Case Report

Congenital Erythropoietic Porphyria: A Comprehensive Case Report and Review of Management Strategies

Maria Agha,[1] Humaira Shamim,[2] Shazia Agha,[3] Asad ullah Khan,[4] Fatima Haroon,[5]

Abstract

Congenital Erythropoietic Porphyria (CEP) is a rare, autosomal recessive disorder of porphyrin metabolism, also known as Gunther's disease or "pink-tooth" disease. The mutation in the heme biosynthesis pathway leads to the accumulation of immature porphyrin intermediates (protoporphyrin) in various tissues of the human body. CEP is a rare genetic disorder, occurring in fewer than 1 in 1,000,000 children, with fewer than 280 cases reported worldwide. Due to impaired enzyme function, excessive amounts of porphyrin accumulate in various tissues, such as plasma, bone marrow, red blood cells, urine, teeth, and bones. We report a 7 years old boy with multiple blisters, scarring and elevated liver enzymes .He had orthodontia, red colored urine and severe anaemia. His skin biopsy showed deposition of porphyrin under dermis thus confirming diagnosis of Cogenital Erythropoietic Porphyria.

Keywords: Gunther's Disease, Congenital Erythropoietic Porphyria (CEP), , Erythrodontia, , Wood's Lamp.

How to cite: Agha M, Shamim H, Agha S, Khan AU, Haroon F. Impact of Hirsutism on Quality of Life of Patients Using Dermatology Life Quality Index. Esculapio - JSIMS 2024;20(04): 612-615

DOI: https://doi.org/10.51273/esc24.25204.28

Introduction

Congenital Erythropoeitic Porphyria (CEP)is also known as pink tooth or Gunther disease.[1]

There is accumulation of immature Protoporphyrin in various tissues of human body due to enzyme mutation in heme biosynthesis.[2]

Photosensitivity causes severe skin reaction like blisters formation, scarring and secondary infections. Abnormal heme synthesis leads tohemolysis and child may present with severe anemia. Other clinical manifestations include red coloured urine , skin blistering, scarring and erythrodontia.[5]

CEP is an autosomal recessive hereditary disorder which is very rare. There is decrease or lack of Uroprophrinogen lll synthetase. This is the major pathogenic factor without any specific treatment.

The term "Porphyria" is derived from the Greek word "Porphyra," meaning purple pigment, and refers to a group of disorders resulting from defects in the heme biosynthesis pathway. Congenital Erythropoietic Porphyria (CEP), first identified in 1911, is an autosomal recessive disorder caused by a deficiency of Uroporphyrinogen III Cosynthase (UROS), leading to excessive accumulation of porphyrin.[7]

CEP is also called Gunther disease which is a rare variant of Porphyria with autosomal recessive inheritance.[8]

Child may present clinically with severe anaemia, photosensitivity, blistering, red colored urine, erythrodontia and defect in bone mineralization.[9]

Clinical manifestations may vary in intensity and in very severe form, may reduce life expectancy of the child.[10]

This enzyme deficiency affects various organs, including bone marrow, red blood cells, skin, and teeth. Symptoms include mutilating skin lesions, pink teeth (erythrodontia), dark urine, and pronounced photosensitivity. Recent advances in genetic testing have enhanced early diagnosis, particularly in cases with atypical or ambiguous

1,2. Department of Dermatology, AIMC, Jinnah Hospital, Lahore.
3,5. Department of Obst. & Gynae Unit1, SIMS/ Services Hospital, Lahore.
4. Department of Paediatric Medicine, Saira Memorial Hospital, Lahore.

Correspondence:
Dr. Maria Agha, *House Office, Department of Dermatology, AIMC, Jinnah Hospital, Lahore. Pakistan E-mail: mariaagha31@gmail.com*

Submission Date: 16-10-2024
1st Revision Date: 30-10-2024
Acceptance Date: 10-12-2024

presentations. The mutation spectrum of UROS varies among populations, with certain alleles more prevalent in specific ethnicities, further complicating diagnosis.[11]

Management typically involves avoiding sun exposure, while bone marrow transplantation and stem cell therapy offer curative options. However, the availability of these treatments in resource-limited settings is often restricted due to high costs.[12]

Case Report

We report a 7-year-old male child diagnosed with Congenital Erythropoietic Porphyria (CEP). He presented to the outpatient Dermatology department at Services hospital Lahore on 23-08-2024 with blistering on his face and scars on his hands and feet, which were present since infancy. The child was born out of a non-consanguineous marriage, with three siblings, none of whom were affected.

