

Delayed photosensitivity in a child with erythropoietic protoporphyria : a case report

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Abstract

Erythropoietic protoporphyria (EPP) is a genetically inherited disease that causes protoporphyrin accumulation in erythrocytes, skin, liver, bile, and stool. Clinically this manifests as photosensitivity with painful, edematous cutaneous porphyria. We present the case of a four-year-old boy with a delayed photosensitivity reaction to sunlight. In the evening following sun exposure, he would develop swelling and a violaceous rash on the dorsal surface of his hands and occasionally the helix of his ears. His reactions were severe, requiring morphine on more than one occasion prior to diagnosis. He later developed waxy depressed scars on his nose and cheeks. On laboratory investigation, both total and free protoporphyrin were elevated. Photosensitivity in EPP usually occurs minutes after sun exposure, but our patient had significantly delayed reactions. Genetic testing revealed mutation in the FECH gene that confirmed the diagnosis of EPP. Although rare, presentations of photosensitivity in the pediatric population should be carefully evaluated.

Keywords

Pediatric, dermatology

Introduction

Erythropoietic protoporphyria (EPP) is a rare inherited disorder with a prevalence ranging from 1 per 75,000–200,000.^{1,2} The majority of EPP cases are mutations in the FECH gene that lead to a ferrochelatase enzyme deficiency.³ Inheritance is complex, and families have been described with EPP following an autosomal recessive inheritance pattern.⁴

Ferrochelatase catalyzes the final step of the heme biosynthesis pathway. Patients with EPP accumulate protoporphyrin IX (PPIX) in erythrocytes, skin, liver, bile, and stool.⁵ When PPIX that has been deposited into the skin is exposed to light, free radicals are generated, causing skin injury.⁵ This reaction promotes complement activation and mast cell degranulation. EPP presents as photosensitivity that causes cutaneous changes characterized by erythema, pruritus, and pain. The classic presentation of EPP shows scarring on the dorsal surface of the hands, bridge of the nose, and cheeks.

In EPP, photosensitivity is usually immediate. Here, we describe a case report of EPP with reactions that were delayed for up to several hours.

Case report

A 4-year-old Caucasian boy was referred to our dermatology clinic with a history of photosensitivity. His parent's first

noticed this when he was approximately 18 months old. In the evening following sun exposure, he would develop edema and non-persistent violaceous eruptions on the dorsal surface of his hands and the helix of his ears. He would develop some swelling on his face and mild erythema on his nose, and rarely, he would have a rash on his ankles. This was associated with significant pain which often required morphine for pain management. The skin changes would last 12 h and would clear without residual erythema, pigmentation, papules, blisters, or scarring. Pain would not occur when he was directly under sunlight, but in as little as 20 min or up to 4 h following sun exposure. The family had tried various sunscreens but found them to be ineffective at controlling his symptoms.

Past medical history included aortic stenosis that was surgically corrected. He was not on any medications. Physical

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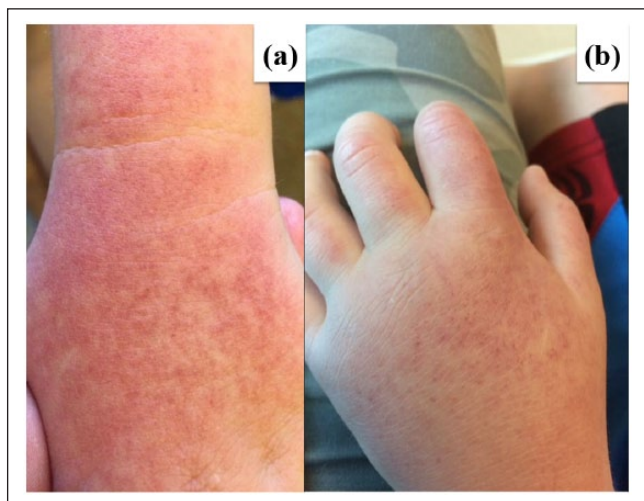


Figure 1. (a) Mottled erythema on the dorsal surface of the hands. (b) Significant edematous changes to the hand and digits.

