

Porphyria Cutanea Tarda Associated With an Acute Gastrointestinal Bleed: The Roles of Supplemental Iron and Blood Transfusion

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We describe a case of porphyria cutanea tarda (PCT) induced by blood transfusion and oral iron supplementation in an 80-year-old white woman. The patient experienced acute blood loss from 2 duodenal ulcers 2 months prior to presentation. During her hospitalization for the gastrointestinal bleed, her anemia was treated with blood transfusion, iron supplementation, and erythropoietin. Multiple blistering lesions developed on her skin 2 months after hospital discharge. Clinical and laboratory findings were consistent with a diagnosis of porphyria cutanea tarda. Treatment included discontinuation of iron therapy, local skin care, and phlebotomy, which prevented the development of more lesions. The roles of iron overload and chronic renal disease in the pathogenesis of the porphyria are discussed.

Porphyria cutanea tarda (PCT), recognized as a bullous dermatosis, was named more than 60 years ago by Jan Waldenström.¹⁻⁴ In this disease, bullae and erosions are often present on sunlight-exposed areas, including the face and, most commonly, the dorsa of the hands.^{2,4} These lesions may form scars and milia during the healing process.⁴ Additionally, hypertrichosis and areas of increased pigmentation sometimes develop.⁴

The most prevalent of the porphyrias, PCT is caused by the reduced activity or deficiency of the hepatic enzyme uroporphyrinogen decarboxylase (UROD).²⁻⁵ In porphyrias, intermediate metabolites in the production of the heme moiety accumulate because of specific enzymatic deficiencies.⁶ In PCT, uroporphyrinogen III is not metabolized as a

result of the deficiency of functional UROD.^{4,7} Auto-oxidation of uroporphyrinogen III produces photosensitizing porphyrins that collect in the skin, predisposing to the development of the cutaneous lesions.⁴

PCT is associated with several etiologic agents and conditions, including exogenous estrogens, alcohol, viral hepatitis, iron supplementation, and others.²⁻⁶ Hepatocyte damage seems to be the common pathway for all of the substances known to precipitate this disease.^{3,4,6-8} In addition, because most patients with PCT have excess iron within their hepatocytes, iron is believed to have an essential role in this elusive process.^{2-7,9} Iron may come from various sources, including oral supplementation and blood transfusion.^{5,8,10,11} We report a case of PCT in a patient with an acute gastrointestinal bleed and chronic renal insufficiency.

Case Report

An 80-year-old white woman was hospitalized for an acute gastrointestinal bleed from 2 large duodenal ulcers. Immediately after her admission to the hospital, she was transfused with 2 units of packed red blood cells because her hemoglobin level was 7.7 g/dL (normal: 12–16 g/dL). The patient required an additional 2 units of blood several days later because her hemoglobin level remained low at 8.2 g/dL. Erythropoietin therapy (3000 U/d, 3 d/wk) was also initiated because her recovery was complicated by anemia of chronic renal disease. The patient was already receiving oral iron supplementation (300 mg twice a day), which was started 1 week before admission to the hospital. These interventions, as well as specific therapy for the duodenal ulcers, raised her hemoglobin level to 11.5 g/dL by the time of discharge (3 weeks after hospital admission).

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Within 2 months of this hospitalization, the patient presented with multiple blistering lesions on her face, hands, arms, and legs. A review of her medical history revealed that she carried the additional diagnoses of chronic renal insufficiency, adult-onset diabetes mellitus, hypertension, and malnutrition. The patient denied a history of ethanol use and was not receiving estrogen replacement therapy. She also had no family history of similar skin disease. Physical examination revealed several superficial ulcerations and vesicles present on the face, neck, hands, and arms (Figures 1 and 2). Black terminal hair growth also was noted on the cheeks, temples, and forehead. Laboratory findings demonstrated a hemoglobin level of 13.5 g/dL and a ferritin level of 1215 ng/mL (normal: 10–200 ng/mL). Aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase were elevated at 120 U/L (normal, 15–45 U/L), 123 U/L (normal, 7–56 U/L), and 828 U/L (normal, 20–150 U/L), respectively. Other abnormal laboratories included a serum urea nitrogen level of 74 mg/dL (normal, 5–20 mg/dL) and a serum creatinine level of 2.7 mg/dL (normal, 0.5–1.5 mg/dL). The results of a urine porphyrin screen showed 3+ fluorescence, further supporting the diagnosis of PCT.

