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CASA REPORT

A case report : Featuring a young boy presenting with excessive hair growth & red colored urine

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Abstract:

A four-year-old boy from a rural town in Saudi Arabia presented at the pediatric clinic at King Abdul-Aziz University Hospital complaining of hypertrichosis, skin pigmentations, abdominal pain, vomiting and red urine. We discovered upon laboratory investigations, disturbed liver enzymes, elevated serum ferritin and high uroporphyrin values. The constellation of symptoms and the elevated uroporphyrin suggested the diagnosis of Porphyria. We would like to believe this is an interesting case, which demonstrates a number of combined clinical features in a child, who is the product of a first-degree consanguineous marriage.

Keywords: hypertrichosis, red urine, porphyria, hyperpigmentation

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Introduction

Porphyria is a medical term, encompassing a group of disorders, in which the activity of the heme synthetic enzyme uroporphyrinogen decarboxylase (UROD) is deficient. The incidence of porphyria varies significantly by type, with porphyria cutanea tarda (PCT) being the most common and Congenital Erythropoietic Porphyria (CEP) being the rarest [1]. Porphyrias are classified into two types according to the predominant symptoms, neurovisceral or acute porphyria, presenting usually with abdominal pain, neuropathy, autonomic instability, and psychosis, and cutaneous porphyria presenting with symptoms of photosensitive lesions on the skin [2].

The clinical presentation of the commonest type of porphyria, PCT both familial and acquired, often follows exposure to pathogens or conditions that adversely affect hepatocytes and lead to hemosiderosis. These pathogens or conditions include ethanol, estrogen, hepatitis,

human immunodeficiency viruses and the hemochromatosis genes. Excess iron enhances the formation of toxic oxygen species, thusly increasing the oxidative stress facilitating

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porphyrinogenesis by catalyzing the formation of the oxidation products that ultimately inhibit uroporphyrinogen decarboxylase (UROD). The reduction of UROD activity to approximately 25% of the norm, leads to the clinical expression of the disease.

We present a case of porphyria, featuring a combination of hypertrichosis; hyperpigmentation over sun exposed areas, disturbed liver enzymes and elevated urinary levels of porphyrins. Other causative agents such as HIV, HCV were negative, which favors a sporadic etiology. There has been no association between porphyria and the renal anomalies found in this patient (single kidney), which we believe might have been a coincident.

Case Report

A 4-year-old boy of Arabian ancestry, who is the ninth child of a first-degree consanguineous marriage, was referred to King Abdulaziz University Hospital (KAUH) Jeddah Kingdom of Saudi Arabia, as a case of excessive body hair growth and skin hyper-pigmentation for further evaluation.

This boy was a product of full term pregnancy, via emergency caesarean section due to maternal pre-eclampsia. He was born with a good Apgar score and a birth weight of 3.5 kg. The patient's mother is diabetic, and was not compliant on any diabetic medication. Furthermore, the patient did not have a family history of porphyria. His antenatal, natal and postnatal medical records were normal. At the age of one year, the parents noticed that their child started to have repeated episodes of abdominal pain, dull – aching in nature, generalized, mild to moderate in severity, aggravated by food and relieved by vomiting, the pain was not associated with constipation or dysuria. The vomiting was non-projectile and non-bilious. A few months after the development of the abdominal pain, facial hair started to grow mainly on the forehead and then progressively started covering most aspects of the face (Figure

I). The parents noticed hair growing over the upper parts of both arms and legs (Figure II-A & II-B). The previous symptoms were associated with recurrent episodes of painless red colored urine (Figure II). The skin pigmentation was increasing in darkness upon sun exposure. The patient had no significant past medical or surgical history, neither history of similar condition in the family nor any known allergies. On examination, his growth parameters were within the 10th percentile for his age. The patient's excessive hair growth covered the following areas: forehead, malar area, upper limbs, and lower limbs, with hyperpigmentation over sun exposed areas as seen in (Figure II-A & II-B). The patient had a normal neurological examination and there were no axillary or pubic hair growth. He also had normal male genitalia.

