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Case Report

Porphyria cutanea tarda: A case report

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ABSTRACT

Background: The porphyria's are a rare group of metabolic disorders produced by acquired or hereditary deficiency of the enzyme UROD, fifth enzyme in the chain of production of the heme group, which results in an accumulation of photosensitive by products, such as uroporphyrinogen, which leads to the fragility and blistering of sun-exposed skin. Porphyria can manifest with neurovisceral and/or cutaneous symptoms, depending on the defective enzyme. Prevalence of porphyria's varies, from 1 in 500 to 1 in 50,000 people worldwide. PCT, the most common.

Case Presentation: A 59-year-old Indian man presented with multiple non healing ulcers on dorsum of right hand and scalp associated with photosensitivity and reddish discoloration of urine, and surrounding depigmentation with scarring. He was diagnosed as having PCT after clinical investigation and was treated symptomatically.

Conclusion: PCT is the most common of the seven porphyrin metabolism disorders. The misdiagnosis and mismanagement of this disease can have a significant impact on a patient's life and does management of PCT in our case is focused on the signs and symptoms and findings.

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1. Introduction

The porphyria cutanea tarda (PCT) is the most common type of porphyria without a well-defined pattern of inheritance. Porphyria cutanea tarda may be acquired without inherited mutation in Uroporphyrinogen decarboxylase (UROD) enzyme. UROD enzyme is needed to metabolize certain body chemicals that are known as porphyrins.¹ It is the fifth enzyme of heme biosynthesis and inverts to uroporphyrinogen protoporphyrin.² Low level of UROD enzyme leads to accumulation of porphyrin in the body especially liver and skin.

The prevalence of all PCT is 1:5000-1:70,000.³⁻⁶ The disease has been classified into three subtypes. The acquired or sporadic type (Type 1) and Inherited type (Type 2). The acquired accounts for approximately

80% of the patients, the remainder are of the inherited type (Type 2) which is transmitted as an autosomal-dominant trait with a weak penetrance. In this subtype, UROD activity is deficient in hepatocytes but not in RBCs. Mutation in the UROD gene is seen in 20-30% of patients with familial PCT. In this subtype, UROD activity is reduced in all tissues. Type 3 PCT occurs in <5% cases, there is normal Erythrocyte UROD activity.⁷ Genetic defect or environmental risk factors are unknown. Homozygous mutation of the UROD gene results in a very rare form, Hepatoerythropoietic porphyria (HEP), which manifests during childhood, while the familial and sporadic forms appear at mid to late adulthood.⁸ A variety of agents are known to precipitate type 1, these include alcohol, cigarette smoking, iron overload, end-stage renal disease, estrogens, griseofulvin, hydantoin, and Hepatic siderosis. Excess alcohol intake enhances Intestinal

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absorption of iron, precipitating PCT. Toxic Chemicals, such as hexachlorobenzene,^{9,10} chlorinated Hydrocarbons, such as tetrachlorodibenzo-p-dioxin, and pentachlorophenol cause toxic PCT. There is a strong correlation between sporadic form of PCT and Hepatitis C infection, and this is well established in many studies. Several reports have described PCT in patients with HIV infection and hereditary Hemochromatosis (HH). Typical mutations linked to HH are C282Y, H63D, and HFE locus. Hemochromatosis gene plays a role in the determination of PCT.¹ HFE gene mutation prevalence is increased in PCT.^{11,12} HFE gene mutation might also cause hemochromatosis. There are several postulations regarding pathomechanism of HIV Induced PCT. These include HIV-induced altered Porphyrin metabolism, direct hepatic damage, altered porphyrin biosynthesis and functional Impairment of cytochrome p-450 mixed function Oxidases. Co-infection with Hepatitis C virus is a more potent risk factor for the development of PCT. However, in most cases, a relationship between symptoms and assumed etiological factors cannot be demonstrated.

2. Case Presentation

A 59-year-old man presented with multiple non healing ulcer largest of which measuring around 9x9 cm over dorsum of left hand and 3x3 cm scalp since 3 months.

Clinical examination revealed multiple, ulcers with well-defined margin present over scalp and dorsum of hand.



