CONGENITAL ERYTHROPOIETIC PORPHYRIA ABOUT A SUCCCESSFUL EVOLUTION CASE

Diana Espitia-Hernandez [a,1], **Nicolle Guiot-Isaaca** [a], **Daniela Chaparro-Reyesa** [a,b], **Carolina Cortes-Correa** [a,b] **and Elkin, Peñaranda-Contreras** [a,b]

[a] Dermatology Department, Hospital de la Samaritana, Bogotá, Colombia. , [b] DERMAS Research Group, Hospital de la Samaritana, Bogotá, Colombia.

ABSTRACT Background: Congenital erythropoietic porphyria is an extremely rare autosomal recessive disease caused by the deficient enzymatic activity of uroporphyrinogen synthase III (UROS), leading to the accumulation of type I porphyrin isomers and impaired heme group synthesis, which cause the clinical manifestations, mainly cutaneous, hematologic, ophthalmic and osseous. The diagnosis is based on high levels of uroporphyrinogen type I in the urine, coproporphyrinogen in faeces, and the clinical findings. **Clinical case:** A 31-year-old female patient with a longstanding history since childhood of multiple hyper and hypopigmented spots on the back of the hands and the face, mild destruction of the nasal cartilage, scarring and perioral retraction, sclerodermiform changes, erythrodontia and marked phalangeal retraction. She was diagnosed with congenital hematopoietic porphyria and put on conservative treatment, resulting in a favourable course and clinical stability. **Conclusions:** It is important to know the different manifestations of this disease in order to make a timely diagnosis and avoid progression. Although rare, this disease can be associated with high morbidity if untreated.

KEYWORDS Porphyria, erythropoietic, porphyrins, Urobilinogen

Introduction

Congenital erythropoietic porphyria, or Günther's disease, is an autosomal recessive condition of approximately 200-300 cases worldwide [1,2]. The pathophysiology is a deficiency in the enzymatic activity of uroporphyrinogen III synthase (UROS) [3]. The gene that encodes the enzyme is located on the long arm of chromosome 10. However, the disease has been associated with 49 types of mutations, the most common being the C73R mutation, where cysteine is replaced by arginine, modifying the structure of the enzyme while at the same time affecting its function [4]. Heme group synthesis results from 8 enzymatic processes, where UROS is the fourth enzyme responsible for hydroxymethylbilane rearrangement and cyclization to generate uroporphyrinogen IIII [4]. A deficiency of this enzyme causes an accumulation of hydroxymethylbilane, which metabolizes to coproporphyrinogen I [5]. Accumulating these two components generates uroporphyrin I and coproporphyrin I from autoxidation [5]. These porphyrins accumulate mainly in the bone marrow, skin and bone, giving rise to the main symptoms of the disease [6]. The most severe clinical picture develops from the first months of life. It is characterized by hemolytic anaemia, erythrodontia, hypertrichosis, irregular skin hyper and hypopigmentation, cicatricial alopecia and extreme sensitivity to sunlight resulting in the formation of vesicles and subepidermal blisters. Frequent infections, a delayed repair and healing process, bone resorption and nasal and auricular cartilage destruction create progressive mutilation of body areas exposed to light (face and hands) [7,8]. Adult forms of late onset of the disease are less severe because of mild skin photosensitivity associated with thrombocytopenia or myelodysplasia [5].

Case report

A 31-year-old female patient with no significant family history who, since infancy, presented lesions in the face and hands. The dermatology service has followed the patient because of a diagnosis of congenital erythropoietic porphyria. On physical examination, there was evidence of multiple hyper and hypopigmented spots on the back of the hands and the face, with mild destruction of the nasal cartilage, zones of scarring and perioral retraction, sclerodermiform changes, erythrodontia and marked

DOI: 10.5455/IJMRCR.172-1669134895
First Received: November 22, 2022
Accepted: April 1, 2023
Associate Editor: Ivan Inkov (BG);
[1]Corresponding author: D Espitia-Hernandez dm.espitia171@uniandes.edu.co

phalangeal retraction (Figure 1-3).

Laboratory tests were ordered based on the clinical findings. The results included increased porphobilinogen in 24-hour urine (2.9 mg/24 hours; normal range: 0-2mg/24 hours). Genetic testing showed the pathogenic variant c.217T>C (p.Cys73Arg) in the UROS gene and the uncertain significance variant c.50A >G (p.Asp17Gly: Het) in the UROS gene, confirming the diagnosis of congenital erythropoietic porphyria.

The patient was advised to avoid sun exposure and use sunscreen and physical photoprotection items. With these recommendations, the patient has remained stable, with no new skin lesions. She is on follow-up by a multidisciplinary team that includes physiatry and occupational therapy to address hand retractions and haematology due to the presence of thrombocytopenia and splenomegaly without anaemia.