During his first presentation, we conducted laboratory investigations in order to rule out the possibility of congenital adrenal hyperplasia, which is a common cause of hyperpigmentation. The following laboratory investigations had been performed at KAUH Clinical Chemistry Laboratory for the assessments of different parameters. The laboratory investigations revealed normal serum sodium of 136 mmol/L (135-145), serum potassium of 4.6 mmol/L (3.5-5.1), elevated transferrin saturation 58% (15–50%) and elevated serum ferritin levels of 489 ng/mL (30 - 400 ng/ml) and no metabolic acidosis pH: 7.35 (7.37-7.45). A hormonal study showed normal serum cortisol levels of 454 nmol/L (138-636), normal levels of 17-hydroxyprogesterone of 3.2 ng/ml (0.6-7), normal ACTH levels of 18.76 pmol/L (9-52), normal thyroid stimulating hormone levels 4.2 u/L (0.27 - 4.8), normal free T4 levels 16.02 pmol/l (12 - 22) and normal testosterone levels of 10 pmol/l (9.1 - 55.2). His liver enzymes were disturbed; aspartate aminotransferase (AST) was high, 593 (15-37 IU/L), serum alanine aminotransferase (ALT) was also high, 612 (30-65 IU/L). Hepatitis C virus (HCV) and human immunodeficiency



Figure I: Excessive hair growth including; forehead, malar area, with pigmentations over sun exposed areas.



Figure II-A & II-B: These two pictures demonstrate the excessive hair growth over upper limbs (A) and lower limbs (B) with apparent pigmentations over sun exposed areas.

viruses (HIV) antibody screening were negative. We conducted a liver isotope scan; it revealed a decrease in the uptake of radioactive substances by hepatocytes, suggesting hepatic inflammation.

Urinary investigations including dipstick, urine analysis and urine culture surprisingly revealed no red blood cells, casts or any bacterial organisms, while the renal ultrasound



Figure III: The red appearance of the urine collected from the subject; the microscopical analysis showed no evidence of red blood cells or casts.

incidentally showed single right kidney. We collected a twenty-four hours urine sample for the assessment of a urinary porphyrin profile. The sample revealed very high uroporphyrin levels (Table 1). The investigations and the constellation of symptoms deemed the diagnosis of porphyria as very likely. The patient was started on a low dose chloroquine therapy of 125 mg orally twice per week (each 125 mg contained 75 mg base) and he was advised to avoid sun exposure.

Table I. The porphyrin profile

| | Result (nmol/l) | Normal Range (nmol/l) |
|--------------------------------|------------------------|------------------------------|
| Hepatacarboxy Porphyrin | > 2340 | up to 24 |
| Hexacarboxy Porphyrin | >3060 | up to 4 |
| Coproporphyrin 1 | >150 | up to 40 |
| Total Porphyrins (HPLC) | >6630 | up to 143 |

Discussion

Porphyria is a group of genetic and acquired deficiencies affecting the activities of enzymes in the heme-biosynthetic pathway. The enzymatic

deficiencies result in excessive production of and excretion of metabolic intermediates. These metabolites accumulate in tissues and result in neurovisceral (abdominal pain, psychiatric disorder, neurological symptoms and / or photocutaneous symptoms). Porphyria is a group of inherited disorders, some are autosomal dominant and others are autosomal recessive. Because of the nature of consanguinity in this case, we believe it is more likely to be an autosomal recessive condition [3]. However, we lack the facilities to conduct genetic testing for this particular disorder.

