CASE REPORT

Congenital Erythropoietic Porphyria: A Rare Case Report

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ABSTRACT

Congenital erythropoietic porphyria belongs to the group of erythropoietic porphyria which are primarily inborn errors of bone marrow heme synthesis. Congenital erythropoietic porphyrrias are inherited as autosomal recessive entities due to two mutant alleles coding for the enzyme uroporphyrin III synthetase. So, parent of the patients may just be carriers rather than carrying active disease. Clinical manifestations are due to excess porphyrin in the blood which is responsible for hemolytic anemia and photosensitivity. Treatment include avoidance of sun exposure, oral beta carotene, alpha tocopherol and splenectomy.

Keywords: Porphyria, Gunther’s disease, Congenital erythropoietic porphyria, Erythropoietic porphyria.


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INTRODUCTION

Erythropoietic porphyria is classified in to 3 types based on the clinical features.
1. Mixed type.
2. Porphyria with neuropsychiatric manifestation.
3. Porphyria with predominant cutaneous manifestation.

Congenital erythropoietic porphyria belong to the third category.

Erythropoietic porphyria is reported in diverse populations. The total number of cases reported worldwide is less than 200. Remarkable clinical variability exists in erythropoietic porphyria. Despite the limited treatments that are currently available, the prognosis is not invariably poor.

Most patients with erythropoietic porphyria survive into adulthood, with a life expectancy of 40 to 60 years. No racial predilection is reported for erythropoietic porphyria. Erythropoietic porphyria occurs in both males and females with approximately equal frequencies. Erythropoietic porphyria typically occurs in infants or young children; however, several adult-onset cases are reported. Staple clinical features of congenital erythropoietic porphyria (CEP) include persistent damage to skin, cartilage and bone due to photosensitivity based on severity. The other prominent features include erythrodontia, burgundy colored urine, hypertrichosis and osseous fragility.¹

CASE REPORT

An 8-year-old boy came to the Department of Oral Medicine Diagnosis and Radiology with the chief complaint of discolored teeth since child hood. History (as revealed by his mother) revealed that the discoloration of teeth was not present at the time of birth and it developed days after his birth. She also revealed that photosensitivity developed during the third week of life. The history also revealed that the patient was passing burgundy colored urine.

On clinical examination, the patient was well oriented to time and place for his age. Signs of photosensitivity like scarring was seen in face and hands (sun exposed part) (Fig. 1).

On intraoral examination, exfoliation of deciduous and eruption of permanent teeth were not affected much. The teeth showed brownish red hue. The distribution of brownish red hue was not uniform among the teeth, i.e. the anteriors showing the deeper hue than the posteriors (Fig. 2).

Fig. 1: Signs of photosensitivity (scarring) seen in face and hands
Intraoral periapical radiograph and panoramic radiograph showed normal trabecular pattern and eruption of successors for his age. Posterior anterior view of the skull showed no evidence of pathology in the skull (Figs 3 to 5).

Hemogram revealed anemia (reduced RBC count), reduced total and differential count of WBCs and reduced platelet count, i.e. pancytopenia. It should be noted that the reduction in count was moderate rather than severe. Based on history, clinical features, and radiographic examination, the condition was diagnosed as CEP.

**DISCUSSION**

Congenital erythropoietic porphyria or Gunther’s disease belong to the group of erythropoietic porphyrias with predominant cutaneous manifestations. Erythropoietic porphyria is primarily a disorder of heme synthesis that occurs in the bone marrow. Inactivity of the enzyme uroporphyrinogen III synthase in erythrocyte precursor cells causes reduction in the production of isomer III porphyrinogen production that can affect the end-product heme; So, isomer I porphyrinogens that cannot be used to form heme may be overproduced. The accumulated isomer I porphyrinogens are spontaneously oxidized to their corresponding porphyrins, which are water-soluble photosensitizers with a reddish hue.

These porphyrins are released from the maturing erythrocytes into the plasma and are excreted by renal mechanisms; urine with a port-wine color is produced. The interaction of excess porphyrins in the skin and light radiation causes phototoxic damage of biomolecular targets that is manifested as mechanical fragility and blistering that may result in severe scarring.

The hemolytic anemia of erythropoietic porphyria can cause hypersplenism in more serious cases. Hypertrophy of the bone marrow in such cases can lead to osseous fragility and pathologic fractures. Acral osteolysis and onycholysis may occur; bones and teeth are stained red by the deposition of porphyrin pigment. Ocular damage can lead to blindness. The photoactive nature of porphyrin molecules results in the bright pink fluorescence of these pigments in urine, teeth, and bones under Wood light illumination.

