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Single Case

Porphyria Cutanea Tarda Presenting with Scleroderma, Ichthyosis, Alopecia, and Vitiligo

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Abstract
Porphyria cutanea tarda (PCT) is a cutaneous porphyria that presents later in life with cutaneous findings in sun-exposed sites. We report a complex case of PCT in a 67-year-old woman with an unusual constellation of cutaneous findings: scleroderma, acquired ichthyosis, and nonscarring alopecia. Possible triggers for her PCT include tamoxifen treatment for breast cancer and carrier status of the hemochromatosis gene. High-dose chloroquine was used to successfully achieve clinical remission and normalize her uroporphyrins. While on chloroquine she developed extensive classic vitiligo. It is not clear if this is another feature of her complex and unusual PCT, or a consequence of her antimalarial therapy.

Introduction

Porphyria cutanea tarda (PCT) is a cutaneous porphyria resulting from an acquired or inherited deficiency of the enzyme uroporphyrinogen decarboxylase. In the acquired form, the enzyme deficiency develops only in the liver. Typically, in the inherited form, the enzyme deficiency is present in both the erythrocytes and the liver [1, 2]. In acquired PCT, the enzyme

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deficiency is most often secondary to alcohol intake, smoking, iron overload, hepatitis C infection, and estrogens [3]. PCT presents later in life with cutaneous findings in sun-exposed sites. Characteristically, PCT results in skin fragility, hyperpigmentation, bullae of the dorsal hands, erosions, hypertrichosis, and sclerodermoid changes [1]. Herein, we describe a patient with previously unreported constellation of cutaneous findings including significant scleroderma of the upper limbs and face with bilateral cicatricial ectropion, acquired ichthyosis, alopecia, and vitiligo.

Case Report

A 67-year-old woman presented to the dermatology department with a 2-year history of a generalized skin rash. She also reported concerns with her vision and constant tearing from both eyes. She had no past history of any skin conditions. Her past medical history was notable for smoking, hypothyroidism for which she was treated with levothyroxine, and invasive ductal carcinoma of the right breast 2 years prior for which she underwent a right-sided mastectomy and was treated with tamoxifen. She did not require any chemotherapy or radiation for her breast cancer. Her family history was notable for a sister with breast cancer and a daughter with vitiligo.

Cutaneous examination revealed: significant sclerodermatous changes of the entire head, neck, and upper trunk; multiple atrophic, sclerotic plaques of the neck and face; extensive ichthyotic patches on the limbs and trunk; diffuse alopecia; and erythema of the sclera with erosions and ectropion of the lower lids bilaterally (Fig. 1, 2). Sclerodactyly was not present. The patient reported that she infrequently developed a few erosions to her arms and/or lower legs. She denied skin fragility and/or blisters of the hands.

Laboratory findings included a normocytic anemia with an Hgb of 111 g/L, an elevated ferritin of 684 μg/L, and slightly elevated aspartate aminotransferase. Hepatitis C, hepatitis B, and HIV testing were negative. An immunologic panel including antinuclear antibody, extractable nuclear antigens, anti-double stranded DNA, anti-histone antibodies, and anti-Scl-70 was negative. Quantitative porphyrins from a 24-h urine collection revealed uroporphyrin I of 1,947 (<46 nmol/day), uroporphyrin III of 594 (<20 nmol/day), elevated coproporphyrin III of 117 (15–242 nmol/day), and elevated hepatocarboxylic, hexacarboxylic, and pentacarboxylic porphyrins. HFE testing for hemochromatosis found a mutation in the H63D gene. Multiple punch biopsies demonstrated changes consistent with scleroderma/morphea and lacked interface changes.

The patient was diagnosed with PCT, likely multifactorial in etiology including carrier state for hemochromatosis and possibly tamoxifen-induced. The diagnosis of PCT was based primarily on her laboratory investigations as her clinical findings were atypical and biopsies demonstrated primarily scleroderma.