The child exhibited classic signs of photosensitivity, reddish urine, and pink teeth since the age of four. There was facial hyperpigmentation and mild hypertrichosis. Blistering was observed on sun-exposed areas, including the hands, feet, and face. On examination, reddish brown teeth and blisters and scars were seen. On Wood's lamp examination of teeth, there was erythrodontia. His haemoglobin was 7g/dl, AST & ALT were raised. Urine for urinary prophobilinogen was raised. Skin biopsy from blister sites confirmed the diagnosis of Congenital Erythropoeitic Porphyria.

Figure 1: *Facial hyperpigmentation blistering, scarring and erythrodontia in a 7-year-old patient with CEP.*

Wood's Lamp Examination revealed the characteristic pink teeth and reddish urine, confirming the diagnosis of CEP. Hemoglobin levels were 7 g/dL, and platelet count was 7,000/mm^3. Liver enzymes—Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST)—were mildly elevated. Urinary porphyrin levels were significantly elevated, consistent with a diagnosis of CEP.

Figure 2: *Pink teeth due to the excessive porphyrin deposition in dental structures.*

Diagnostic tests confirmed elevated levels of porphyrins in the red blood cells and bone marrow, as well as the presence of splenomegaly. Skin biopsy samples also revealed changes typical of CEP.

Figure 3: *Urine sample from the patient showing a dark reddish hue due to elevated porphyrin levels.*

Given the clinical presentation and laboratory findings, other causes of photosensitivity, such as Epidermolysis Bullosa, Pseudoporphyria, and Porphyria Cutanea Tarda, were considered but ruled out based on serum porphyrin levels and the presence of erythrodontia.

Discussion

CEP is a condition that typically presents early in life and is characterized by severe photosensitivity, blistering, and scarring of the skin. The primary pathophysiological abnormality is a defect in the heme synthesis pathway, leading to the accumulation of porphyrins. In many cases, chronic hemolysis requires frequent blood transfusions, as in this case. If the disorder manifests later in life, the symptoms may be milder, with less frequent need for blood transfusions.[11]

Recent advances in gene-editing technologies, such as CRISPR/Cas9, hold promise in treating CEP, as they allow for direct correction of mutations in the UROS gene. These therapies are still experimental and not yet widely available. However, early studies have demonstrated significant potential in addressing the genetic root cause of CEP and other related disorders.[12]

The main approach to managing CEP involves preventing exposure to ultraviolet (UV) radiation. Physical barriers, such as protective clothing and high-SPF sunscreens, are essential for minimizing photosensitivity. Bone marrow transplantation and stem cell therapy offer potential curative treatments, but are often inaccessible in resource-limited settings due to the complexity and cost of the interventions.[13]

Emerging pharmacological treatments, such as synthetic heme analogs, are being investigated as less invasive alternatives to bone marrow transplantation. These therapies aim to bypass the defective enzyme and provide a stable source of heme. Although promising, these treatments are still in the experimental phase and are not yet part of the standard treatment regimen.[14]

The differential diagnoses for CEP include:

1. Epidermolysis Bullosa: A condition marked by skin fragility, where serum porphyrin levels are normal.
2. Pseudoporphyria: A drug-induced condition with normal serum porphyrin levels.
3. Hereditary Porphyria: Typically, latent until puberty.
4. Porphyria Cutanea Tarda: Characterized by skin blisters but without erythrodontia.

Global Disparities in CEP Management

In many low- and middle-income countries, access to curative treatments such as bone marrow transplantation is limited due to high costs and lack of infrastructure. Consequently, management often revolves around symptomatic care, including frequent blood transfusions and iron chelation to prevent complications from chronic hemolysis[15]. In such regions, genetic counselling and increased awareness about sun protection can help mitigate disease progression.

