CASE REPORT

GUNTHERS WITH HAEMOLYTIC ANAEMIA EXTREMLY RARE: A CASE REPORT

Nilesh Kumar, Ankur Varshney, Arvind Anand, Dibyaranjan Behera, Ravi Anand, Ashutosh Tiwari
Institute of medical sciences, BHU, Varanasi, UP, India

Correspondence to: Nilesh Kumar (nilesh19arreno@gmail.com)

DOI: 10.5455/ijmsph.2013.2.313-315 Received Date: 25.12.12012 Accepted Date: 26.12.2012

ABSTRACT
Congenital erythropoietic porphyria (CEP), also called Gunthers is the rarest of the porphyrias, with a prevalence estimated at 1 in 1,000,000 or less. Only approximately 200 cases of CEP have been reported till now worldwide. CEP affects males and females equally, and occurs in all ethnic groups. Clinically it is a subacute to chronic type of porphyria, defect is expressed in infancy and clinical features such as extreme cutaneous photosensitivity, blistering, scarring, hyper and hypo pigmentation of photo exposed parts. Haemolytic anaemia with splenomegaly and retarded growth may also be present. Due to its rarity we are presenting Congenital erythropoietic porphyria with haemolytic anaemia.

KEY-WORDS: Gunthers; Porphyria; Haemolytic Anaemia; Photosensitivity; Genetic

Introduction

Cutaneous porphyria is a nonacute porphyria and is also called erythropoietic porphyria. Erythro-poietic porphyria divided in erythropoietic protoporphyria (EPP) and congenital erythropoietic porphyria (CEP).[1] The disease cutaneous porphyria has been around since the beginning of time, however it has just recently been given this name. The disease is one that is a genetically inherited metabolic disorder and the result of this is a deficiency of an enzyme vital in the making of heme.[1,2] The disruption in the production of the heme leads to an over-abundance of the heme and this excess amount can reach toxic levels, causing cutaneous porphyria.[1,2] Primary abnormality in CEP is due to decreased uroporphyrinogen III cosynthase activity resulting in accumulation and hyper-excretion of biologically inactive type I porphyrins. Clinically CEP is non-acute porphyria and defect is expressed in infancy and peculiar clinical features include extreme cutaneous photo-sensitivity, blistering, scarring, milia formation, hypo- and hyper pigmentation of photo exposed parts. Life span is usually decreased.[1] This is the first case we observed in our clinics, and with such rarity and missed easily due to its simple presentation we are going to present.

Case Report

A 14 year old male, born of consanguineous marriage as full term normal delivery, with normal milestone and development presented with the history of Blackish discoloration of skin over face and dorsum of foot and hands for the past 12 years, Yellowish discoloration of eyes and urine (initially intermittent then continuous since 3 months) for 5 Years, passage of red colored urine for the past 6 months, Progressive abdominal distension with heaviness in left upper quadrant for 3 months only, without any drug history, and significant family and personal history. Striking features on physical examination were pallor, icterus, blister and scaly lesion over face and dorsum of upper limb and lower limb [Figure-1,2].

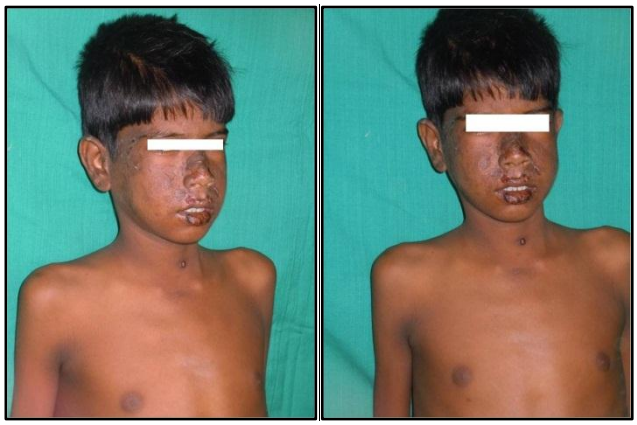

Figure-1: Clinical Photograph showing blister, hyperpigmentation, scar over face.