The tamoxifen was discontinued. She treated the sclerodermoid areas with high-potency topical steroids. Given her anemia of chronic disease, she was unable to initiate monthly phlebotomies. She was started on chloroquine 125 mg p.o. twice weekly and over a 5-month period this was gradually increased to 250 mg p.o. daily, which she tolerated well with no liver toxicity or other side effects. Within 1 month of discontinuing tamoxifen and initiating treatment, there was decreased sclerosis and ichthyosis noted on examination. Additionally, her urine porphyrins gradually declined to near-normal levels. However, during her treatment course she also developed extensive acrofacial vitiligo (Fig. 3).

After 3 years of treatment with chloroquine, her scleroderma was significantly improved and stable. Her ichthyosis had resolved, and she had noticeable hair regrowth. She was taken off the chloroquine treatment and was subsequently monitored. She achieved 2 years of remission. After 2 years of remission, she developed a solitary blister to her dorsal hand after spending time in the sun and consuming some alcoholic beverages. It then progressed and she developed a few erosions to her neck and lateral face. Her uroporphyrins were found to be elevated and she was diagnosed with recurrent PCT. Of great interest, a noticeable ichthyosis also returned to her back and lower legs.

Discussion

PCT presents with cutaneous findings in sun-exposed sites. These findings typically include skin fragility, hyperpigmentation, bullae and erosions of the dorsal hands, facial hypertrichosis, and sclerodermoid changes [1]. Characteristically, the bullae are on the dorsum of the hands and heal with scarring and milia. A combined retro- and prospective analysis of 152 patients by Muñoz-Santos et al. [2] found that skin fragility and hand blisters were the most frequent cutaneous findings in PCT; this finding was seen in approximately 80% of patients. Thereafter, facial hypertrichosis and facial hyperpigmentation were seen in 63.8 and 42.1%, respectively [2]. Sclerodermoid changes were seen in only 1.3% of patients [2].

Our patient presented with features not previously reported with PCT. Typical skin findings such as blisters and erosions with scarring and hypertrichosis were minimal to absent. Despite sclerodermoid changes representing a less common manifestation of PCT, our patient had extensive sclerodermatous changes. More extensive scleroderma has been reported previously in the literature [4, 5]. Thomas et al. [5] reported a patient with numerous similarities to our case: alopecia, extensive sclerodermatous changes, and cicatricial ectropion. This patient had a familial form of PCT and the sclerodermoid changes improved with venesection and hydroxychloroquine treatment [5].

Lastly, our review of the literature did not find any cases of acquired ichthyosis associated with PCT. Most often, acquired ichthyosis is seen as a paraneoplastic phenomenon and occasionally associated with autoimmune diseases such as lupus [6, 7]. The combination of a sclerodermoid-ichthyosis overlap has been reported in association with both systemic lupus erythematosus and scleroderma, but not PCT [8, 9].

It is possible that her PCT was tamoxifen-induced. There are three reports in the literature that make this causal relationship [10–12]. Interestingly, a well-known precipitant for PCT is estrogens. Tamoxifen is an inhibitor of estrogen so the link between PCT and tamoxifen is not clear. It has been postulated that the mechanism of action is nonalcoholic steatohepatitis. Perhaps her underlying HFE heterozygosity contributed to liver dysfunction and iron overload. In previous reports, tamoxifen-induced PCT resolved with discontinuation of tamoxifen and venesection.

Given the severity of our patient's symptoms and lack of venesection as a treatment option, we opted to treat our patient with chloroquine. Our patient responded very well and the treatment resolved the patient's uroporphyrins and PCT-related cutaneous findings. The patient sustained 2 years of remission with this treatment. It is unclear whether the development of extensive vitiligo was idiopathic, associated with the PCT, or related to the chloroquine. There are case reports of vitiligo being induced by chloroquine in the literature [13].