Conclusion

Congenital Erythropoietic Porphyria is a rare genetic disorder that poses significant challenges in management, particularly in resource-limited settings. Early diagnosis, combined with appropriate symptomatic management and advanced therapies when available, is key to preventing complications. Emerging therapies, including gene-editing techniques and synthetic heme analogs, hold the potential to revolutionize CEP treatment, offering a possible cure for this lifelong condition. However, for many patients, access to these treatments remains a significant barrier, necessitating ongoing efforts to improve access to care globally.

References

1. Khan J, Hashmi MU, Noor N, Khan AJ, Shrateh ON, Tahir MJ. Congenital erythropoietic porphyria presenting with recurrent epistaxis: a case report. J Med Case Rep. 2023;17:472. Published 14 Nov 2023.
2. Bhusal M, Bhattarai S, Shah M, Khedka A. Congenital erythropoietic porphyria: a case series of rare uroporphyrinogen III synthase gene mutation in Nepalese patients. JAAD Case Rep. 2021;7(2):102-106. Published 2021 Feb 25. doi:10.1016/j.jdcr.2021.02.017.
3. Kahila A, Zamlout A, Mazloum A, Laila O and Badran A." Congenital erythropoietic porphyria (Gunther disease): Oxford Medical Case Reports, 2020; 7,227–230 doi: 10.1093/omcr/omaa051.
4. Kamalyan M, Mohammadi M. Oxford Medical Case Reports. Congenital erythropoietic porphyria five years observation with standard treatment: a case report. Oxford Med Case Rep. 2024;1(2):122. doi:10.1093/omcr/omd451.
5. Ciftci V, Kılavuz S, Bulut FD, Mungan HN, Bisgin A, Dogan MC. Congenital erythropoietic porphyria with erythrodontia: a case report. Int J Paediatr Dent. 2019; 29(4):542-548. doi:10.1111/ipd.12473. Published 01 Feb 2019.
6. Li XL. Congenital erythropoietic porphyria: a rare case report. Med Case Rep Study Protoc. 2021;2(4). doi: 10. 1097/MD9.0000000000000098.
7. Shirazi N, Chauhan P, Jindal R, Ahmad S "Congenital erythropoietic pophyria: A rare of photosensitivity with hemolytic anemia and mental retardation. Journal of CPSP Pakistan 2019, Vol.29(Special Supplement 1 of case report): S23-S25.
8. Singal A, Kayarkatte MN, Pandhi D. Congenital erythropoietic porphyria in an Indian child. Indian J Paediatr Dermatol. 2019;20(2):141-144.doi:10.4103/ijpd. IJPD _67_18. Published Apr-Jun 2019.
9. Gupta M. Congenital erythropoietic porphyria: A case report. Pak Assoc Dermatol. 2017;27(1):89-91. Available from: http://www.pad.com.pk/jpad-article/view/1036. Published 13 June 2017.

10. Pecchini PM, Bonnecarrère G, Guillaume A, Jullien M, Duarte F, Mosser G. Successful treatment of congenital erythropoietic porphyria using matched unrelated hematopoietic stem cell transplantation in an adult: A case report. Transplantation. 2022;106(1):e21-22. doi: 10.1002/xsa.342. Published 17 January 2022.
11. Smith SG, Desnick RJ. Heme synthesis and the porphyrias. Molecular Medicine. 2021;11:56-71.
12. Erwin AL, Desnick RJ. Congenital Erythropoietic Porphyria. NORD. Updated July 23, 2024. Available from: https://rarediseases.org/rare-diseases/ congenital-erythropoietic-porphyria.
13. Smith HJ, et al. Gene therapy in rare erythropoietic porphyrias: Advances and challenges. Orphanet J Rare Dis. 2022;17(1):123.
14. Gillams A, et al. Advances in genetic therapies for porphyria. J Inherited Metabolic Disease. 2022; 45:98-112.
15. Sudrié-Arnaud B, Legendre M, Snanoudj S, Pellaurd F, Bekri S, Tebani A. An atypical case of congenital erythropoietic porphyria. Genes. 2021;12(11):1828. doi:10.3390/genes12111828.

Authors Contribution

MA, HS: Conceptualization of Project
HS, SA: Data Collection
HS, SA: Literature Search
HS, SA: Statistical Analysis
AUK: Drafting, Revision
MA: Writing of Manuscript