

Splenectomy as a cure to pancytopenia in congenital erythropoietic porphyria

Farah Arshad Khan, Fatima Raza, Nazish Saqlain

Abstract

Congenital erythropoietic porphyria (CEP) is a rare genetic disorder caused by mutations in the uroporphyrinogen III synthase (UROS) gene, resulting in the accumulation of toxic porphyrins in various tissues such as the skin, red blood cells, bones, and teeth. We report the case of a 34-year-old Pakistani male who presented with a history of photosensitivity, skin deformities, and red urine since childhood. Over the past 13 months, he developed pancytopenia and required multiple blood transfusions. Clinical examination revealed splenomegaly, haemolytic anaemia, and characteristic skin changes. Despite ongoing dermatological treatment, the patient underwent splenectomy due to transfusion dependence and hypersplenism. Post-splenectomy, his blood counts normalized. The patient was advised strict photoprotection, vaccination, and long-term follow-up. This case underscores the importance of early diagnosis, transfusion management, and the role of splenectomy in patients with CEP complicated by pancytopenia, highlighting the need for continuous care and long-term disease management.

Keywords: Congenital Erythropoietic Porphyria, Porphyria, Pancytopenia, Splenectomy, Photosensitivity.

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Introduction

Congenital erythropoietic porphyria (CEP), also known as Gunther's disease, is an inherited autosomal recessive disorder which is caused by mutations in the gene responsible for uroporphyrinogen III synthase (UROS) expression. This condition leads to phototoxic reactions due to the buildup of biologically inactive type I porphyrins, which accumulate in the different tissues particularly, the skin, red blood cells, bones, and teeth.¹ CEP is a rare genetic disease, affecting less than 1 in 1,000,000 children, with approximately 280 cases reported in the

literature, of which very few present with pancytopenia.²

We report the case of a male with characteristic clinical features of CEP undergoing multiple blood products' transfusions due to pancytopenia. Massive splenomegaly was identified as the underlying cause of pancytopenia and was successfully treated with splenectomy.

Case report

A 34-year-old male, born of a nonconsanguineous marriage and diagnosed with Congenital Erythropoietic Porphyria at the age of 13-years, presented to the Haematology clinic with complaints of pain in his left hypochondrium for the past four months and generalized weakness for almost 14 months. The pain was dull in nature, and was associated with jaundice which developed gradually. He also gave a history of two recent episodes of haemoptysis and frequent gum bleeding over the past one month.

The past medical history revealed that he had life-long history of photosensitivity over his exposed areas and blistering that healed with scarring, leading to progressive deformities of the hands, ears and nose. (Figure 1). His mother reported a red discharge in his diapers, along with redness and matting of both eyes, since early childhood, however, these findings were not appropriately investigated until his early teens. The passing of red-coloured urine remained persistent since then. He



Figure-1: Thickened facial skin with abnormal pigmentation and scarring, hypertrichosis, reddish-brown discoloration of the teeth and ears and nasal deformities. Severe ectropion, trichiasis, and corneal scarring are visible.

Department of Pathology (Haematology), Lahore General Hospital, Lahore, Pakistan.

Correspondence: Nazish Saqlain. e-mail: nazish68@yahoo.com

ORCID ID: 0000-0003-2537-1257

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Figure-2: Bilateral fingers deformities extending to the proximal interphalangeal joints.

gradually developed deformities of his hands with mutilated fingers (Figure 2) which made him acquire medical consultation leading to his final diagnosis. He was first seen in the Dermatology and Haematology departments of Lahore General Hospital (a public sector Hospital in Lahore) on 6th June, 2012. Since then, he has been on regular follow-up at the same hospital. None of his siblings were affected, and both parents were phenotypically normal. The diagnosis of CEP was established based on his clinical features and supportive skin biopsy findings. Genetic or molecular confirmation of UROS mutation was not performed, which we acknowledge as a limitation of this report.

The patient was on a treatment regimen prescribed by the dermatology department, which included multivitamins, topical ointments for sun protection, and eye ointments. Notably, the patient was not taking any systemic antibiotics.

Over the past few months, his routine Full Blood Count (FBC) showed persistent pancytopenia. (Table 1) The blood smear showed dimorphic red blood cells, along with polychromasia and few schistocytes, suggesting haemolysis. No platelet clumps were appreciated. The morphology of white blood cells and platelets was unremarkable.

Over the last 13 months, the patient had received ten units of packed red blood cells and eight units of random donor platelet concentrates, with a marked increase in transfusion frequency during the last month.

On examination, the patient exhibited thickened skin with hypopigmented and hyperpigmented patches, as well as scarring predominantly on photo-exposed areas. Facial hypertrichosis was noted, along with reddish-brown discolouration of the teeth. Deformities involving the nose, ears, and fingertips were observed bilaterally, extending to

Table-1: Serial Full Blood Counts (FBC) before Splenectomy showing pancytopenia.