In conclusion, we report a complex patient with unique manifestations of PCT that include:

(1) Atypical cutaneous manifestations including significant scleroderma, sclerotic plaques of the face and neck, extensive acquired ichthyosis, diffuse alopecia, and bilateral ectropion of the lower lids
(2) Anemia of chronic disease
(3) Possibly induced by tamoxifen
(4) Carrier for hemochromatosis
(5) Remission with daily chloroquine
(6) Concurrent vitiligo

Statement of Ethics

The patient outlined in this case provided informed written consent and there was no conflict of interest. No ethics approval was required for reporting of a single case.

Disclosure Statement

The authors have no conflict of interest to declare. There was no funding for this work.

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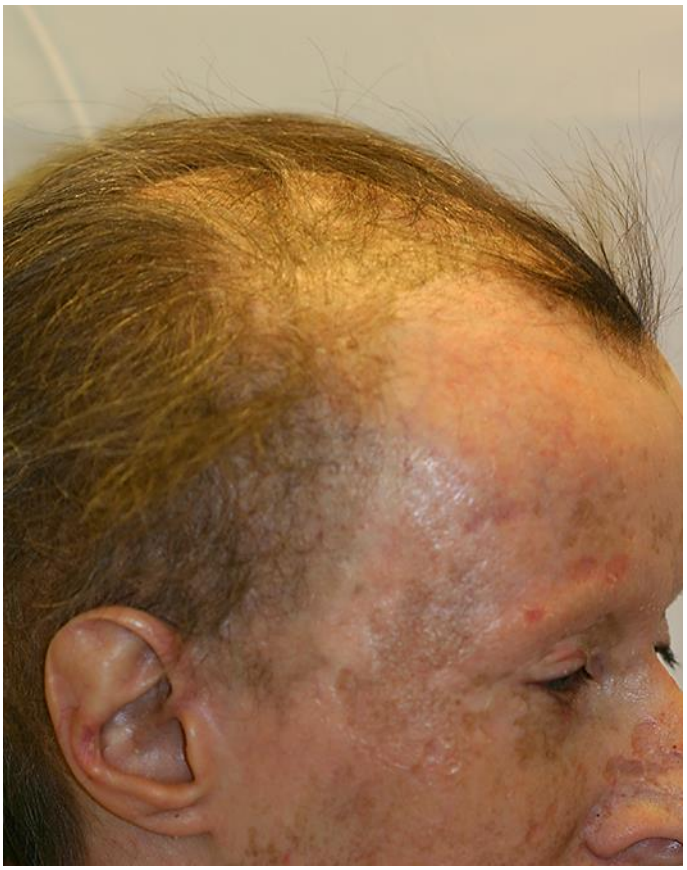

Fig. 1. Porphyria cutanea tarda – alopecia, sclerotic plaques over the face, and bilateral lower lid ectropion.

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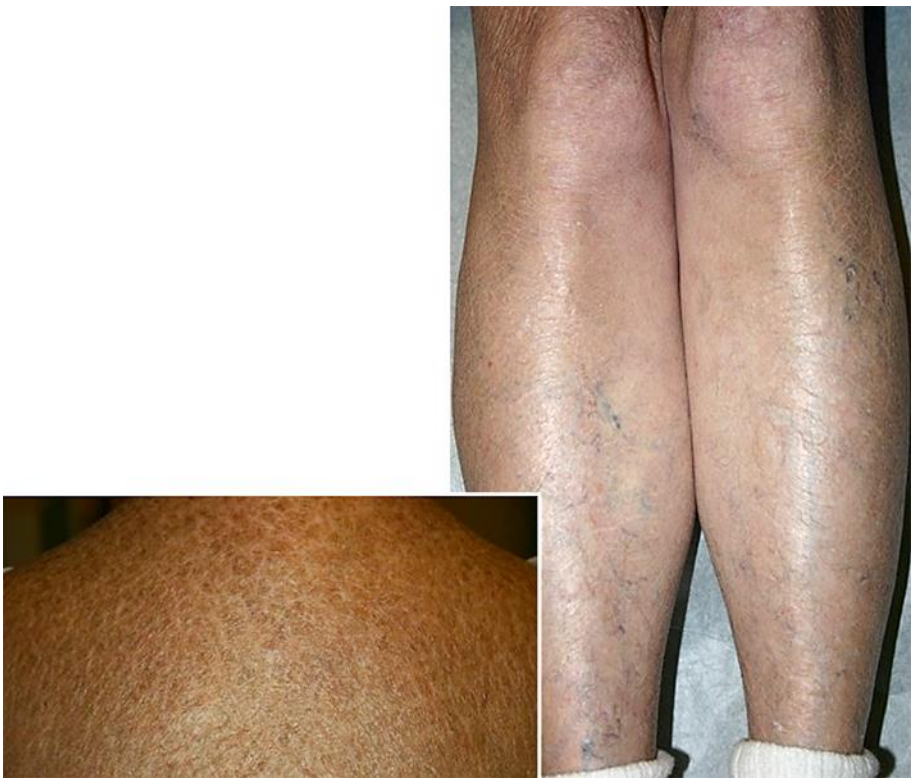