The clinical features of porphyria vary greatly. Acute porphyria could present with severe abdominal pain, neurological and psychiatric symptoms [4]. Muscular weakness and mild sensory changes, often in a “bathing trunk” distribution, along with constipation, nausea, vomiting, postural hypotension, and hypertension are also common features of acute porphyria [5]. Cutaneous porphyria usually present in childhood with skin lesions, pigmentation, dark red urine and hypertrichosis, particularly on the forehead and upper cheeks, the lesions occur on skin areas that are exposed to the sun, such lesions are most severe in congenital erythropoietic porphyria [6,7]. These lesions are due to the accumulation of porphyrins in the skin and the liver, which also explains the hepatic involvement of the disease such as cholelithiasis and occasionally liver failure. PCT is the commonest of all the porphyries, it has two forms; sporadic PCT, accounts for 80 - 90% of all cases and familial PCT, accounts for 10 - 20%. Etiological factors for PCT include alcohol, oestrogens, iron, and chemicals (for example, hexachlorobenzene). There is also an association with hepatitis C. Mild iron overload is nearly always present. People with genetic haemochromatosis, are four times more likely than otherwise normal subjects to have sporadic PCT [8]. The patient in this study presented with hypertrichosis, skin pigmentations, abdominal pain, vomiting and red urine. His laboratory

investigations showed disturbed liver enzymes and elevated serum ferritin.

The diagnosis of porphyria can be rather challenging, mainly due to the scarcity of advanced facilities with sufficient technology to conduct the analysis required to establish the diagnosis and subtype of porphyria. During acute attacks of porphyria a raised urinary excretion of aminolaevulinic acid (ALA) and porphobilinogen (PBG) occurs. A fresh urine sample, protected from light, should be sent to a specialist laboratory for accurate quantitation of aminolaevulinic acid (ALA) and porphobilinogen (PBG) concentrations [9]. However, between acute attacks the concentrations of urinary PBG and ALA are often normal. In variegate porphyria plasma fluorescence is usually increased, which is a valuable tool both diagnostically and for family studies [10,11]. Acute intermittent porphyria, variegate porphyria, and hereditary coproporphyria can be differentiated by analysis of faecal porphyrins, patients who are suspected of having cutaneous porphyrias must have their urine and faeces investigated for excess porphyrins as the water solubility (and hence route of excretion) of the individual porphyrins differs [12]. It is particularly important to distinguish between patients with variegate porphyria and hereditary coproporphyria presenting with skin lesions alone, who are at risk of life threatening acute neurological attacks, and those with PCT or congenital erythropoietic porphyria, who are not at risk from such attacks [12]. In the presented study, we measured urine porphyrins via high performance liquid chromatography. For calibration, we used the uroporphyrin I Fluorescence Standard Kit and the Coproporphyrin III Fluorescence Standard Kit (Sigma Porphyrin Products, Logan, Utah, USA). We refer to these standard kits as calibrators. Accurate porphyrin concentrations were calculated after spectrophotometric measurement with known molar extinction coefficients in 1 mol/l. The demonstration of reduced red cell

hydroxymethylbilane synthase activity, could confirm diagnosis of acute intermittent porphyria [13]. Iron overload is commonly associated with porphyria, mainly PCT [14]; in the presented study, the patient had elevated serum ferritin and transferrin saturation. Classification of the subtypes of porphyria among affected patients is not essential for clinical management. In the presented study, the liver enzymes were elevated so we conducted a HCV serology and a liver isotope scan. When patients present with elevated liver enzymes or signs of hepatic stress, testing for associated disorders such as HIV, HCV, and iron overload via liver imaging studies to exclude other causes of hepatic involvement and to serve as a baseline for follow up evaluation is important.

Treatment modalities for porphyria include avoidance of sun exposure and low doses chloroquine therapy (125 to 250 mg orally twice per week) or Hydroxychloroquine (100 mg orally twice per week), which improves the removal of excess uroporphyrin from the tissue and enhances urinary excretion [15]. In the presented study, we advised the patient's family on the importance of avoiding sun exposure and we started the patient on low dose chloroquine therapy. The management modality used showed signs of improvement on the child during his hospital stay. We used the low dose chloroquine therapy mainly because; it offered a cheap long-term solution for the family, whom lived in a rural town in the kingdom of Saudi Arabia. We feared they might not be able to attend follow up appointments so we sought out a more suitable and permanent solution.