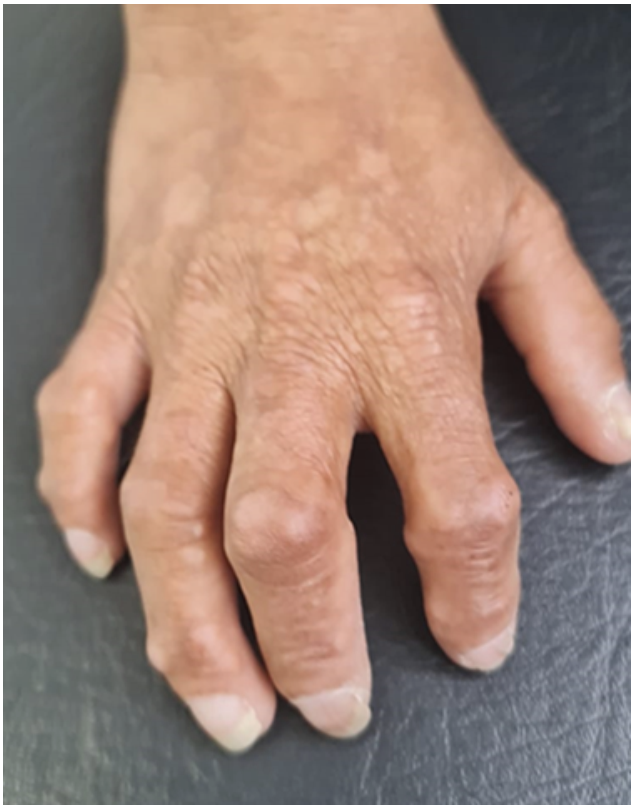

Figure 1: Multiple hypopigmented spots in the right hand, with phalangeal retraction.

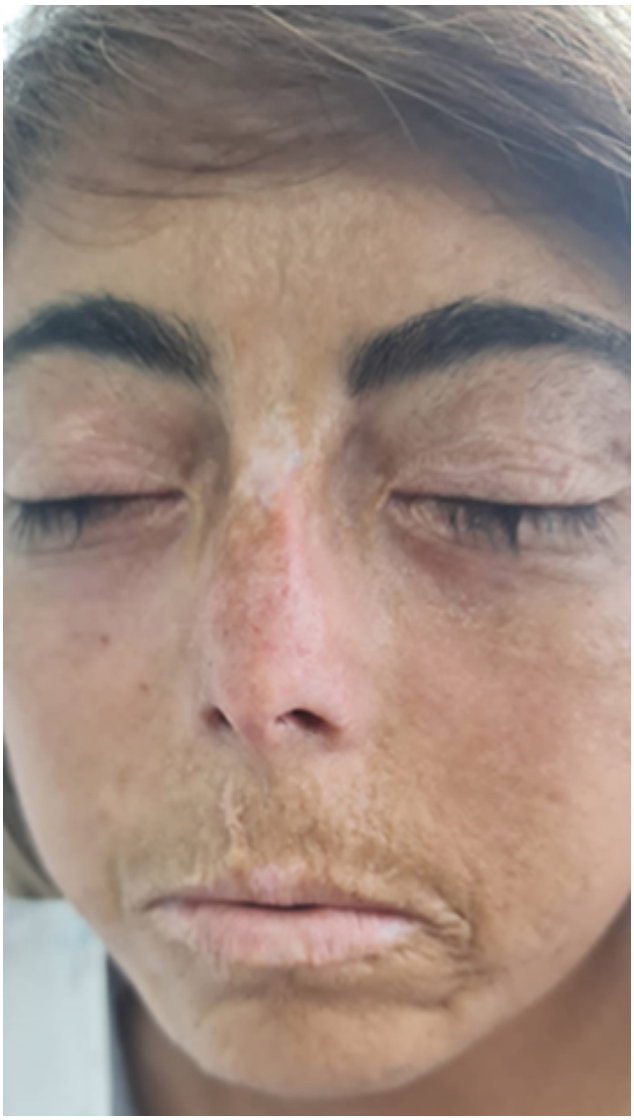

Figure 2: Bird-like facies, hypopigmented spots in the upper part of the nasal bridge, multiple hyperpigmented spots on the nasal bridge and upper lip, and areas of residual scarring in the perioral region.

Discussion

Günther's porphyria is a rare hereditary disease secondary to a deficiency in the enzymatic activity of uroporphyrinogen synthase III [3]. This metabolic defect leads to the accumulation of porphyrins, uroporphyrin and coproporphyrin, mainly in the skin, giving rise to phototoxic lesions [3,4]. The diagnosis is based on clinical and paraclinical findings, including high porphyrin levels in urine, faecal samples, or uroporphyrinogen III inactivity [5].