The patient was treated with daily skin cleaning and bacitracin ointment applied to open sores in addition to discontinuation of the oral iron therapy. For 2 weeks, her hemoglobin level was allowed to drift down on its own. At that time, new vesicles were still appearing on her hands, though they were cropping up less frequently, and most of the lesions were found to be in various stages of healing. Her hemoglobin level was 11.4 g/dL and 400 mL of blood was withdrawn by phlebotomy. Three weeks later, examination revealed only a few small eschars on her hands, and a hemoglobin level of 9.3 g/dL. Phlebotomy was then discontinued. The patient now remains free of new skin lesions.

Comment

With respect to the previously reported cases of PCT associated with blood transfusion, to our knowledge, this case is the first in which acutely bleeding duodenal ulcers were the initiating events.^{5,8,10,11} Review of the literature reveals that blood transfusion has contributed to the development of PCT in patients with several other medical conditions, including alcoholism, end-stage renal disease, hemophilia A, acute nonlymphocytic leukemia, viral hepatitis, estrogen supplementation, hepatotoxic drugs, and chronic lymphocytic leukemia.^{5,8-11} Of these case accounts, the patient with hemophilia was the only patient with gastrointestinal bleeding, which was

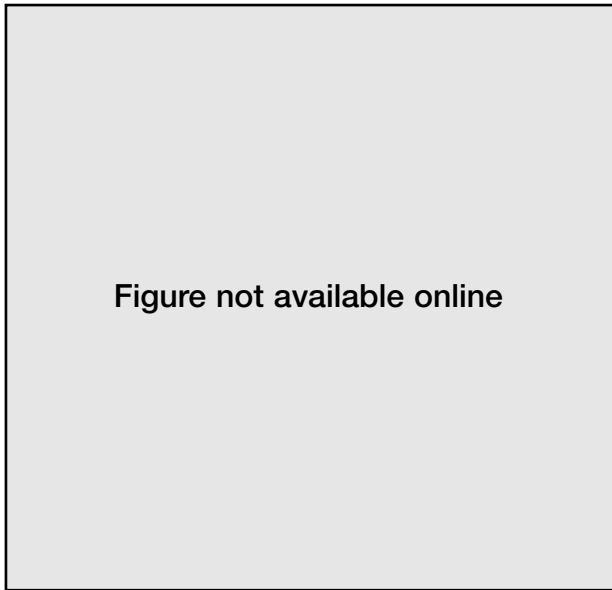


Figure 1. Healing ulcerations present on the dorsa of the hands and wrists.

later attributed to gastric ulceration.¹¹ Blood transfusions promote the development of PCT through the accumulation of excess iron.^{8,10,11} Our patient also was receiving iron supplementation, which has been associated with the development of PCT independent of blood transfusion.¹¹ In all, we calculate that the patient received 41 g of iron around the time of her hospitalization.³ Much of this iron may never have been absorbed; however, the transfusions alone provided the patient with nearly 800 mg of iron intravenously.³

The presence of renal disease in patients with PCT can complicate both diagnosis and treatment.^{9,12} It is known that PCT is sometimes found in association with end-stage renal disease because of several mechanisms, including reduced activity of UROD because of azotemia and reduced clearance of porphyrins by diseased kidneys or dialysis membranes.^{9,12,13} End-stage renal disease is also associated with anemia that results from endogenous erythropoietin deficiency. Our patient, in fact, was receiving exogenous erythropoietin. Erythropoietin replacement may actually be therapeutic in patients with renal disease and PCT.^{4,5,9,12} Alone or in combination with phlebotomy, erythropoietin facilitates the reduction of excess iron.^{4,5,9} Although our patient had chronic renal insufficiency that did not yet require dialysis, it is clear that the erythropoietin did not contribute to the development of PCT in this case.

The diagnosis of PCT in our patient was based on a classic presentation, history, random urine porphyrin screen, elevated liver function tests, and increased ferritin; however, some experts recommend

