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Porphyria cutanea tarda is a biochemical and not histological diagnosis

Abstract

Porphyria cutanea tarda is the most common porphyria, due to acquired deficiency of hepatic uroporphyrinogen decarboxylase (UROD) enzyme, presenting with photosensitivity and blistering skin lesions. Factors making an individual susceptible to PCT include alcohol consumption, smoking, hepatitis C, HIV, estrogen use, and UROD mutation. Diagnosis of PCT is made with typical porphyrin profile of elevated plasma porphyrins (maximum fluorescence at 620nm) and urine porphyrins (predominant hexa-, penta-, hepta-carboxyporphyrins). Skin biopsy may show features consistent with PCT, however by themselves may not be diagnostic. PCT is readily treatable with either phlebotomy schedule or low dose hydroxychloroquine regimen. We present two cases referred to our centre, all of them diagnosed with PCT based on a skin biopsy. An 81 year old man presented with blistering skin lesions and photosensitivity on dorsal hands and scalp. Skin biopsy from dorsal hand performed by his dermatologist showed dilated blood vessels in dermis with collagen deposition, consistent with PCT. He had no susceptibility factors for PCT. The porphyrin profile was normal with plasma porphyrins of 0.1mcg/dl (normal <0.9) and urine porphyrins of 35nmol/L (normal <300). A 28year old female was diagnosed with PCT based on skin biopsy. She had 4year history of photosensitivity and plaque like lesions on dorsal hands, which were progressive in spite of being treated with hydroxychloroquine. Except history of smoking, she had no other susceptibility factors of PCT. Biochemical porphyrin profile was normal. She is being treated for pseudoporphyria secondary to doxycycline and is doing well. Conclusions: Biochemical porphyrin profile and not skin histology is the confirmatory test for the diagnosis of PCT.

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Introduction

Porphyria cutanea tarda (PCT), the most common human porphyria, is acquired due to deficient activity of hepatic uroporphyrinogen decarboxylase (UROD) in the heme biosynthetic pathway, secondary to production of its inhibitor uroporphomethene, which is produced in the presence of mild to moderate iron overload.[1–4] Decreased activity of UROD leads to increased accumulation of uroporphyrinogen and the partially decarboxylated intermediates hepta-, hexa- and penta-carboxylate porphyrinogens, which are auto-oxidized to the corresponding porphyrins. PCT has a characteristic biochemical pattern of porphyrins in urine (>300nmol/L, with predominant fraction of uroporphyrins and intermediates) and plasma (>0.9mcg/dL, with maximum fluorescence at 681-621nm wavelength at neutral pH), which is diagnostic of this disorder.[1–3] Skin histology shows sub-epidermal blister formation with deposition of periodic-acid-Schiff positive hyaline material containing immunoglobulin around the vessel walls, with little inflammation.[1,5] Damage to the epidermis may lead to coalescing of the lesions and bullae formation. Surrounding fibrosis may be prominent in chronic lesions. PCT is a heterogeneous disorder with most cases precipitated in the presence of multiple environmental and hereditary susceptibility factors.[1,6,7] Common susceptibility factors are alcohol use, smoking, hepatitis C virus (HCV) infection, HIV infection, hemochromatosis gene mutations, estrogen use, and inherited UROD mutation. Clinically, PCT patient's present photosensitivity on sun exposed areas, with blistering lesions, plaque like lesions, or skin friability as most common clinical presentations. PCT is readily and effectively treatable by repeated phlebotomy schedule or with low dose hydroxychloroquine (HCQ) given as 100mg twice a week orally. Both the treatments are equally effective and safe in the treatment of PCT.[1,2,6]

Methods and results

We describe three cases with photosensitive skin lesions referred to our centre with diagnosis of PCT, determined based on skin biopsy. Biochemical porphyrins profile in urine and serum in these patients confirmed diagnosis of PCT in only one patient, while other two patients did not have PCT and were diagnosed with pseudoporphyria.

Case 1

81 year old white male reported two years history of photosensitivity with skin blistering on dorsum of hands and on scalp. Other comorbidities were diabetes, hypertension, chronic kidney disease, dyslipidemia, and chronic obstructive pulmonary disease. He was also on anticoagulation for patent foramen ovale. He was seen by a dermatologist and skin biopsy from dorsal hand lesion showed bullae formation at the dermal-epidermal junction with prominent dilated vessels and focal areas of collagen deposition within the epidermis (Figure 1a). Based on these findings, PCT was diagnosed and he was treated with phlebotomy schedule, every 2–4weeks. This was discontinued after about 15months due to anemia, requiring two units of packed red blood cells.

