



Erythematous patches on the hands

Our patient's history of obsessive-compulsive disorder may have masked the true diagnosis for years.

A 49-YEAR-OLD CAUCASIAN MAN sought care at our clinic for erythematous patches on the dorsal surface of his hands. The patient indicated that these lesions had appeared approximately 2 to 3 years earlier and that they had become increasingly painful when exposed to sunlight. The patient's mother also recalled multiple sunburns that he'd suffered in the past.

The patient had a mild mental impairment and struggled with obsessive-compulsive disorder. He admitted to washing his hands 10 to 15 times a day, and was previously given a diagnosis of dyshidrosis secondary to excessive hand washing. The patient was treated with moisturizing creams,

but his symptoms did not improve.

Examination of the dorsal surface of his hands revealed multiple erythematous patches, blisters, and calluses, as well as ulcerations on the proximal and distal interphalangeal joints (FIGURE 1). There were also scarred and linear plaques on the bilateral proximal and distal interphalangeal joints. The patient had no other lesions on his body.

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

FIGURE 1

Erythematous patches, blisters, calluses, and ulcerations



PHOTOS COURTESY OF: DAVID A. KASPER, DO, MBA

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➤ **Hepatobiliary disease is present in about 25% of patients, and may be the only manifestation of the disease.**

Diagnosis: Erythropoietic protoporphyria

Erythropoietic protoporphyria (EPP) is a metabolic disease that is caused by a deficiency in ferrochelatase enzyme activity.^{1,2} Ferrochelatase is the last enzyme in the heme biosynthetic pathway, which is responsible for the incorporation of iron onto protoporphyrin IX.¹ Ferrochelatase activity in patients with EPP is typically 10% to 25% of normal, resulting in an accumulation of protoporphyrin IX in the skin, erythrocytes, liver, and plasma.^{1,3} There are both autosomal dominant and recessive forms of EPP, and it is the most common porphyria found in children.^{1,3}

■ **A characteristic that distinguishes EPP** from other porphyrias is the rapid onset of photosensitivity associated with pruritus and a stinging or burning sensation on the sun-exposed areas of the body—typically, the cheeks, nose, and dorsal surface of the hands.⁴ These symptoms are commonly followed by edema, erythema, and in more severe cases, petechiae.^{3,4} With repeated sun exposure, the affected skin may develop a waxy thickening with shallow linear or elliptical scars, making the patient's skin appear much older than it actually is.^{3,4} Although blisters, erosions, and crusting are not always present, they can manifest with prolonged sun exposure.¹

What you may also see

Hepatobiliary disease is present in about 25% of patients, and may be the only manifestation of the disease.¹ The deleterious effects of protoporphyrin are concentration dependent, so a wide variation in the severity of hepatobiliary disease exists. Cholelithiasis and microcytic hypochromic anemia are common on the mild end of the spectrum, but life-threatening complications such as hepatic failure have been reported in about 2% to 5% of cases.^{1,5}

■ **When it's diagnosed.** EPP usually manifests by 2 to 5 years of age, but it may not be diagnosed until adulthood.³ Such a delay may occur because of a lack of cutaneous lesions, mild symptoms, or a late onset of symptoms.¹

Consider these conditions in the differential

Contact dermatitis. This inflammatory skin

condition can occur when a foreign substance irritates the skin (irritant contact dermatitis) or result from a delayed hypersensitivity reaction that's evoked by reexposure to a substance (allergic contact dermatitis). Acute lesions are typically well defined and confined to the site of exposure. They are characterized by erythema, vesicles or bullae, erosions, and crusts. In chronic cases, the lesions are ill-defined and involve plaques, fissures, scaling, and/or crusts.^{4,6}

■ **Porphyria cutanea tarda.** This most common form of porphyria is characterized by increased sensitivity and fragility of the skin.³ (For more information, see "Genetic blood disorders: Questions you need to ask," *J Fam Pract*. 2012;61:30-37.) Vesicles and bullae will form after minimal trauma, typically on the dorsal surface of the hands, extensor surfaces of the forearms, and the face. These lesions will eventually form erosions and heal slowly to form atrophic scars. Excessive hair growth on the face, postinflammatory hyperpigmentation, scarring alopecia, and scleroderma-like changes with yellowish-white plaques have also been described in porphyria cutanea tarda. Wood's lamp examination of urine will reveal a coral-red fluorescence.^{4,7}