Fig. 1:

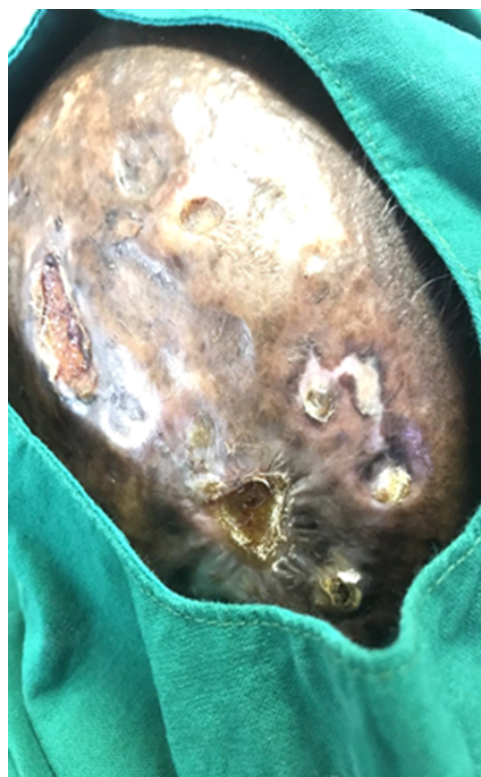


Fig. 2:

Few areas showing healing with depigmentation and Scarring.

History of Blisters which break upon leaving painful sores initially started over dorsum of hands, feet and scalp since 10 years. Patient also has Red coloured urine since childhood. (Figure 3)



Fig. 3:

History of similar illness in brother is also appreciated.

Differential diagnosis: PCT, scleroderma, photo aggravated Bullous dermatoses.

Histopathology of skin: Epidermis showed hyperkeratosis, Subepidermal separation.

Upper dermis- scattered lymphocytes, few thick walled Capillaries with PAS positive materials.

Woods lamp: pinkish fluorescence of urine and teeth.

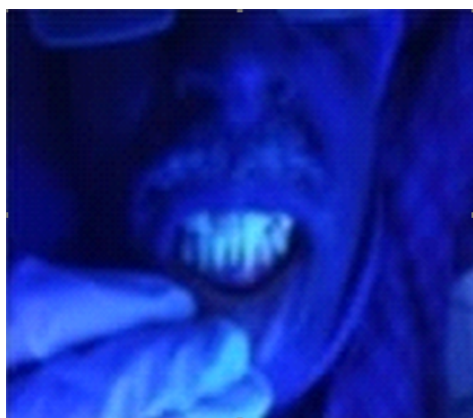


Fig. 4:

Ocular examination: Scleromalacia perforans.

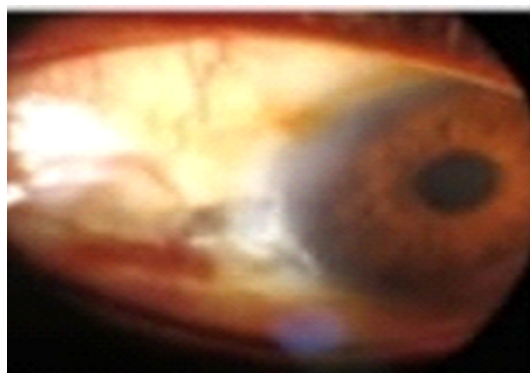


Fig. 5:

2.1. Investigations done were

1. Urine and stool porphyrins- elevated.
2. Genomic testing: heterozygous UROD pathogenic variant.
3. Liver function tests: within normal limit.
4. Serology: HIV, hep B, hep C was negative.
5. Autoimmune screening was negative.

3. Discussion

Type I PCT typically presents in adulthood, whereas the onset of symptoms in childhood is suggestive of Type II PCT. The cutaneous lesions of both are indistinguishable and occur on sun exposed areas, especially the dorsum of hands, forearms, and on the face.¹ Patients present with skin fragility, pigmentation, hypertrichosis and bullous lesions due to photosensitivity. Bullous lesions appear in 85% of patients in summer, each time the patient indulges in a spree with hard liquor together with solar exposure. In the Quiescent stage, the lesions heal with scarring, hypo- and hyperpigmentation, milia on the fingers, and less often on

