Picture of the Month

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A 5-YEAR-OLD BOY, born in the United States to Pakistani parents, had a history of skin problems and the passage of pink-red urine since birth. He developed severe phototoxic reactions, including vesicles and bullae with resultant scarring, in areas of the skin exposed to the sun. His face was most severely affected (Figure 1). The dorsum of both hands demonstrated hyperpigmentation with irregular areas of hypopigmentation and skin atrophy (Figure 2). In addition to the cutaneous changes, on physical examination he was found to have hepatosplenomegaly and red-stained teeth.

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Denouement and Discussion

Congenital Erythropoietic Porphyria (Günther Disease)

Figure 1. The skin of the face, particularly the nose and perioral areas, shows severe phototoxic damage with bullae, vesicles, hemorrhagic crusts, and scarring.

Figure 2. The dorsa of the hands are hyperpigmented with areas of hypopigmentation and skin atrophy.

Congenital erythropoietic porphyria (CEP), also known as Günther disease, is a rare inherited disorder of porphyrin metabolism caused by a deficiency of uroporphyrinogen III synthase (or cosynthase). Although first described by Schultz in 1874, CEP was named after Günther who described the disorder, which he named *hematoporphyra congenita*, in detail in 1911. To date, only 130 cases of CEP have been published in the world literature.

The diagnosis of CEP is often first suspected by the presence of reddish or brown staining of the diapers in neonates or infants. Photosensitivity becomes apparent within the first few months of life and is manifested by the development of vesicles and bullae in light-exposed areas of the skin that become crusted and superinfected. Scarring associated with hyperpigmentation and mutilation is commonly seen, particularly involving the phalanges, ears, and nose. Hypertrichosis in the form of fine, downy hair over the face and extremities is common. Porphyrin deposits in the teeth are responsible for the reddish or brown discoloration. Additional characteristic manifestations include hemolytic anemia, splenomegaly, gallstones, and pathologic fractures of bone.

The mode of inheritance of CEP is autosomal recessive. The biochemical defect is a homozgyous deficiency of the enzyme uroporphyrinogen III synthase. The defect results in the marked overproduction of uroporphyrin I and coproporphyrin I in circulating erythrocytes and bone marrow cells, which then accumulate throughout the body. The porphyrins are excited by radiant energy, resulting in the release of energy that reacts with oxygen to produce free radicals and singlet oxygen, which in turn damage surrounding tissues and cells.

The enzyme activity in erythrocytes and fibroblasts of affected individuals is typically 2% to 10% of normal, while the activity level is intermediate in carriers of the disorder who are otherwise healthy. Mutations causing CEP are heterogeneous.

The clinical picture, consisting of the early onset of vesicular or bulbous photosensitive skin lesions, resulting in mutilating scarring, the passage of pinkish-red urine, and erythodontia, should rapidly suggest the diagnosis. Teeth and urine will fluoresce reddish-pink under the Wood light. The diagnosis can be confirmed by finding elevated levels of urinary and erythrocyte porphyrins, a pattern that is specific for CEP.

The differential diagnosis of CEP includes other types of porphyria that are characterized by photosensitivity, such as hepatoerythropoietic porphyria and porphyria cutanea tarda. Although hepatoerythropoietic porphyria and porphyria cutanea tarda may present within the first few years of life, the photosensitivity seems to diminish with age and is followed by hypertrichosis, hyperpigmentation, and sclerodermalike scarring. Erythropoietic protoporphyria usually presents in childhood with burning or stinging sensations of the skin followed later by phototcutaneous lesions. Vesicles and bullae are rare in this form of porphyria. Children with xeroderma pigmentosum have severe photosensitivity but normal porphyrin metabolism.

The prognosis of CEP is poor, frequently culminating in death in early adulthood and occasionally in the neonatal period. The only preventive measure is the absolute avoidance of sunlight exposure. Protection from trauma to the skin and aggressive treatment of cutaneous infections may help delay scarring and mutilation. Other therapies that have shown some benefit are oral beta carotene to reduce sun sensitivity, erythrocyte transfusions and splenectomy for the hemolytic anemia, and the oral administration of adsorbents such as charcoal and cholestyramine. Allogenic bone marrow transplantation may be curative in patients with severe phenotypes.

Some students of the porphyrias believe that the clinical picture of individuals with CEP, particularly their avoidance of sunlight, the mutilated skin, red teeth, and hypertrichosis, led to the development of the folklore of the werewolf in medieval Europe.

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REFERENCES


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