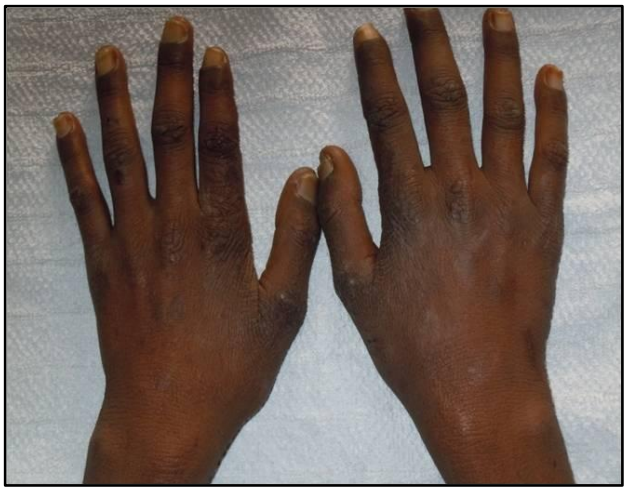

Figure-2: Clinical Photograph showing blister, hyperpigmentation, scar over dorsum of hand

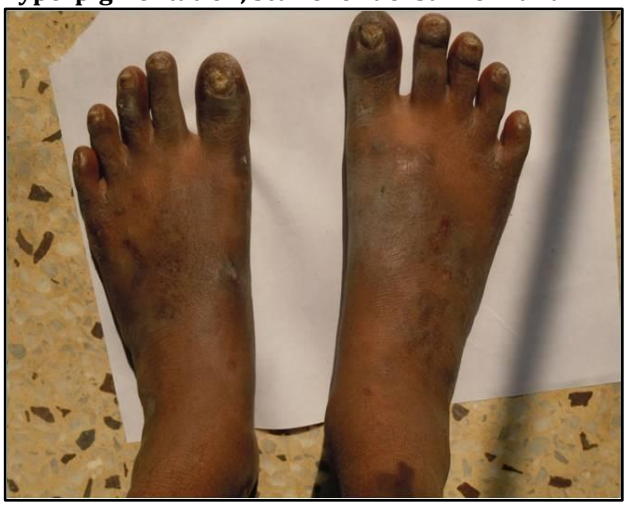

Figure-3: Clinical Photograph showing blister, hyperpigmentation, scar over dorsum of foot

Systemic examination revealed splenomegaly, rest of systemic examination was non-contributory. Many symptoms of porphyria are very similar to those experienced in other more common diseases such as Systemic Lupus Erythematosus, Wilson's disease, and Hemochromatosis. Thus laboratory testing based on the definite pattern of accumulation and hyper-excretion of porphyrins and porphyrin precursor is most effective for diagnosis and typing of porphyrias. Investigations which we planned included routine laboratory investigations significantly revealed decreased Hb (7.2 g/dl), increased reticulocyte count (12% of circulating erythrocytes). Peripheral blood film show erythrocytes exhibited anisocytosis, a dimorphic picture, hypochromia with poikilocytosis. Coombs test was positive. Hemoglobin electrophoresis show HbF 5%, HbA2 2.2%. Platelets and WBC were normal. LDH was increased (728 U/l). Serum Iron was increased (184ug /dl) with normal total iron binding capacity (379ug/dl). Liver function tests showed an elevated serum bilirubin with raised alkaline phosphatase levels. ANA- 49.63 (normal), Serum Ceruloplasmin- 16.9 (20-60), 24- hr Urinary Copper- 150 (normal), All other routine investigations were within normal limits. As per porphyria profile Porphobilinogen and delta amino levaleunate was absent in urine. Porphyrin levels were raised in urine, stool and blood as observed by bright red fluorescence under Wood's lamp. Quantitive studies revealed that urinary porphyrins were elevated 70 times than normal (uroporphyrin levels being more than coproporphyrins). Fecal porphyrin levels too were greatly elevated (coproporphyrin levels were higher than uroporphyrins). Erythrocytes showed greatly increased levels of copro-porphyrins with much lesser amounts of uro-porphyrins, protoporphyrins were negligible. Firm diagnosis was established on the basis of this pattern of increase in porphyrin levels and clinical picture by a systematic ruling out mechanism.

Discussion

Porphyrias are classified as hepatic or erythropoietic based on the sites of accumulation of heme precursors, either in the liver or bone marrow and red blood cells.[3] Symptomatically, acute porphyrias primarily present with nervous system involvement, often with severe abdominal pain, vomiting, neuropathy and mental disturbances. Cutaneous porphyrias present with skin manifestations often after exposure to sun due to the accumulation of excess porphyrins near the surface of the skin.[3] CEP is extremely rare and till recent times less than 200 cases have been reported in world literature. CEP is due to deficiency of the enzyme uroporphyrinogen III cosynthase (UIIIC). The mutation that causes the most severe deficiency of the enzyme uro-porphyrinogen III synthase is C73R. It results in an increase in uroporphyrin I and coproporphyrin I in plasma, red blood cells, urine, feces, and in different tissues.[10] The cutaneous, or erythropoietic, porphyrias primarily affect the skin, causing photosensitivity (photodermatitis), blisters, necrosis of the skin and gums, itching, and swelling, and increased hair growth on areas such as the forehead. Often there is no abdominal pain, distinguishing it from other porphyrias. In some forms of porphyria, accumulated heme

