Case Report

A Rare Case of Porphyria

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Abstract

Introduction: Congenital erythropoietic porphyria is one of the rare forms of an intriguing group of metabolic disorders known as porphyrias. Less than 200 cases have been reported in the literature. Clinical Presentation: We report the case of a 27-year-old gentleman who had the clinical profile suggestive of porphyria, now presenting with anaemia. The type of porphyria was found to be congenital erythropoietic porphyria by biochemical assay and cause for anaemia was haemolysis, a well-known association with the erythropoietic porphyrias. Treatment: The management of porphyrias is essentially symptomatic. He was treated with blood transfusions and haematinics. Conclusion: The patient improved symptomatically and he is on regular follow-up. With the development of gene therapy, a specific cure for this rare type of porphyria is expected in the near future.

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Key words: Gene therapy, Splenectomy

Introduction

Porphyrias are a rare and intriguing group of metabolic disorders. We report a case of congenital erythropoietic porphyria, one of the infrequent forms of porphyria.

Case Report

The symptoms of our patient, a 27-year-old gentleman born of a non-consanguineous marriage, began soon after birth when it was noted that he was passing red coloured urine (Fig. 1). Soon afterwards, blisters were noted over the exposed parts of the body and would breakdown, leaving behind raw areas. The parents had been advised not to expose the child to direct sunlight. Though precautions were taken initially, as the child began to attend school, he was exposed to sunlight and developed mutilating skin lesions over the exposed parts. He was doing well and studying for his degree when he was referred to us for persistent anaemia.

On examination, he has hypertrichosis of the face, arm and legs; erosions over the sclera, deformed pointed nose, deformed small ears, brownish pink teeth, dry skin with pseudoscleroderma appearance, hyperpigmented and hypopigmented macular lesions over the exposed parts and resorption of fingers and toes (Figs. 2 and 3). Pallor and moderate splenomegaly were also noted.

Investigations revealed increased urobilinogen in the urine, without bile pigments or elevated porphobilinogen. Haemoglobin was 5.0 gm/dL with reticulocyte production index more than 3. Total white cell count was 3300/mm^3, while P_{48} L_{51} E_1 and platelet count was 60,000/mm^3. Peripheral smear revealed pancytopenia. Serum bilirubin was 4.3 mg/dL, liver enzymes were normal and lactate dehydrogenase level was 1773 U/L (normal, <300). Red cell coproporphyrin level was 338.91 nmol/L (normal, 3 to 10 nmol/L) and red cell protoporphyrin level was 2513.7 nmol/L (normal, 6 to 10 nmol/L).

Based on clinical and laboratory findings, a diagnosis of congenital erythropoietic porphyria with associated haemolytic anaemia was made. Pancytopenia was attributed to hypersplenism. He is being treated symptomatically with red cell transfusions and folic acid and is on regular follow-up. The patient was not keen on splenectomy. Urine and blood samples from all members of the family were screened and there was no evidence of porphyria in the entire family.

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Fig. 1. Photograph showing red coloured urine.

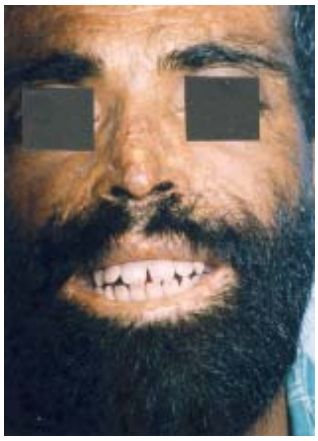

Fig. 2. Photograph showing deformed ear and nose, erythrodontia.

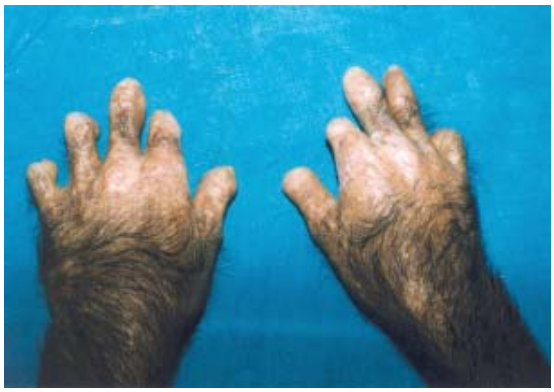

Fig. 3. Photograph showing finger resorption.

