

# Large, Nonhealing Scalp Ulcer Associated With Scarring Alopecia and Sclerodermatous Change in a Patient With Porphyria Cutanea Tarda

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*Porphyria cutanea tarda (PCT) is a disorder caused by deficient activity of a liver enzyme that leads to the accumulation of photoactive metabolites in the skin. The initial clinical presentation commonly includes mechanical fragility of the skin and blisters in sun-exposed areas. Sclerodermatous skin changes and scarring alopecia are described in up to 20% of patients. Although these unique skin changes have been reported in the literature, information regarding nonhealing ulcers of extraordinary size is lacking. We report a unique cutaneous manifestation of PCT that is not well documented: unusually large, nonhealing ulcers in the setting of sclerodermatous skin changes and scarring alopecia.*

*Cutis.* 2005;76:329-333.

**P**orphyria cutanea tarda (PCT) is a disorder caused by deficient activity of the liver enzyme uroporphyrinogen decarboxylase. Various liver insults, including viral hepatitis and alcohol abuse, may be the etiology in many cases of PCT. The decreased activity of uroporphyrinogen decarboxylase can lead to the accumulation of photoactive porphyrins in the skin, which cause damage when activated by light. This cutaneous photosensitivity can lead to increased mechanical fragility of the skin, blisters, erosions, sclerodermatous skin changes, and scarring alopecia.<sup>1,2</sup>

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## Accepted for publication June 22, 2004.

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The authors report no conflict of interest.

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## Case Report

A 61-year-old white man was seen in late June 2002 by his primary care physician for a sore on the scalp. The sore began as a bump on the head 10 days prior, when the patient hit his head while exiting his vehicle. The sore continued to enlarge, became painful and bruised, and began interfering with his sleep. At the time of the incident, the patient also scratched his chin and also developed a similar lesion there. He reported that for the previous 2 to 3 years, he had had "thin skin" and that minimal trauma often led to lesions on his head and hands that turned into difficult-to-heal ulcerations. The patient's medical history was significant for osteoarthritis and idiopathic thrombocytopenic purpura, for which he underwent a splenectomy. His surgical history also included inguinal hernia repair and treatment of cataracts. At the time of his visit, the patient was taking no medications or supplements and reported having had an allergy to penicillin as a child. He reported smoking one pack of cigarettes per day and consuming 2 to 3 beers per weekend. A review of the patient's systems was negative for cough, sputum, hemoptysis, paroxysmal nocturnal dyspnea, gastrointestinal symptoms, and dysuria. In addition, he denied headache, jaw claudication, or visual changes.

Results of a physical examination demonstrated a 5×6-cm ulcer with a thick dry eschar surrounded by ecchymoses on the left frontotemporal scalp (Figure 1). There was no surrounding erythema. A laboratory workup taken that day showed a white blood cell count of 12,100/cm<sup>3</sup> and a hematocrit level of 47.1%; results of a urinalysis, basic metabolic panel, and chest x-ray were within reference range. The patient's erythrocyte sedimentation rate was 43 mm/h (reference

range, 0–20 mm/h), up from 8 mm/h in August 2001; and his liver function test result was elevated, which prompted screening for hepatitis C. Results of both the enzyme-linked immunosorbent assay and the recombinant immunoblot assay were positive. Due to the large ulceration on the scalp, vasculitis was suspected and the primary care physician referred him to a rheumatologist.

A few days later, the patient was seen by a rheumatologist, who also suspected temporal arteritis. Cutaneous anthrax was considered in the differential diagnosis. A temporal artery biopsy and a culture were performed. The biopsy result showed no inflammation involving the muscular artery, and the culture result was negative. By early July, there was a new lesion on the right jaw. Results of a biopsy specimen of this site showed parakeratosis, ulceration, necrosis, and acute and chronic inflammation. No fungal elements or granulomas were seen.

Our patient returned for follow-up with his primary care physician in mid July, with no improvement. The lesion on his scalp had expanded, and he presented with 3 new lesions on his face (Figure 2) and a sore on his left index finger. He also reported malaise and fatigue as well as 3 days of facial numbness and decreased vision in his left eye. Results of a physical examination showed the scalp ulcer to be 8×6 cm; additionally, the patient now had a 2.5×1.5-cm lesion on the left maxilla, a 1.5-cm lesion on each mandibular ramus, a small eschar on the left index finger, a blood-filled blister on the left third finger, and ecchymoses on both arms. He was prescribed oral prednisone 60 mg/d for possible vasculitis, even though cryoglobulin, antinuclear antibody, and antineutrophil cytoplasmic antibody test results were negative.

The patient was subsequently referred to the Department of Dermatology at the University of Alabama at Birmingham, where he presented in early September 2002 with an erythrocyte sedimentation rate down to 9 mm/h (reference range, 0–20 mm/h) and aspartate aminotransferase and alanine aminotransferase levels still elevated at 80 U/L (reference range, 10–34 U/L) and 123 U/L (reference range, 6–59 U/L), respectively. Systemic steroids were discontinued. Results of a physical examination demonstrated erosions, with crust and collarettes of scale on the dorsum of the hands (Figure 3) and large gray-white crusted plaques on the scalp and jaw. There were smooth, indurated sclerodermoid plaques on the central chest (Figure 4), as well as periorbital hypertrichosis (Figure 5). PCT was suspected.



Figure 1. Primary scalp lesion.



Figure 2. Facial lesions and scarring alopecia.