The typical complaint is blistering and fragility of light-exposed skin in an individual with discolored urine. The presentation of erythropoietic porphyria at birth in a patient with a history of a difficult perinatal course and concomitant jaundice usually indicates severe disease. Patients may have a history of hemolytic anemia before the complete diagnosis was recognized. Very early prenatal expression with nonimmune hydrops fetalis has been reported.

Findings at physical examination may include the following:

- **Skin**
  - Photosensitivity, with formation of vesicles and bullae, occurs early in the course of the disease.
  - Increased fragility and erosions can contribute to mutilation, especially on the face (e.g. nose, mouth, ears) and hands.
  - Hypertrichosis of the face and extremities is common.
- **Oral**
  - The teeth have a reddish color.
  - The teeth fluorescence under a wood light due to porphyrin deposition in dentine and enamel.
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• Urine
  – Pink staining of the diapers in the neonatal period is common.
  – This staining is due to the porphyrin pigment in the urine.

• Ocular
  – Ocular manifestations of erythropoietic porphyria include blepharitis, cicatricial ectropion, and conjunctivitis. Lagophthalmos is a major cause of light-induced ocular surface aggravation.
  – Scleral findings include interpalpebral fissures and pink fluorescence of the perilimbal sclera under a wood light.
  – Subsequent bilateral corneal scarring may occur, with eventual blindness. The risk for malignant conjunctival degeneration is low.

• Skeletal
  – Porphyrins are also deposited in the bone, where they cause an orange-red fluorescence.
  – The severe loss of bone with subsequent contractures and deformities occurs in most adults with erythropoietic porphyria.
  – X-ray studies show osteopenia and acro-osteolysis.

Erythropoietic porphyria is caused by autosomal recessive inheritance of genes that encode abnormal uroporphyrinogen III synthase enzyme protein. The resultant deficient activity of this enzyme leads to hemolytic anemia, cutaneous photosensitivity and their complications. The mutation that causes the most severe deficiency of the enzyme uroporphyrinogen III synthase is C73R.

The GATA gene family, a group of transcription factors, has a crucial role in normal human hematopoiesis. A mutation in GATA1, an X-linked transcription factor, has been reported in association with erythropoietic porphyria.

Porphyrin analyses

– Urinary porphyrin concentrations are increased 100 to 1000 times and involve predominantly uroporphyrin I.

– The combination of elevated urinary and erythrocyte isomer I porphyrin levels is specific for erythropoietic porphyria.

– Coproporphyrin preferentially accumulates as fecal porphyrin after the decarboxylation of uroporphyrin.

– Excessive uroporphyrins in red blood cells appear to cause fragility; therefore, a hemolytic anemia is common.

– Consequent splenomegaly and hepatomegaly are observed.

– Fluorescence microscopy of peripheral blood or bone marrow specimens.

– Red porphyrin fluorescence in intact erythrocytes and erythroid precursor cells can be observed in smears of bone marrow specimens illuminated by violet or blue light against a dark-field background.

– The brilliant fluorescence of nuclei in erythrocyte precursor cells is specific for erythropoietic porphyria.

Medical care: Avoidance of sunlight is most important. Vitamin and mineral deficiencies should be prevented. Blood transfusions to correct anemia are required in severe cases, and this may reduce porphyrin production by the marrow. Splenectomy is sometimes considered to increase the lifespan of RBC’s. Identifying the mutations in a family enables diagnosis before birth in subsequent pregnancies. Gene therapy may be an option in the future. Oral beta-carotene has been used with limited benefit. The use of oral alpha-tocopherol and ascorbic acid to quench reactive oxygen radicals has been advocated to reduce porphyrin-sensitized photodamage to skin elements and circulating erythrocytes. Topical lubrication of the eyes improves the dry eye symptoms and may stabilize visual function. Bone marrow transplantation is reported to be successful;
however, the long-term results are unknown. Life-threatening infectious complications limit the applicability of this therapeutic approach.6-8 Stem cell cord blood transplantation has also been reported successful in a few patients.9

• Oral care
  – Because of pancytopenia, risk of bleeding and infection can be encountered during dental procedures.
  – So elective dental procedures and minor oral surgical procedures should be done under the umbrella of antibiotics.
  – Regular oral prophylaxis should be advocated.
  – Ceramic veneers and crowns with or without root canal treatment can be done to improve the esthetic value of the teeth.

• Prognosis
  – With strict adherence to sun avoidance, scarring and mutilation can be minimized.
  – Normal life spans are possible in many cases.
  – Despite the limited treatments that are currently available, the prognosis is not invariably poor.
  – Most patients with erythropoietic porphyria survive into adulthood, with a life expectancy of 40 to 60 years.10

REFERENCES


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