Clinically, this porphyria subtype is characterized by severe compromise due to photosensitivity-induced lesions with blister and scar formation and mutilation of phalanxes, ears and nose. These mutilations were present in our patient, together with perioral scarring, erythrodontia, areas of hypo and hyperpigmentation and phalangeal retractions, which are some other manifestations of the disease [5]. Other frequent findings include hypertrichosis and cicatricial alopecia, but none of these were present in this case.

On the other hand, haematological manifestations are found in the more severe forms of the disease, including myelodysplasia or hemolytic anaemia requiring transfusions [6]. In our case, the patient had mild thrombocytopenia sustained over the years, with no cell line abnormalities found in the peripheral blood smear and the latest laboratory results showing moderate basophilia and neutropenia. Other manifestations have been described, such as corneal ulcers and scars that may result in blindness and osteopenia due to demineralization. However, these have not affected our patient despite her longstanding condition. So far, no highly effective treatment has been reported for curing this condition; however, the fundamental pillar in managing these patients is photoprotection, hence the need to

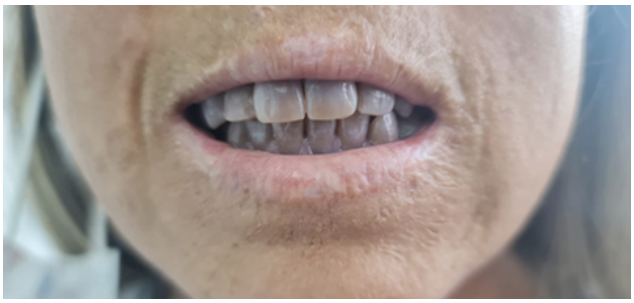

Figure 3: Erythrodontia

recommend the use of hats, glasses and clothing to limit exposure [4]. Other protection and light tolerance therapies that have been described are beta-carotenes and mineral sunscreens [5]. Activated charcoal and colestyramine are options to alter porphyrin enterohepatic circulation to increase excretion; however, issues have been associated with their use because of the need for high doses [3,5]. On the other hand, splenectomy, subcutaneous erythropoietin and chronic hypertransfusion have been used to reduce endogenous porphyrin production and improve anaemia [3,5]. Cases of successful use of bone marrow transplant as curative therapy have been described. This treatment is based on bone marrow replacement with unaltered hematopoietic stem cells to impact porphyrin overproduction; however, this therapeutic approach must be studied in advance because of its associated risks and complications [3,5]. Our patient is still on treatment with primary prevention measures, using physical photoprotection barriers and with regular interdisciplinary follow-up and has not required pharmacological treatment. The clinical course has been satisfactory, considering how severe the disease can be.

Informed Consent:

Written informed consent was obtained from all the participants.

Ethics Committee Approval

According ethics consent.

Conflict of Interest:

No potential conflict of interest relevant to this article was reported.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

References

1. Darwich E, Herrero C. Novedades en las porfirias eritropoyéticas. Actas Dermosifiliogr [Internet]. 2013;104(3):212–9. Available from: https://www.sciencedirect.com/science/article/pii/S0001731012002190

2. Fritsch C, Bolsen K, Ruzicka T, Goerz G. Congenital erythropoietic porphyria. J Am Acad Dermatol [Internet]. 1997 Apr 1;36(4):594–610. Available from: https://doi.org/10.1016/S0190-9622(97)70249-4

3. Desnick RJ, Balwani M. The Porphyrias. In: Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson JL, editors. Harrison's Principles of Internal Medicine, 21e [Internet]. New York, NY: McGraw-Hill Education; 2022. Available from: accessmedicine.mhmedical.com/content.aspx?aid=1190503045

4. Fernando González L, Motta A. Porfiria eritropoyética congénita Congenital erythropoietic porphyria Correspondencia. Vol. 22, Porfiria eritropoyética congénita Rev Asoc Colomb Dermatol. 2014.

5. di Pierro E, Brancaleoni V, Granata F. Advances in understanding the pathogenesis of congenital erythropoietic porphyria. Br J Haematol [Internet]. 2016 May 1;173(3):365–79. Available from: https://doi.org/10.1111/bjh.13978

6. Howard M, Hall A, Ramsay D. Congenital erythropoietic porphyria (Gunther disease) – Long-term follow up of a case and review. Dermatol Online J. 2016 Jan 1;23.

7. Erwin AL, Desnick RJ. Congenital erythropoietic porphyria: Recent advances. Mol Genet Metab [Internet]. 2019;128(3):288–97. Available from: https://www.sciencedirect.com/science/article/pii/S1096719218306474

8. Salomone CB, Ogueta IC, Reyes C v., Durán GS, Aguirre N, Wietstruck A. Congenital erythropoietic porphyria: Case report and management recommendations. Arch Argent Pediatr. 2018 Apr 1;116(2):e300–2.