the face and other exposed parts pseudoscleroderma may occur. Hypertrichosis is seen over the face, particularly the cheeks, temples, and above the eyebrows, giving a monkey-like face.¹ The limbs may also be involved. In coloured races, hypopigmented patches may occur at the sites of erosions. Sclerodermoid changes and dystrophic calcification are rarely seen in children. Rarely patients present with Ocular manifestations such as conjunctivitis, photophobia, and excessive tearing. Systemic features such as insomnia, anorexia, constipation, or diarrhea can also occur. Monochromatic photobiological tests reveal spectral sensitivity at about 400 nm and sometimes also at 500-600 nm. Impaired liver function tests are frequent, with elevated serum transaminases. Iron overload in PCT is suggested either by increase Serum iron levels or by hepatic siderosis. Liver Biopsy specimens show variable degrees of fatty Infiltration, inflammation, necrosis, and portal Fibrosis. Patients with PCI have a higher incidence of hepatocellular carcinoma than the general population. Other conditions with which PCT maybe associated include diabetes mellitus, SLE, Chronic renal failure on dialysis (hemodialysis-Related PCT), and HIV infection. PCT has also been reported as Bantu porphyria in the Bantus of South Africa and Zimbabwe due to the hepatotoxic effect of adulterated drinks brewed locally.¹ The cutaneous features are similar to those of other forms of hepatic porphyria, but extensive erosions with secondary infection, subungual, fingertip or palmar bullae and gross secondary scleroderma are more common. In southeast Turkey, PCT was reported to occur after the accidental consumption of wheat dressed with hexachlorobenzene. The prognosis in PCT is better than that in CEP or AIP. It is usually not fatal unless the liver function is profoundly affected or acute manifestations of a grave nature supervene. The tendency of skin photosensitivity may burn itself out after middle age, although the porphyrin dyscrasia remains. Risk of hepatocellular carcinoma has been observed mostly among northern European population. An iron-deficient state is protective for recurrence of symptoms, whereas inadvertent administration of iron precipitates it. Pregnancy outcomes in women suffering from various porphyrias are not definitely known. First attack of AIP may be precipitated during Pregnancy. PCT may improve or exacerbate during this period. Primigravidas with sporadic PCT may have premature delivery and low birth weight babies. Incidence of small for gestational age fetus is more in multiparous women. Familial PCT is associated with 3-fold increased risk of perinatal death. All acute porphyrias are the risk factors for intra-uterine growth retardation, premature delivery, spontaneous abortion, and perinatal death.¹ However, pregnancy during latent disease may not be associated with adverse outcomes. The major differential diagnosis is to be made from VP and other dermatoses such as epidermolysis

Bullosa, hydroa vacciniforme, hydroa aestivale, Drug-induced photosensitivity, polymorphic light eruption, and scleroderma.

Diagnosis of PCT depends on histology of the skin, which shows a subepidermal blister with minimal inflammatory cell infiltrate in the dermis. A characteristic elongated structure called “caterpillar bodies” is seen at the roof of the bullae. There is festooning of dermal papillae into the bullae. There is deposition of PAS-positive material in the papillary capillaries. Electron microscopy shows reduplication of the dermoepidermal basement membrane and a reduction in the number of collagen fibers, which may account for easy susceptibility to mild mechanical trauma.^{10,13,14} DIF shows deposition of C3, IgG, and IgM in and around the dermal capillary walls and also the dermoepidermal junction. Urine of the affected patients is dark brown in all types of PCT and emits red fluorescence under Wood’s light. The porphyrin profile in PCT reflects the partial defect in uroporphyrinogen decarboxylase activity. Owing to their water solubility, uroporphyrin (Isomers I > III) and 7-carboxyl-porphyrin (Isomers III > I) are excreted in the urine. The less water-soluble 6, 5, and 4-carboxyl porphyrins (coproporphyrin) are also present in the urine, but in much smaller amounts, although they predominate in feces. Isocoproporphyrin III is most elevated in feces with lesser amounts of coproporphyrin, 7-carboxyl Porphyrin, and uroporphyrin. The erythrocyte Porphyrin profile in patients with PCT is normal.