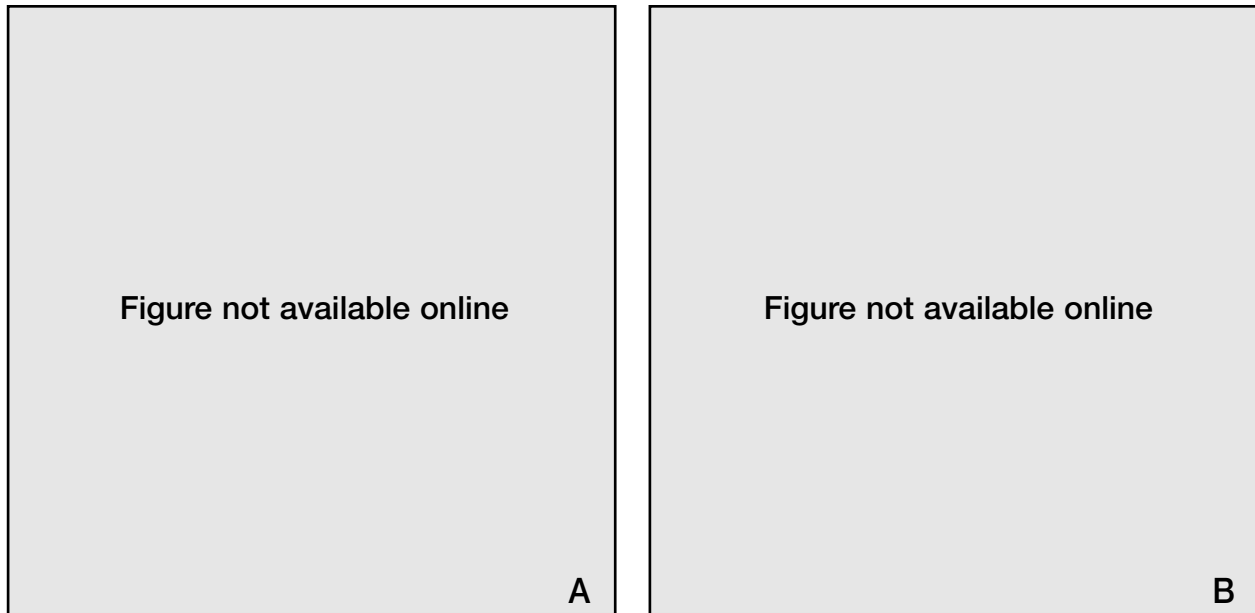


Figure 2. Multiple ulcerations and vesicles distributed evenly over the face. Note the presence of facial hypertrichosis (A). Close-up view of the lesions on the forehead (B).

additional laboratory evaluation. A simple urine screen, which involves Wood's lamp–induced fluorescence of urine that contains elevated uroporphyrins, is suggested as the initial screening laboratory test.¹⁴ If this is positive, a quantitative test for porphyrins in the urine may confirm the diagnosis.¹⁴ In PCT, uroporphyrins sometimes reach levels of 1000 µg or higher in a 24-hour collection specimen; nevertheless, the urinary porphyrin profile of PCT is nonspecific.^{4,8,10} For this reason, porphyrin levels from either the plasma or feces also may be needed to firmly establish a diagnosis.⁴ Though not diagnostic, other abnormal laboratory findings in PCT include elevated ferritin levels and mildly elevated liver function tests.^{2,4,5,8} Biopsy was not necessary to establish a diagnosis in our case. In actuality, the histopathology of PCT is also nonspecific among the cutaneous porphyrias, sometimes showing deposits of eosinophilic material, subepidermal bullae, and sclerotic changes in older lesions.^{4,15}

There are standard approaches to the treatment of PCT. Most of the therapies used produce remission through promoting recovery of the activity of UROD via a reduction in iron levels.^{4,5,7} Abstention from alcohol, iron supplements, and other substances known to precipitate PCT is usually mandatory.^{2,9} For more than 3 decades, phlebotomy has been used with great success.^{2,16,17} Phlebotomy results in remission of PCT through the accompanying depletion of excess iron.^{2,4,17} A reduction of serum ferritin to the normal range and a decrease of hemoglobin levels to about 11 to 12 g/dL generally

result in clinical improvement.⁴ The iron chelating agent deferoxamine mesylate also is used for the treatment of PCT and likewise works through iron depletion.⁴ Used alone or in combination with phlebotomy, chloroquine is reported to be effective.⁴ Finally, local skin care measures may be instituted to prevent further skin traumatization, relieve symptoms, and treat bacterial superinfection.^{2,8}

Both sporadic and familial forms of PCT are recognized.^{4,8} Based on our patient's history, we believe that she developed the sporadic form of the disease. However, the 2 types may have identical clinical features, and a negative family history does not rule out the possibility of familial PCT.^{4,8} Nevertheless, sporadic PCT has a much higher prevalence rate.^{4,8} The patient's continued remission also supports iron overloading from exogenous sources as the causative factor.

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