FBC parameter	10-7-24	5-8-24	FBC on presentation (6-12-24)
HB (g/dL)	8.8	11	9.1
Platelets (*10 ³ /uL)	88	104	85
TLC (*10 ³ /uL)	4.7	2.5	2.6
AST (U/L)	115	115	112
ALT (U/L)	63	72	81
Serum bilirubin (mg/dL)	3.1	3	3.5
Unconjugated bilirubin	1.9	2.1	1.1
Conjugated bilirubin	1.2	0.9	2.4
Reticulocytes count (%)	3.8	4.3	3.5
Blood urea (mg/dL)	23	17	17
Blood creatinine (mg/dL)	0.8	0.4	0.4

HB: Haemoglobin; TLC: Total Leukocyte Count; AST: Aspartate Transaminase; ALT: Alanine Transaminase.

Table-2: Post- splenectomy serial FBC.

FBC parameter	Post- op Day 2	Post-op Day 4	Post-op Day 15
HB (mg/dL)	10.3	12.7	13.6
RBC counts (*10 ⁶ /uL)	3.04	4.46	4.84
TLC (*10 ³ /uL)	3.4	5.9	6.6
Platelets (*10 ³ /uL)	102	162	323

the proximal interphalangeal joints. Ocular examination revealed severe ectropion, trichiasis, and corneal scarring. Gingivitis was noted, however, no bruising or petechiae were present.

Abdominal examination revealed a massive spleen, measuring 19 cm below the left costal margin. Laboratory investigations showed an elevated erythrocyte sedimentation rate, raised reticulocytes, increased lactate dehydrogenase, and a normal serum iron profile. The urine examination showed 3+ red blood cells, and the Coombs test and autoimmune profile were negative. Overall, the clinical findings and laboratory investigations were strongly suggestive of haemolytic anaemia with features of hypersplenism.

The patient was advised splenectomy on the basis of transfusion dependence (>6 units/month), severe splenomegaly (>15 cm) and hypersplenism (thrombocytopenia, leukopenia). The patient received the Pneumococcal, Meningococcal, and Hib vaccine, and the Influenza vaccines. A laparoscopic splenectomy was performed. After splenectomy patient was observed for CBC parameters which returned to normal by 4th post-op day (Table 2). He was advised penicillin prophylaxis and to get pneumococcal and meningococcal vaccine boosters every 5-10 years along with annual influenza vaccine. He was advised to use strict photoprotection and emollients. He was discharged and counselled about the genetic inheritance of disease, and the need for long-term follow-up.

Discussion

Congenital Erythropoietic Porphyria (CEP) leads to haemolytic anaemia due to a deficiency of the enzyme uroporphyrinogen III synthase (UROS), resulting in disruption of the heme biosynthesis pathway.³ This results in the accumulation of toxic porphyrins in red blood cells, causing oxidative damage to the cell membrane and making the cells fragile.⁴ These damaged cells undergo haemolysis, both intravascularly and via sequestration in the spleen. The bone marrow compensates by increasing erythropoiesis, but the ongoing damage leads to a continuous cycle of haemolysis, causing symptoms of anaemia such as fatigue and jaundice. Pancytopenia results from bone marrow suppression due to toxic porphyrins and chronic haemolysis, which impair the production of red blood cells, white blood cells, and platelets. Splenomegaly develops as the spleen becomes enlarged from the increased workload of filtering damaged red blood cells and cellular debris due to ongoing haemolysis.⁵

The management of haemolytic anaemia in Congenital Erythropoietic Porphyria (CEP) involves a combination of supportive therapies and interventions to address both the anaemia and the underlying haemolysis. Blood transfusions are commonly used to manage symptomatic anaemia.² Previous reports have described the use of splenectomy to alleviate pancytopenia secondary to hypersplenism in CEP with improvement in haematological parameters following the procedure, as was done in this case.^{6,7} In severe cases, haematopoietic stem cell transplantation (HSCT) may be considered, particularly for patients with unresolved pancytopenia.⁸ Photoprotection is crucial, with patients advised to avoid sun exposure and use of UV protective clothing and sunscreen. Additional supportive care includes pain management for skin lesions, infection control, and monitoring for organ complications such as liver or renal dysfunction due to porphyrin accumulation. Phlebotomy and iron chelation strategies are under investigation with the aim to reduce haemolysis and cut the accumulation of porphyrins.^{9,10} Patient education is essential to improve treatment compliance, decrease the risk of complications, and ensure proper management of symptoms via regular follow-up appointments and lab investigations.

Informed consent was obtained from the patient regarding publication of his clinical details and photographs in this case report purely for academic purpose. IRB approval was taken via letter number: 00-1-C-2025, dated 15th Jan, 2025.

Conclusion

This case demonstrates that in Congenital Erythropoietic Porphyria, worsening pancytopenia may result from severe hypersplenism secondary to chronic haemolysis and massive splenomegaly. In our patient, transfusion dependence, splenic enlargement, and persistent cytopenias improved markedly after splenectomy, with normalization of haematological parameters. The case supports splenectomy as a useful therapeutic option in carefully selected CEP patients with hypersplenism-related pancytopenia. Long-term management should include strict photoprotection, vaccination, infection prophylaxis, genetic counselling, and regular haematological follow-up.

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Author Contribution:

FAK: History taking, clinical examination, follow up of the patient and writing.

FR: Lab tests, report compilation and writing.

NS: Case discussion, writing, final review and references.