3.1. Treatment of PCT consists of three elements

Avoidance of triggering factors (alcohol, estrogens), depletion of iron (phlebotomy), and elimination of porphyrin (low-dose chloroquine therapy).¹⁵ A nutritionally adequate intake of ascorbic acid is also beneficial. Combined treatment with repeated phlebotomy and chloroquine results in remission in an average of 3.5 months. The time necessary for remission with chloroquine alone is 10.2 months; the time for remission with phlebotomy alone is 12.5 months. Complete elimination of alcohol and exposure to other hepatotoxins resulted in complete clinical clearing of bullae and skin fragility in 2 months to 2 years. Elimination of risk factors include: 1. Stopping oestrogen therapy, if it has not been used for more than 2 years, can induce remission. However, elimination of the underlying cause by abstaining from alcohol, or by treating hepatitis C with interferon does not always induce remission. 2. Photoprotection visible light sunscreens containing pigmentary grade titanium dioxide or zinc oxide, sometimes with added iron oxide, filter films for car and home windows, gloves, hats and clothes play an important role in controlling symptoms during the period of several months before specific therapies take effect.

3.2. Phlebotomy

Venesection depletes iron stores and eliminates hepatic iron overload, thus restoring normal enzyme activity. It reduces hepatic iron stores and produces remissions of several years duration. One unit of blood should be removed every 2 to 4 weeks until the hemoglobin level drops to 10 gm/dl or until the serum iron level drops to 50 mg/dl. The average number of units required for remission varies between 8 and 14. Measurement of plasma uroporphyrin level is an effective way to monitor the progress of patients with PCT.¹⁵ Treatment should continue until plasma uroporphyrin levels drop below 10 mmol/L. Plasma ferritin levels can also be used as a guide to treatment by venesection. Phlebotomy can be terminated when iron stores, as reflected by plasma ferritin concentration, have fallen to low-normal limits.¹⁵ Desferrioxamine leads to earlier remission than venesection because it rapidly chelates hepatic iron, and it may be of value in PCT with renal failure but it is expensive and requires the use of a subcutaneous pump at night. Erythropoietin mobilizes hepatic iron to hemoglobin and is the treatment of choice for PCT in renal failure where patients are too anaemic for venesection.

3.3. Chloroquine therapy

Chloroquine in very low dosages may also be used. Chloroquine causes the release of hepatic tissue bound uroporphyrin, and subsequently it is rapidly eliminated by the plasma and excreted by the urine. A release of porphyrins that is too rapid might severely affect liver function.¹⁵ Hence daily doses of chloroquine cause a potentially dangerous acute hepatitis, but chloroquine at the low dose of 125 mg or 250 mg taken twice a week is safe and effective. It leads to clinical remission within 6 months or so and biochemical remission after 6-15 months, at which point treatment is stopped. Retinopathy does not seem to occur with such low doses of chloroquine. Hydroxychloroquine (100 mg twice Weekly) is also effective. In patients with chronic hemodialysis-associated PCT, chloroquine is ineffective. Erythropoietin, desferrioxamine, and small-volume phlebotomy have been employed to control the disease.¹⁵ Blistering usually resolves within 2-3 months, skin fragility within 6-9 months, and porphyrin concentrations generally normalize within 13 months or so at which point treatment should be stopped. Hypertrichosis and sclerodermoid lesions respond more slowly during the years after treatment has stopped. Excision and grafting may be needed for ulcerated sclerodermoid lesions.

3.4. After treatment

4. Conclusion

This case was misdiagnosed as discoid lupus erythematosus for several months due to the symptoms of photo sensitivity



Fig. 6:



Fig. 7:

and scarring alopecia. But a proper history elicited that along with photo sensitivity and alopecia, patient also had red coloured urine and history of a similar illness in family which raised the suspicion of porphyria cutanea tarda. A simple wood's lamp examination of urine and teeth could help us differentiate this from its close differentials like scleroderma and photoaggravated bullous dermatoses. The familial porphyria cutanea tarda has a very less chance of similar symptomatic illness in the family due to its low penetrance but was present in our case. Also, as per literature, familial porphyria cutanea tarda usually has a younger age of onset but was manifested only by the early

6th decade in our case.

In our opinion, inspite of porphyria cutanea tarda being not very common among general population, its familial nature, late onset and associated family history makes it a rare and exceptional case.

5. Author's Contributions

Dr. Sana diagnosed the patient and had the idea of the case report.

Dr. Iqbal and Dr. Amreen followed the patient and designed the report, reviewed the literature, wrote the case report, and approved the final text.

6. Acknowledgement

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8. Conflict of Interest


None.


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