■ **Dyshidrotic eczema.** This disease is characterized by the sudden onset of pruritic, clear vesicles on the fingers, palms, and soles. The vesicles are deep-seated and are typically devoid of surrounding erythema. Each episode will spontaneously regress in 2 to 3 weeks, but this disease can be disabling due to the recurring nature of the outbreaks.^{4,8}

■ **Solar urticaria.** Within minutes of sun exposure, erythematous patches with or without wheals will appear. The lesions typically last less than 24 hours, and are most commonly found on the chest and upper arms. Pruritus and a burning sensation frequently accompany flares of solar urticaria, and pain may be present but is not a common symptom. In severe cases, an anaphylactoid reaction can occur, with light-headedness, nausea, bronchospasm, and syncope.^{4,9}

■ **Hydroa vacciniforme.** Within hours of sun exposure, erythematous macules will appear. They will progress to papules and vesicles, and may become hemorrhagic. These

lesions are typically found on the face, ears, and dorsa of the hands in a symmetric, clustered pattern. Pruritus and a stinging sensation may accompany the lesions, as well as general malaise or fever. Over the course of a few days, the lesions will become necrotic, form a hemorrhagic crust, and heal with "pox-like" vacciniform scars.^{4,9}

Confirm your suspicions with testing

There should be a high degree of suspicion for EPP when any child or adult presents with photosensitivity.^{10,11} The absence or delayed onset of visible lesions can make the diagnosis difficult and cause the patient considerable suffering.¹²

■ **If EPP is suspected**, order lab work for confirmation. The most diagnostically useful test is the erythrocyte protoporphyrin level, which will be increased in patients with EPP. These levels can range from several hundred to several thousand $\mu\text{g}/100\text{ mL}$ of packed red blood cells (normal = $<35\ \mu\text{g}/100\text{ mL}$).³ In addition, elevated levels of protoporphyrin are found in the feces. However, unlike other porphyrias, the level of urine porphyrins is normal (because protoporphyrin IX is water-soluble).^{1,3}

Due to the incidence of hepatobiliary disease in EPP, liver enzymes should be drawn and the proper imaging performed if abnormal values are obtained. Biopsy of the involved skin, with histologic review, will also aid in the diagnosis if other testing is inconclusive.^{1,4}

Treatment: Protection from sun is key

While complete sun exposure avoidance would prevent most sequelae in EPP, this is not always a feasible option. Covering the skin with sun-protective clothing and using sunscreen that contains titanium oxide or zinc oxide are acceptable alternatives to overt avoidance^{1,3,10,13} (strength of recommendation [SOR]: **A**). Beta-carotene at doses of 60 to 180 mg/d for adults or 30 to 90 mg/d for children to achieve a serum level of 600 mcg/dL has also been shown to be effective in reducing photosensitivity in some

cases^{1,2,5} (SOR: **B**). Cysteine, antihistamines, phototherapy, pyroxidine, and vitamin C have also been used to treat EPP, but have demonstrated limited efficacy^{1,3,10} (SOR: **B**).

■ **Hepatobiliary complications.** Treating hepatobiliary complications is dependent upon the degree of dysfunction. Cholestyramine can be used to increase the fecal excretion of protoporphyrins in liver dysfunction^{1,3,10} (SOR: **A**). In severe liver dysfunction, blood transfusions can be utilized until a liver transplant can be performed^{1,3,10} (SOR: **A**). Liver transplantation, however, does not correct the metabolic error, and damage to the transplanted liver can occur.¹

Sun block and supplements for our patient

After discussing the risks and benefits of treatment, our patient elected to use an over-

FIGURE 2

A dramatic improvement



After minimizing his exposure to the sun, using tacrolimus 0.1% ointment and a skin moisturizer, and taking a beta-carotene supplement, the appearance of our patient's hands improved. His hands were less erythematous and there were no ulcerations. Callus formation persisted.

the-counter zinc oxide sun block, as well as begin beta-carotene supplementation at 60 mg/d. We slowly increased the beta-carotene to therapeutic levels, and reevaluated for efficacy. To treat the lesions on his hands, we started the patient on tacrolimus (Protopic) 0.1% ointment once daily (to avoid using a topical steroid due to his skin fragility) and a skin protectant/moisturizer (Theraseal) 2 to

3 times daily to reduce irritation.

After treatment and minimal sun exposure for several months, our patient saw a dramatic improvement in his disease, with no blistering or ulcerations noted (FIGURE 2). **JFP**

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