precursors excreted in the urine may cause various changes in color, after exposure to sunlight, to a dark reddish or dark brown color. Even a purple hue or red urine may be been.[4] Porphyria is diagnosed through biochemical analysis of blood urine and stool.[5] Confirmation of the diagnosis of cutaneous porphyria can be made by initial screening of the total porphyrin with a spectrophotometer (semi-quantitation of porphyrins can be achieved by scanning acidified urine or fecal extracts between 350 nm and 450 nm) or a spectrofluorometer. The specimens analysed are urine and plasma (if a spectro-fluorometer is available) or feces (if a spectro-fluorometer is not available). The spectrofluoro-meter is a better instrument as it gives specific curves for VP and EPP.[11] CEP has severe presentation in early childhood and its management is very critical. The only available prophylactic measure for CEP is total avoidance of sun light.[12] Betacarotene, and splenectomy for intractable cases of CEP. Activated charcoal given by mouth is sometimes effective and Bone Marrow Transplantation is a known cure.[6-9]

Conclusion

CEP is a disease that can cause physical and mental distress to child as well as psychological distress to parents and whole family. This distress may be further aggravated by a delayed diagnosis. Delay in diagnosis may even become life threatening. The distress and sequel of this disease can be relieved by awareness of CEP in patients who present with photosensitivity. With this awareness early diagnosis of CEP can ultimately be made resulting in proper management of the patient.

References

1. Murphy GM. Diagnosis and management of the erythropoietic porphyrias. Dermatol Ther; 2003;16(1):57-64.
2. Lane N. Born to the purple: the story of porphyria. Scientific American. Scientific American. 2002. Dec 16. Available at: URL: http://www.scientificamerican.com/article.cfm?id=born-to-the-purple-the-st
3. Lourenco CM, Lee C, Anderson KE. Disorders of Haem Biosynthesis. In: Saudubray JM, Berghe G, Walter JH. (in English). Inborn Metabolic Diseases: Diagnosis and Treatment .5th ed. New York: Springer; 2012:p. 521–532.
4. Stokvis BJ . Over twee zeldzame kleurstoffen in urine van zieken" (in Dutch). Ned Tijdschr Geneeskd1889; 133 (51): 2562–70.
5. Thadani H, Deacon A, Peters T. Diagnosis and management of porphyria". BMJ 2000;320(7250): 1647–1651.
6. Bickers DR, Pathak MA,LIMHW. The Porphyrias . In: Fitzpatrick TB, Eisen AZ, Wolff K (eds.). Dermatology in general medicine . Mc Graw Hill Inc.New York :1993: p 1854-93.
7. Gupta S, Gupta U, Tiwari NK, Saraswat PK, Gupta DK. Gunthers disease . Indian J Dermatol. 1998:43(2):79-81.
8. Poh Fitzpatrick MB. Erythropoietic Porphyria : Current mechanistic , diagnostic and therapeutic considerations . Semin. Hematol. 1977 ;14 : 211-215.
9. Majid S, Massod QA, Hassan I, Veshnavi S, Hussain ST . Feasibility of diagnosis and typing of Porphyrias in developing countries like India-its biochemical basis . JK Practitioner 2006:13(1) 30-33.
10. Hebel JL, Poh-Fitzpatrick MB. Congenital Erythropoietic Porphyria. [Updated 2009 Jan 12]. Available from: http://emedicine.medscape.com/article/1103274-overview
11. Massod QA, Hassan I, Khan D, Sameem F, Quadri MI, Hussain ST, et al. Congenital erythropoietic porphyria with hemolytic anemia. Indian J Dermatol 2005;50:155-7.
12. Dawe SA, Peters J, Du Vivier A, Creamer JD. Congenital erythropoietic porphyria: Dilemmas in present day management. Clin Exp Dermatol. 2002;27:680-3.

Cite this article as: Kumar N, Varshney A, Anand A, Behera D, Anand R, Tiwari A. Gunthers with haemolytic anaemia extremly rare: A case report. Int J Med Sci Public Health 2013; 2:472-474.
Source of Support: Nil
Conflict of interest: None declared