The following laboratory workup results were obtained: negative human immunodeficiency virus, a ferritin level of 572 ng/mL (reference range, 23–336 ng/mL), and an iron level of 200 µg/dL (reference range, 49–181 µg/dL). A 24-hour urine specimen contained the following levels: total

uroporphyrin of 2286  $\mu\text{g}/24\text{ h}$  (reference range, 3.3–20.5  $\mu\text{g}/24\text{ h}$ ), heptacarboxyporphyrin level of 2030  $\mu\text{g}/24\text{ h}$  (reference range, 0–6.8  $\mu\text{g}/24\text{ h}$ ), pentacarboxyporphyrin level of 502  $\mu\text{g}/24\text{ h}$  (reference range, 0–4.7  $\mu\text{g}/24\text{ h}$ ), coproporphyrin level of 507  $\text{mg}/24\text{ h}$  (reference range, 0–155  $\text{mg}/24\text{ h}$ ), and total plasma porphyrin level of 54.4  $\mu\text{g}/\text{L}$  (reference range, 1.0–5.6  $\mu\text{g}/\text{L}$ ).

The biopsy results of the indurated plaque of the chest showed diffuse fibrosis of the

dermis with trapping of adnexal structures consistent with scleroderma. The biopsy results of the large scalp ulceration showed superficial and mid dermal perivascular lymphocytes and plasma cells without any evidence of vasculitis. We concluded that this patient had PCT associated with a large nonhealing scalp ulcer, sclerodermatous skin changes, and hepatitis C. This conclusion was made after biopsy results ruled out other possible etiologies, such as skin malignancy, vasculitis,



**Figure 3.** Milia, erosions, and scarring on the hands.



**Figure 4.** Sclerodermatous change on the chest.



**Figure 5.** Periorbital hypertrichosis.



or other necrosing pathology. Treatment recommendations included diligent wound care, therapeutic serial phlebotomy, and evaluation for treatment of hepatitis C.

Upon removal of the eschar on the scalp, the ulcer was found to extend to the periosteum (Figure 6). The wound was debrided, and the patient was instructed how to care for a moist wound, including covering the entire scalp lesion with silver sulfadiazine cream and then dressing the area with gauze or nonstick dressing pads. As the wound healed, the patient was told he could replace the silver sulfadiazine with a thin layer of petroleum jelly. He was instructed to change the dressing twice a day and to clean the wound bed with soap and water or a diluted solution of vinegar and water before applying each new dressing. His cutaneous lesions resolved completely after 6 months of diligent wound care to the scalp and serial phlebotomy treatments (7 treatments scheduled 2 weeks apart). Approximately 500 cc of blood were removed during each phlebotomy. At the end of the phlebotomy treatments, ferritin levels had decreased from 572 ng/mL to 9.5 ng/mL (reference range, 23–336 ng/mL), and total plasma porphyrin levels had decreased from 54.4 µg/L to 9.5 µg/L (reference range, 1.0–5.6 µg/L). Liver function test results also returned to reference range.

### Comment

PCT is the most common porphyria, occurring in up to 1 in 25,000 individuals as either a sporadic type or an inherited type. Approximately 80% of patients have the sporadic type, with the enzyme deficiency restricted to the liver. The familial type is autosomal dominant and characterized by reduced uroporphyrinogen decarboxylase activity in erythrocytes and other tissues. Alcohol, estrogen, iron, and viral infections such as hepatitis can induce clinical expression of PCT in susceptible individuals.<sup>3</sup>

Of all potential inciting factors, hepatitis C has the highest association with PCT. The prevalence of hepatitis C virus in patients with PCT has been shown to be up to 91% in certain European populations.<sup>4</sup> The prevalence of hepatitis C in patients with PCT in North America has been reported to be between 56% and 94%.<sup>5,6</sup> However, this strong association is with the acquired form of PCT and has not been documented with the familial form.<sup>7</sup> Other diseases associated with PCT include diabetes mellitus, systemic lupus erythematosus, Sjögren syndrome, rheumatoid arthritis, human



**Figure 6.** Scalp lesion with eschar removed.

immunodeficiency virus, Wilson disease, renal failure, and hemochromatosis.<sup>8</sup>

The pathogenesis of the skin lesions in PCT is likely multifactorial. The water-soluble porphyrins that accumulate within the skin are activated by light and result in skin damage from the release of proteolytic enzymes into the cytoplasm.<sup>9,10</sup> Complement activation also may have a role in the tissue damage. Complement deposition has been noted at the dermal-epidermal junction near involved skin, and complement degradation products have been isolated from the bullous lesions.<sup>11</sup> In addition, both immunoglobulins G and M have been found around dermal vessels by immunofluorescence and at the dermal-epidermal junction.<sup>8</sup> The skin lesions of PCT do not occur exclusively because of this acute photosensitivity. In addition to sun exposure, the lesions require mild trauma or other physical insult. Subsequently, the backs of the hands and forearms are affected first and often have the worst lesions.<sup>1</sup>

A total of 15% to 20% of patients with PCT develop sclerodermatous skin changes and scarring alopecia.<sup>1</sup> The proposed mechanism is the photoindependent stimulation of fibroblast collagen formation by uroporphyrin I.<sup>12</sup> These areas of sclerodermatous change can develop dystrophic calcifications with nonhealing ulcers and rarely respond to treatment.<sup>1</sup> Such sclerodermatous changes are sometimes referred to as *pseudoscleroderma of PCT* and can occur in areas with little sun exposure.<sup>13,14</sup>

Treatment of PCT has traditionally included serial phlebotomies and antimalarial drugs such as chloroquine or hydroxyquin. Abstinence from alcohol, estrogens, iron supplements, and foods

rich in iron also is recommended. Because complete suppression of viral replication may lead to improvement or remission of PCT, treatment with interferon also has been used.<sup>1</sup> However, interferon therapy for PCT induced by hepatitis C has not consistently improved the disease.<sup>15</sup> Some reports have suggested that interferon treatment after phlebotomy may have better results.<sup>16</sup>

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