the presence of antinuclear antibodies in high titers (> 1:80), as well as other circulating auto-antibodies.

■ **Skin lesions of EBA** usually manifest with skin fragility and noninflammatory tense bullae in traumatized skin, such as the extensor surfaces of the hands, feet, and fingers.

None of the above-mentioned diagnoses

manifest with hypertrichosis or red-pink fluorescent urine on Wood lamp, and results of porphyrin studies would be normal.<sup>3</sup>

### Address triggers, provide treatment

Once the diagnosis is confirmed, steps must be taken to avoid triggering factors, such as any alcohol consumption, use of estrogen, sun exposure (until plasma porphyrin levels are normal), and potential sources of excessive iron intake.

Two therapeutic options are available for treating PCT—whether it's sporadic or familial. Phlebotomy sessions reduce iron overload and iron depletion and may prevent the formation of a porphomethene inhibitor of UROD. The other treatment option is antimalarial agents—usually hydroxychloroquine—and is indicated for patients with lower serum ferritin levels.<sup>1-4</sup> In patients with HCV-associated PCT, effective treatment of the infection has resulted in resolution of the PCT, in some cases.<sup>3</sup>

Treatment involving phlebotomy or an antimalarial agent can be stopped when plasma porphyrins reach normal levels.

■ **Our patient** was initially managed with 2 sessions of phlebotomy. He subsequently received treatment for the HCV infection at another hospital.

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If plasma or urine porphyrin testing is not readily available, a good first step is a Wood lamp exam.

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