Conclusion

The 4 year old boy in this study presented with abdominal pain, hypertrichosis, and hyperpigmentations over sun exposed areas such symptoms favored the diagnosis of porphyria. Later on, we confirmed the diagnosis by the urinary HPLC analysis, which revealed an elevated urinary porphyrins profile. Other

causative agents such as HIV, HCV were negative, suggesting a sporadic etiology. Upon conducting a literatures review, we found no association between porphyria and renal anomalies (single kidney), thus we believe this maybe a co-incident.

Limitations

Our limitations are mainly due to lack of facilities and the financial and educational level of the patient's family. We were able to send the urinary HPLC profile to establish the diagnosis of porphyria and initiate the proper management. However, we were not able to conduct a stool HPLC profile, urine HPLC profile for the entire family of eleven (nine children + parents), UROD activity, genotyping information, PBG and ALA analysis. The laboratory facilities required to conduct such tests are not available in our country and the family could not afford to send samples abroad for analysis.

REFERENCES

- 1- Desnick RJ, Glass IA, Xu W, et al. Molecular genetics of congenital erythropoietic porphyria. *Semin Liver Dis.* 1998;18:77-84
- 2- Poblete-Gutierrez P, Wiederholt T, Merk HF, Frank J. The porphyrias: clinical presentation, diagnosis and treatment. *Eur J Dermatol.* 2006;16:230-40
- 3- Table 18-1 in: Marks, Dawn B.; Swanson, Todd; Sandra I Kim; Marc Glucksman (2007). *Biochemistry and molecular biology.* Philadelphia: Wolters Kluwer Health/Lippincott Williams&Wilkins. ISBN 0-7817-8624-X.
- 4- Thadani H, Wassif W, Deacon A, Peters T. Neuropsychiatric manifestations of acute intermittent porphyria. *J sychiatric Case Reports* 1997;2:29-35.
- 5- Elder GH, Hift RT, Meissner PN. The acute porphyrias. *Lancet* 1997;349:1613-7.
- 6- Fritsch C, Bolsen K, Ruzicka T, Goerz G. Congenital erythropoietic porphyria. *J Am Acad Dermatol* 1997;36:594-610.
- 7- Guennoun N, Gerolami-Colombani V, Sebti A, Aquaron R. Sporadic porphyria cutanea tarda: a case report in a Moroccan man. *Med Trop (Mars).* 2003;63:183-7.
- 8- Elder GH, Worwood M. Mutations in the hemochromatosis gene, porphyria cutanea tarda, and iron overload. *Hepatology* 1998;289-90.
- 9- Buttery JE. Is the Watson-Schwartz screening method for porphobilinogen reliable? *Clin Chem* 1995;41:1670-1.
- 10- Poh-Fitzpatrick MB. A plasma fluorescence marker for variegate porphyria. *Arch Dermatol* 1980;116:543-7.
- 11- Long C, Smyth SJS, Woolf J, Murphy GM. Detection of latent variegate porphyria by fluorescence. *Br J Dermatol* 1993;129:9-13.
- 12- Helen Thadani, Allan Deacon, Timothy Peters. Diagnosis and management of porphyria. *BMJ* 2000;320:1647.
- 13- Kappas A, Sassa S, Galbraith RA, Nardaman Y. The porphyrias. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. *The metabolic basis of inherited diseases.* 6th ed. New York: McGraw-Hill, 1989:1305-66
- 14- Martinelli AL, Zago MA, Roselino AM, Filho AB, Villanova MG, Secaf M, et al. Porphyria cutanea tarda in Brazilian patients: association with hemochromatosis C282Y mutation and hepatitis C virus infection. *Am J Gastroenterol* 2000;95:3516-21.
- 15- Valls, V, Ena, J, Enriquez-De-Salamanca, R. low-dose oral chloroquine in patients with porphyria cutanea tarda and low- moderate iron overload. *J dermatol sci* 1994; 7:169.