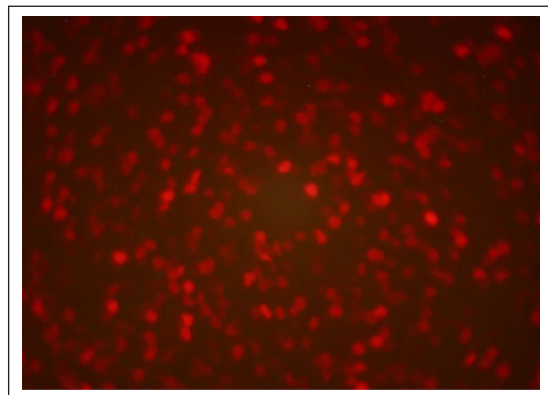


Figure 2. Fluorescence scan at 634 nm, confirming abundant porphyrin.

examination revealed subtle depressed scars on the dorsal surface of his nose and malar cheeks. His mother brought photos of the patient's hands when he was having a reaction (Figure 1). There was mottled reticulate violaceous erythema that involved the dorsal surface of the hands that extended a few centimeters above the wrist. There was no evidence of permanent poikilodermatous changes. He wore a superhero costume that covered most of his face and body, when he was outside to prevent sun exposure.

On laboratory investigation, total protoporphyrin in whole blood was elevated at 1937 mg/dL (reference: <80 mg/dL). Fractionation showed that free protoporphyrin was markedly elevated at 1894 mg/dL (reference: <20 mg/dL). Urinary porphyrin levels, antinuclear antibodies (ANA) and complement levels were normal. Zinc protoporphyrin level was also elevated at 200 (normal range 20–60). A fluorescence scan was performed; there was prominent fluorescence of red blood cells, indicating elevated protoporphyrin in the erythrocytes (Figure 2). Our patient also had a

microcytic iron deficiency anemia (iron total 9 µg/dL, total iron-binding capacity (TIBC) 73, Ferritin 6.4 ng/mL, Hgb 109 g/L, mean corpuscular volume (MCV) 62.7 fL), which is common in patients with EPP.

Full sequencing of the FECH gene revealed a base change at 315-48T>C and deletions in exons 8 and 9. Segregation studies revealed that these occurred in trans, a more common genotype.⁶ The patient's family was also tested for FECH gene abnormalities and given genetic counseling.

Discussion

EPP is the most common cutaneous porphyria in children. The most common genetic variant associated with EPP has been determined to be co-inheritance of a severe FECH defect along with a common low-expression variant IVS3-48C allele.⁶

Treatment options remain limited. Prevention and reduction of sun exposure to the skin is the mainstay of treatment.^{5,7,8} It has been suggested that opaque (zinc oxide or titanium dioxide) sunscreens offer some protection,⁵ but despite the judicious use of sunscreen in our patient, they found no benefit. We were able to provide the parents of our patient a permit for tinted windows on their family vehicle, so that sun exposure while driving would be limited.

Counseling for EPP includes reducing sun exposure. Population studies have found that patients with EPP often have vitamin D deficiency, and therefore, oral vitamin D supplementation should be given.^{9–11} We recommended that our patient receive oral vitamin D supplementation.

Once sun exposure has occurred, cold compresses and antihistamines help to abate symptoms.⁸ However, in our patient's case, these attacks had been so severe as to require morphine for pain management. Despite the severity of these symptoms, permanent cutaneous changes were almost indiscernible, which, although unusual, has been described in cases previously.^{12,13} It follows that since patients with EPP have a risk of liver failure, hepatotoxic medications should also be avoided. Systemic cimetidine has had promising results in a few cases.¹⁴ We prescribe cimetidine 30 mg/kg/day in two doses for our patient with excellent therapeutic result. Our patient has had remarkable increased tolerance to sunlight since starting cimetidine in conjunction with other routine sun protective measures. Our patient and his family has had an improved quality of life that has been described by the mother as “truly life changing.”

Up to half of all patients with EPP have anemia.¹⁵ Treatment with iron has been found to paradoxically improve patient symptoms but is an area for further study.¹⁶

We present a case of a boy with EPP that had delayed and severe photosensitivity. Although traditionally EPP presents with reactions while in the sun, some may have a delayed photosensitivity reaction. This case serves as a reminder that pediatric patients presenting with photosensitivity need to be evaluated carefully. Our patient unfortunately was not referred to dermatology for evaluation in a timely manner as

the delayed photosensitivity clouded EPP as a diagnosis. This case also adds to the clinical evidence that cimetidine is an effective and well-tolerated treatment option for EPP.

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Informed consent

Consent to perform and submit this case report for publication was given by the patient's mother.

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