

CLINICAL LABORATORY APPROACH IN A CASE OF CONGENITAL ERYTHROPOIETIC PORPHYRIA

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ABSTRACT

Congenital erythropoietic porphyria is a rare inborn error of heme synthesis inherited as autosomal recessive disease. In the present instance, one year old female child born of consanguineous marriage presented with infected bullae and vesicles on the scalp and both upper extremities. There was history of hypersensitivity on exposure to sunlight. Milestones of physical and mental development were adequate. Test for detection of porphyrins in the blood, urine and stool were undertaken. The tests confirmed the presence of porphyrins in the samples and a diagnosis of congenital erythropoietic porphyria was made.

Key Words: Congenital erythropoietic porphyria, Porphyria, Porphyrins.

This article may be cited as: Sinharay M, Deb N, Mukhopadhyay M. Clinical Laboratory approach in a case of congenital erythropoietic porphyria. *Gomal J Med Sci* 2012; 10: 253-6.

INTRODUCTION

Porphyrias are a clinically and genetically heterogeneous group of metabolic diseases that result from either an inherited or an acquired dysfunction of enzymes crucial for heme biosynthesis. Biochemically, the different porphyrias are characterized by particular patterns of accumulation and excretion of porphyrins and/or their precursors. In general, the porphyrins excreted in a specific type of porphyria are the irreversibly oxidized substrates of the deficient enzyme. These intermediates when present in excess amounts exert toxic effects that are responsible for cutaneous and neurologic signs and symptoms of clinically overt porphyria.

The current grouping of the porphyrias is based on the primary site of increased porphyrin production, either liver or bone marrow - the hepatic or erythropoietic porphyrias, respectively. Among the erythropoietic porphyrias, congenital erythropoietic porphyria is the rarest of bullous porphyrias; less than 200 cases have been reported until now.¹

CASE HISTORY

A year old female child presented with itching and uneasiness on exposure to sunlight, develop-

ment of a brownish red coloration of the gums and passage of reddish urine that stained her clothes. The child was born of consanguineous marriage to Muslim parents. She had no sibling. Neither her parents nor any of the first degree relatives in the family had similar complaints. Onset of symptoms was marked by recurrent blistering of scalp since two months of age. Her mother did not specify any episode of acute attacks. The child's mental and physical development was adequate as suggested by attaining the milestones with respect to her age. Her weight was 10.3 kg, height 74.6 cm and head circumference 46.9 cm. This case is being presented here after obtaining informed consent from the guardian and due approval from the local institutional ethics committee.

Examination revealed presence of infected bullae and vesicles on the scalp and both upper extremities, along with areas of hypo and hyper-pigmentations in the later. (Fig. 1,2) Face was affected the least with few blisters along hairline. Brownish discoloration of the lower gums was detected. Disfigurement, hypertrichosis, skin thickening, scarring and mutilation of the fingers in this child was absent. There was significant pallor but no detectable jaundice, no splenomegaly or any lymphadenopathy. Nervous system examination was normal. All her vitals were within normal limits.

Investigations revealed Hb 7.5%, PCV 25%, Total leucocyte count 16,000 with normal differential count (N 50, L 48, E 2). Platelet count was nor-

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Figure 1: Infected blisters on the scalp.

mal (3.5 lacs/mm^3) and reticulocyte count was 2.8%. Liver function test was within normal limits (Total bilirubin 0.6 mg/dl, direct bilirubin 0.2 mg/dl, ALT 24 IU/L, AST 15 IU/L, Alkaline Phosphatase 246 IU/L, Total protein 4.9 g/dl, Albumin 2.7 g/dl). Urinalysis showed pH 6.5 and presence of trace albumin. The parameters of renal function tests were within normal limits.



Figure 2: Vesicles along with areas of hypo and hyper-pigmentations on the upper extremity.

Tests for detection of porphyrins in the blood, urine and stool were undertaken by the method of Haining et al.² Presence of uroporphyrin (+++) and coproporphyrin (+) in the urine was detected by the development of bright red fluorescence under ultraviolet (UV) trans-illuminator, which occurs when concentration of porphyrins is greater than 10 times normal.³ Similarly treated normal urine samples served as controls which showed no fluorescence under UV light. Tests for porphyrin on blood



Figure 3(a): Test for detection of blood porphyrins prior to transillumination by ultraviolet light.



Figure 3(b): Distinct fluorescence seen for blood porphyrins under ultraviolet light.



Figure 4(a): Test for detection of urine porphyrins prior to transillumination by ultraviolet light.



