

MILD CONGENITAL ERYTHROPOIETIC PORPHYRIA WITH PREDOMINANT SCARRING

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Abbreviation **CEP** = congenital erythropoietic porphyria.

Case report. A 15-year-old female, born to third-degree consanguineous parents, presented for evaluation of scarring on the face, neck, chest, and forearms. The patient was in good health until age 6 months, when her parents noticed dark-colored urine. At 18 months of age, she began developing bullae on the scalp, face, neck, chest, forearms, hands, and feet. These lesions healed with scarring. Since age 7, the frequency of bulla formation decreased until complete cessation. The patient denied photosensitivity, trauma-induced blistering, abdominal pain, or jaundice, and had no history of blood transfusions. Her intellectual development was age-appropriate, and there was no family history of similar conditions.

Physical examination revealed facial hypertrichosis (Fig. 1) with intact eyebrows and eyelashes, multiple atrophic scars, a deformed nose (Figs. 1, 2), hypermelanotic macules, and brownish dyschromia of the teeth. Atrophic scars were also noted on the upper back, the dorsum of the feet, and the hands; the latter exhibited short, stubby digits with normal nail plates (Fig. 3). The urine was reddish-brown and exhibited pink fluorescence under Wood's lamp examination; however, the teeth did not show fluorescence.

Based on the clinical history and physical findings, the differential diagnoses considered included congenital erythropoietic porphyria (CEP), hepatoerythropoietic porphyria, epidermolysis bullosa, and chronic bullous disease of childhood.



Fig. 1



Fig. 2

Fig. 1, 2: Congenital erythropoietic porphyria with predominant scarring and hypertrichosis.



Fig. 3

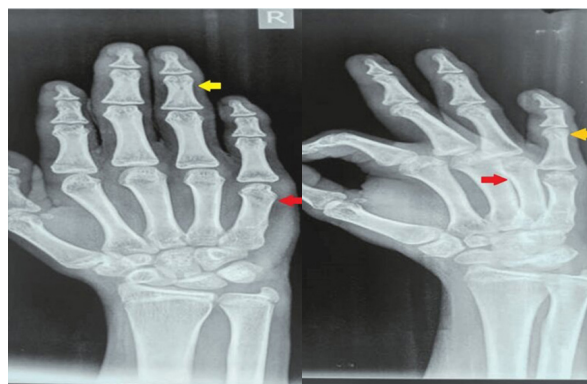


Fig. 4

Fig. 3, 4: Short, stubby fingers with normal nails, scars on the dorsum of the hands and feet (Fig. 3). Premature epiphyseal closure of the metacarpals (red arrows) and phalanges (yellow arrows), with shortening of the fourth and fifth metacarpals (Fig. 4).

Immunohistochemical studies were within normal limits, with the exception of urinary porphyrin levels, which were significantly elevated. Radiographs of the hands demonstrated premature epiphyseal closure of the metacarpals and phalanges, with shortening of the fourth and fifth metacarpals (Fig. 4). Abdominal and pelvic ultrasonography revealed no abnormalities. Histopathological examination of a skin biopsy showed superficial dermal edema and thickened vessel walls. Molecular analysis identified a rare homozygous pathogenic variant in exon 2 of the *UROS* gene: c.56A>G (p.Tyr19Cys). Consequently, a definitive diagnosis of congenital erythropoietic porphyria was established.

The scars were treated with fractional CO₂ laser (FCL) therapy in combination with platelet-rich plasma at 4-week intervals, following a test spot on the forehead. Although the patient reported a localized increase in facial hair, significant improvement in the scarring was observed. Treatment was continued with two additional FCL sessions, resulting in further attenuation of the scars. No new bullae or signs of photosensitivity were observed throughout the treatment and follow-up periods.

Discussion. Congenital erythropoietic porphyria (CEP), also known as Günther disease, is a rare inborn error of heme biosynthesis. It is most commonly caused by an autosomal recessive mutation in the *UROS* gene, though an X-linked mutation in the *GATA1* gene has also been sporadically reported (1).

The genetic alteration is responsible for a deficiency in the enzyme uroporphyrinogen III synthase, which is critical for heme synthesis. This enzymatic deficit leads to the accumulation of type 1 isomeric porphyrins in erythrocytes and plasma, resulting in phototoxicity, hemolytic anemia, and dental and skeletal abnormalities. The accumulation of these abnormal porphyrins varies significantly depending on the specific mutation and its expression level. This variability accounts for the marked phenotypic heterogeneity of CEP, with manifestations ranging from severe prenatal presentations, such as non-immune hydrops fetalis, to mild cutaneous symptoms in adulthood (2).

Photocatalytic and cytotoxic porphyrins, released via erythrocyte lysis, accumulate in plasma and tissues, leading to characteristic clinical features. Cutaneous symptoms include severe photosensitivity with blistering and skin fragility in sun-exposed areas, progressing to scarring, pigmentary changes, hypertrichosis, and potentially the loss of digits or facial features such as the eyelids, nose, and ears.

The current case is unique due to the presence of currently inactive cutaneous lesions in the absence of photosensitivity and systemic involvement. Furthermore, the premature epiphyseal closure of

the metacarpal and phalangeal bones is a notable finding. A similar case was previously described in an 8-year-old child who lacked photosensitivity and systemic involvement, presenting only with erythrodontia, hypertrichosis, and skin fragility with minimal scarring on the dorsal hands and nasal tip; however, genetic analysis was not performed in that instance (3).

In our patient, a rare homozygous pathogenic mutation was identified: c.56A>G (p.Tyr19Cys) in exon 2 of the *UROS* gene. This mutation has been found to cause instability and premature degradation of uroporphyrinogen III synthase, reducing overall normal enzymatic activity to approximately 1.1% (4). A review of the literature revealed that a 13-year-old male harboring the same *UROS* mutation presented with infancy-onset photosensitivity, recurrent blistering in sun-exposed areas, hypertrichosis, erythrodontia, and left cryptorchidism (5). Despite identical homozygous genetic defects, the phenotypic variability between these two cases underscores the complexity of genotype-phenotype correlations, a phenomenon reported in other clinical series (6, 7). These variations may be attributed to several factors, including variability in *UROS* mutations (8), protein misfolding (9), heteroallelic mutations (10), and the influence of modifier genes (11).

Regarding the management of scarring – which can significantly impact social well-being in mild cases – the primary contraindication for laser therapy in porphyria patients is the high risk of severe photosensitivity triggered by the cutaneous photoactivation of porphyrins, which can exacerbate disease activity. To date, only a few cases have reported the use of lasers (Er: YAG, IPL, CO₂ laser) for scar revision in porphyria patients (12). Our patient was treated with fractional CO₂ laser (FCL) without symptom aggravation, achieving moderate clinical improvement.

Conclusion. This case of congenital erythropoietic porphyria is presented to highlight its rarity and to emphasize the significant clinical variability inherent to the disease. The successful use of fractional CO₂ laser in this context suggests it may be a viable option for scar management in select patients with inactive disease.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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