Discussion

The porphyrias are an inherited or acquired group of disorders characterised by deficiency of specific enzymes in the heme biosynthetic pathway, encompassing the cytosol and mitochondria of the cell. They are classified as hepatic or erythropoietic based on the primary site of over-production and accumulation of toxic porphyrin and precursors. Generally, hepatic porphyrias present as a neurological disorder while erythropoietic porphyrias present as a dermatological disorder.[1] Our patient had predominant photosensitivity and hence, the possibility of erythropoietic porphyria was considered. Some non-steroidal anti-inflammatory drugs have phototoxic properties similar to uroporphyrin and cause a syndrome clinically and histologically indistinguishable from porphyria cutanea tarda and is known as pseudoporphyria.[2]

Congenital erythropoeitic porphyria (CEP, Gunther's disease) is an autosomal recessive disorder coded on chromosome 10q26 and is characterised by reduced activity of the cytosolic enzyme, uroporphyrinogen III (URO) synthase enzyme. It catalyses the conversion of hydroxymethylbilane to uroporphyrinogen III. As a result, type 1 isomers of uroporphyrin and coproporphyrin accumulate in the bone marrow, erythrocytes, plasma, urine and faeces.[1,3] Less than 100 cases have been reported in the literature.[3] Gunther documented a detailed clinical profile of the illness and his study was complemented biochemically by Hans Fischer.[4]

Clinical features are marked by cutaneous and haematological manifestations. Cutaneous photosensitivity is the striking feature and begins in early infancy. It is due to photoactivation of porphyrins by light in the 400 nm range (Soret band) and subsequent biological reactivity.[3] Initially manifesting as pruritus and erythema, vesicles and bullae develop subsequently and may contain pink fluorescent fluid. Infection and scarring leave behind hyperpigmentation or rarely hypopigmentation and loss of acral tissues. In fact, CEP causes the most mutilating skin lesions amongst porphyrias. Hypertrichosis or alopecia can occur. Erythrodontia, brownish pink teeth with red fluorescence under ultraviolet light, is pathognomonic of CEP and is due to deposition of porphyrins in the teeth.[1] Anaemia is the striking haematological problem and is due to ineffective erythropoiesis in bone marrow and peripheral haemolysis of the circulating porphyrin-laden erythrocytes. As a result, splenomegaly occurs and it can lead to hypersplenism with subsequent leukopaenia and thrombocytopaenia, as in our patient.[5] While peripheral smear shows normocytic normochromic red cells with polychromasia, bone marrow reveals normoblastic hyperplasia and red fluorescence under ultraviolet light.[3] Histopathology of the bullous lesions reveals subepidermal cleavage with varying degrees of inflammation. Perivascular deposits of porphyrin in skin and liver can also be seen. Reduced uroporphyrinogen III (URO) synthase activity warrants the diagnosis. In CEP, erythrocyte protoporphyrin and coproporphyrin are raised. In the urine, uroporphyrin is the predominant metabolite to get accumulated, coproporphyrin may be occasionally raised while porphobilinogen and aminolevulinic acid levels are normal. In the faeces, coproporphyrin is the predominant metabolite while protoporphyrin may also be raised.[1,3] Prenatal diagnosis can be achieved by amniocentesis.[1]

Treatment of CEP is essentially supportive however unsatisfactory. The prognosis of CEP is poor with death occurring in early adult life. Blood transfusion suppresses erythropoiesis. Splenectomy reduces haemolysis and reduces the need for transfusions. Protection of skin from sunlight and trauma is essential and bacterial infections should be treated promptly. Beta-carotene may be of value. Bone marrow transplantation has been proven to be effective especially in transfusion-dependent children.[1,6] Gene therapy via haematopoietic stem cells is being studied.[1,2]

REFERENCES

1. Desnick RJ. The porphyrias. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. Harrison's Principles of Internal Medicine. 15th ed. New York: McGraw-Hill, 2001:2261-7.
2. Sarkany RP. Porphyria. From Sir Walter Raleigh to molecular biology. Adv Exp Med Biol 1999;455:235-41.
3. McColl KEL, Dover S, Fitzsimons E, Moore MR. Porphyrin metabolism and the porphyrias. In: Weatherall DJ, Ledingham JGG, Warell DA, editors. Oxford Textbook of Medicine. New York: Oxford Univ Press, 1996:1390-5.
4. Fitzpatrick TB, Eisen AZ, Wolff K, Freedberg IM, Austen KF. Dermatology in General Medicine. New York: McGraw-Hill, 1987: 1681-704.
5. Sassa S. Hematologic aspects of the porphyrias. Int J Hematol 2000; 71:1-17.
6. Tezcan I, Xu W, Gurgey A, Tuncer M, Cetin M, Oner C, et al. Congenital erythropoietic porphyria successfully treated by allogenic bone marrow transplantation. Blood 1998;92:4053-8.