

Congenital erythropoietic porphyria – A case report

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Abstract Porphyrins form a group of metabolic disorders caused due to defects in the heme synthetic pathway. Congenital erythropoietic porphyria (CEP) is a rare autosomal recessive form of cutaneous porphyria with less than 200 cases reported in the literature, clinically characterized by marked skin photosensitivity, hypertrichosis, blistering, scarring, milia formation and dyspigmentation of the photo-exposed areas. We report a case of CEP in a four year old male child who presented with features of photosensitivity with darkening of urine color followed by blistering over the photoexposed sites and mutilation of face, hands and feet. Woods lamp examination of teeth and elevated urinary porphyrin levels confirmed the diagnosis.

Key words

Porphyria, congenital erythropoietic porphyria, photosensitivity, Gunther's disease, uroporphyrinogen III cosynthase.

Introduction

Congenital erythropoietic porphyria (CEP), also known as Gunther's disease, is a rare autosomal recessive form of cutaneous porphyria, clinically characterized by severe skin photosensitivity, blistering, scarring, milia formation, hypertrichosis, and dyspigmentation of the photoexposed areas. Mostly it manifests during infancy or early childhood and has a wide spectrum of manifestations ranging from hydrops fetalis *in utero* to severe disease starting in infancy to mild forms presenting during adulthood. In the past, the prognosis of CEP was poor but, now with improved supportive care, it has improved greatly.¹ Herein, we present a case of CEP in a four-year-old male child who presented with features of photosensitivity with darkening of urine followed by blistering over the photoexposed sites and mutilation of face, hands and feet.

Case Report

A four-year-old male child, a single child born of consanguineous marriage, presented with history of recurrent blistering followed by scarring on the photoexposed areas since the age of six months. Since early infancy the mother of the child had noticed reddish coloured urine. There was no history of acute attacks or any history of seizure disorders. There was no history of any similar lesions in the family members. On examination, there was diffuse crusting and scarring over the face and dorsa of hands and feet (**Figure 1**). There was loss of hair over the scalp but hypertrichosis was seen over the shoulders and arms. There was ectropion of both lower lids along with congestion and mucopurulent discharge. There was mottled pigmentation and diffuse scarring over the hands and feet with mutilation and loss of distal part of fingers and nails (**Figure 2**). The teeth were reddish in colour and showed a pink-red fluorescence under Wood's lamp (**Figure 3, 4**). The child had no hepatosplenomegaly or any evidence of hemolysis.

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A clinical diagnosis of CEP was made on the basis of history and clinical examination. Routine laboratory investigation revealed the presence of anemia (Hb-6gm%), whereas other hematological and biochemical parameters were normal. Urinary total porphyrin levels were found to be markedly raised on spectrophotometry (1047 nmol/mmol of creatinine, normal <35 nmol/mmol). Twenty four hour urinary uroporphyrin and coproporphyrin levels were also found to be significantly elevated.

The increased porphyrin and uroporphyrin levels confirmed the diagnosis of CEP. The child was managed symptomatically and was advised sunscreens, oral β -carotene and topical antibiotics for erosions.

Discussion

CEP is a rare variant of cutaneous porphyria, with less than 200 cases being reported in the literature till date. It has an autosomal recessive transmission and is caused due to deficiency of the enzyme uroporphyrinogen III cosynthase, which leads to an increase in uroporphyrin I and coproporphyrin I in plasma, red blood cells, urine, feces, and in different tissues. The C73R mutation is the most frequent, in which cysteine is substituted by arginine.^{1,2} These type I porphyrinogen isomers are oxidized to their corresponding porphyrins leading to photosensitivity which manifests clinically as blistering and erosions over photoexposed sites. Their excretion through the renal route imparts the reddish colour to the urine.²

The clinical manifestations of CEP are variable and range from hydrops fetalis *in utero* to mild cutaneous blistering in the adult onset cases. The hallmark clinical feature is phototoxicity, which is characteristically very severe and even phototherapy for jaundice may precipitate lesions in affected children. Photoexposed skin is very fragile leading to the formation of blisters, and recurrent

blistering and atrophic scarring results in characteristic mutilation of face and fingers. This mutilation may be associated with erosion of terminal phalanges, onycholysis and destructive changes of pinnae and nose. Hypertrichosis of the temples, malar region and extremities is common. Mottled dyspigmentation is seen even in non-exposed areas. Erythrodontia is also a classical finding and pink-red fluorescence of teeth is seen under Wood's lamp due to accumulation of porphyrins in the enamel. Porphyrins are also deposited in the bone resulting in loss of bone and subsequent contractures and deformities. Ocular findings like keratoconjunctivitis, corneal ulcers, ectropion and optic atrophy may also be seen. Hemolytic anemia is also seen in many cases which may be associated with hypersplenism.¹⁻³

The photosensitivity differentiates CEP from other childhood blistering disorders like epidermolysis bullosa but cutaneous features are indistinguishable from porphyria cutanea tarda or variegata porphyria, which can be differentiated by assessment of uroporphyrin levels in blood and urine.

The diagnosis is mainly confirmed by the presence of elevated levels of uro- and coproporphyrin (type I) in the urine and blood. Bright pink fluorescence of urine, teeth and bones under Wood's lamp illumination also helps in diagnosis. The brilliant fluorescence of nuclei in erythrocyte precursor cells with presence of heme inclusion bodies in their nuclei is also seen in CEP.⁴ Skin biopsy shows subepidermal blister with superficial perivascular lymphocytic infiltrate and blood vessels show thickened, hyalinized periodic acid-Schiff (PAS) positive walls.¹

Genetic counselling is important for the parents of an affected offspring. Antenatal diagnosis can be made by measuring the uroporphyrin I concentration in the amniotic fluid which is increased as early as 16 weeks *in utero*.



Figure 1 Diffuse crusting and scarring over the face with ectropion of the eyelids.



Figure 2 Mutilation deformity of the hands.



Figure 3 Reddish discoloration of the teeth.



Figure 4 Reddish fluorescence of teeth seen on Wood's lamp examination.

The management is mainly symptomatic and sun avoidance with strict use of sunscreen is most important. Oral photoprotective agents like β -carotene also help in cutaneous symptoms. Splenectomy to reduce anemia and thrombocytopenia, transfusion regimens, and intravenous haematin therapy to suppress hemoglobin production may be required in severe cases. Allogenic bone marrow transplant is the treatment of choice in severe CEP as it provides a long-term cure, but owing to the complications associated with it, it should be reserved for the severely affected patients. Gene therapy has been successfully tried *in vitro*, but no *in vivo* studies have been done yet.^{2,5}

References

1. Fritsch C, Bolsen K, Ruzicka T, Goerz G. Congenital erythropoietic porphyria. *J Am Acad Dermatol.* 1997;**36**:594-610.
2. Murphy GM. The cutaneous porphyrias: A review. The British Photodermatology Group. *Br J Dermatol.* 1999;**140**:573-81.
3. Bickers DR, Frank J. The Porphyrias. In: Wolff K, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, editors. *Fitzpatrick's Dermatology in General Medicine. 7th edn.* New York: McGraw-Hill; 2008. p.1228-56.
4. Zaider E, Bickers DR. Clinical laboratory methods for diagnosis of the porphyrias. *Clin Dermatol.* 1998;**16**:277-93.
5. Murphy GM. Diagnosis and management of the erythropoietic porphyrias. *Dermatol Ther.* 2003;**16**:57-64.