Fig. 2. Porphyria cutanea tarda – ichthyotic changes to the back and lower extremities. The ichthyosis resolved with treatment and reoccurred with reoccurrence of PCT.

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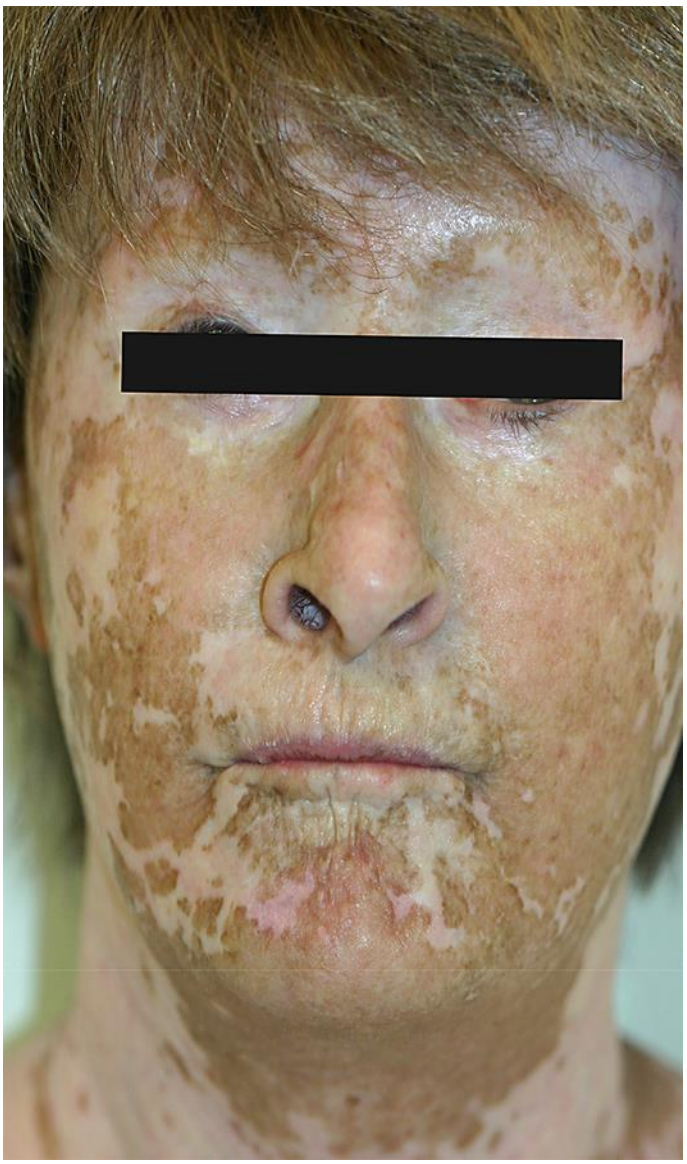

Fig. 3. Extensive acrofacial vitiligo developed during treatment with chloroquine.