Figure 4(b): Bright fluorescence seen for urine porphyrins under ultraviolet light.



Figure 5(a): Test for detection of fecal porphyrins prior to transillumination by ultraviolet light.



Figure 5(b): Brilliant red fluorescence seen for fecal porphyrins under ultraviolet transillumination.

samples, with an UV transilluminator yielded a distinct red fluorescence usually found at concentrations of 2-3 times the normal level.³ Test for detection of fecal porphyrins gave distinguishable orange red fluorescence under UV transilluminator, which is usually due to coproporphyrin in the stool. Quantification was not done because once the presence of porphyrins is detected in urine, blood and stool; quantification has no extra role to play in the diagnosis. (Fig. 3-5) Test for urinary porphobilinogen was done by the method of Schwartz et al⁴ and was negative.

Urine, blood and stool samples from her parents were screened and there was no evidence of porphyria in them.

Skin biopsy was not performed as histopathological findings are non-specific with presence of similar features in all types of porphyria.⁵

DISCUSSION

Congenital erythropoietic porphyria, also known as Günther disease, is one of the first inborn errors of metabolisms to be described.³ This autosomal recessive disorder is caused by deficient activity of uroporphyrinogen III synthase (URO III_s)/ uroporphyrinogen cosynthase in the erythrocyte precursor cells. The inheritance of two mutant alleles for the URO III_s gene leads to mutations, of which C73R is most common. Substitution of cysteine by arginine damages the disulfide bridges which influence the secondary structure of the enzyme. The substrate (uroporphyrinogen I, coproporphyrinogen I) of the deficient enzyme, URO III_s accumulates in bones, erythrocytes, skin, and teeth and is excreted in large quantities in urine and feces.¹ Congenital erythropoietic porphyria is associated with cutaneous lesions and hemolytic anemia. Cutaneous sensitivity to sunlight results from excitation of excess porphyrins in the skin by long wave ultraviolet light, leading to cell damage, scarring, and deformation.⁶ Severe cutaneous photosensitivity starts in the early months of infancy. On exposure to sunlight bullae and vesicle appears on skin which are prone to rupture and infection. Skin thickening, focal hypo and hyperpigmentation, hypertrichosis of face and extremities and disfigurement of face and hands due secondary infection of cutaneous lesions are characteristic. Deposition of Porphyrins in bones and teeth leads to brownish teeth, which fluoresce under long wave UV light. Marked increase in erythrocyte porphyrins leads to hemolytic anemia resulting in Splenomegaly. Adults present with milder form of the disease.

In the present instance, other differential diagnoses were ruled out prior to confirmation.^{5,6} Erythropoietic protoporphyria also occurs in childhood but skin photosensitivity occurs in the form of

pain, itching, erythema and edema. Urine color is also normal. Protoporphyrin levels will be increased in blood, stool. Porphyria Cutanea Tarda presents with skin blistering but there is no erythrodontia and it appears in adults usually. Variegate Porphyria presents with prominent neurovisceral symptoms, urinary ALA and Porphobilinogen are increased and fluorescence emission of porphyrins here occurs at neutral pH, rather than acidic pH used in detection of congenital erythropoietic porphyria. Hereditary coproporphyrin is usually latent before puberty. It presents with prominent neurovisceral symptoms and urinary ALA and porphobilinogen are increased during acute attacks. Epidermolysis bullosa presents with blisters but porphyrin levels are never raised in blood, urine or feces. Pseudoporphyria also presents with skin blistering, but porphyrins are normal. Moreover there is presence of drug history.

The child is now being treated with oral β -carotene, oral antibiotics (all in syrup form), topical antibiotics and the mother was advised to apply sunscreen on child and strictly avoid direct sun exposure. Packed cell transfusion was given to treat anemia. Chronic transfusion of sufficient blood to suppress erythropoiesis is effective in reducing porphyrin production, but results in iron overload.⁶ Recently bone marrow and cord blood transplantation has proved effective but such costly treatments cannot be afforded by people of such low socioeconomic status. Schultz is credited with the first clinical description of congenital erythropoietic porphyria.⁷ Taneja & Sheth published the first report from India in two brothers in 1956.⁸ Subsequently only few cases have been reported internationally.⁹⁻¹²

CONCLUSION

The history of skin blistering, photosensitivity, passage of reddish urine, brownish red gums, presence of anemia, and porphyrins in the blood, urine and feces in this one year old child clinches the diagnosis of congenital erythropoietic porphyria.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
GRANT SUPPORT AND FINANCIAL DISCLOSURE
None declared.