At the time of presentation to our centre, he reported active new lesions on scalp and dorsal hands. He smoked 1 pack per day of cigarettes for 45years and quit over 10 years ago. He denied alcohol or estrogen use, and did not have HCV or HIV infection. Genetic

tests for HFE and UROD mutations were negative. Physical exam was unremarkable except for blistering and scaling lesions on dorsum of hands and on scalp with pain Score of 7 out of 10. Laboratory results were remarkable for haemoglobin 12.5 (normal range: 13.5-17.5gm/dl), fasting glucose (normal range: 70-100mg/dl); and serum creatinine 1.5mg/dl (normal range: 0.7-1.1mg/dl).

Serum ferritin was normal at 24ng/mL. Biochemical porphyrin profile was also normal with urine and plasma porphyrins of 124nmol/L (75% coproporhyrins) and 0.1mcg/dL respectively. The patient is being treated by for pseudoporphyria of unknown etiology, and is doing well.

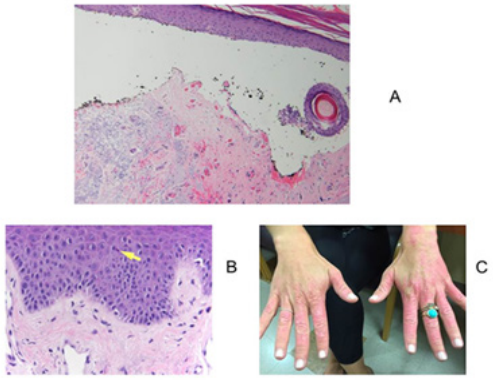

Figure 1 Photosensitive skin lesions.

Case 2

28 year old white female reported bullous lesions with photosensitivity started for 3years. Other comorbidities included gastroesophageal reflux disease and acne, and she was taking proton pump inhibitor and doxycycline. She smoked ½ packs per day for 4years and quit it 4months ago. She was a social drinker using 4-5glasses of wine on the weekends. The patient was seen by a dermatologist and punch biopsy from left dorsal finger lesion showed subtle dermal fibrosis with occasional necrotic keratinocytes with hyalinised blood vessels (Figure 1b). Another punch biopsy from right finger showed immunofluorescence deposits of IgG and C3 around the small blood vessels. With worsening plaque like lesions on hands, lateral arms, and dorsum of feet, she was started on hydroxychloroquine 200mg daily, without any improvement in skin lesions at all after being treated with this drug for six months.

At the time of presentation to use, the skin showed extensive bright erythematous plaque like lesions on dorsal hands, forearms, face, and dorsal aspects of feet (Figure 1C). Other physical examination was unremarkable. Routine laboratory work up was unremarkable. She did not have HCV or HIV infection and genetic testing for HFE or UROD mutations were negative. Routine lab work including serum ferritin was normal. Biochemical porphyrins profile showed normal urine and plasma porphyrins with values of 99nmol/L and 0.1mcg/dl respectively. She was referred back to her dermatologist and is being treated as docycycline induced pseudoporphyria. She is doing very well with improved skin lesions after discontinuing doxycycline. Hydroxychloroquine has been discontinued also.

Discussion

Our case series of two cases demonstrates that histological changes on the skin biopsy alone should not be used to diagnose PCT, and the diagnosis of PCT should be confirmed with a characteristic biochemical porphyrin profile in the urine and plasma.

PCT is the most common human porphyria and is acquired in the presence of susceptibility factors such as smoking, alcohol use, HCV infection, HIV infection, and HFE gene mutations.[1,2] Genetic mutation of the UROD enzyme is a susceptibility factor in about 20% PCT cases, also known as familial PCT.[1,2] Iron overload of mild to moderate degree even in the absence of HFE gene mutations is present in PCT, which is required for the generation of the UROD inhibitor, uroporphomethene.[4] In a large series of PCT cases, about 70% of PCT cases had three or more susceptibility factors.[7] None of the susceptibility factors were present in our first case and smoking was the only susceptibility factor in the second case. Serum ferritin was normal in both these cases. Phlebotomy or low dose hydroxychloroquine are effective and safe in the management of PCT, with all patients achieving remission with the use of one of these modalities.[1,6] Both of our patients did not have any response to the presumed diagnosis of PCT, first one to repeated phlebotomy schedule and the second one to six months of HCQ therapy. Both of these patients turned out to be not having PCT.

Photosensitivity and blistering or bullous skin lesions similar to lesions seen in PCT can occur in other conditions other than PCT, also known as pseudoporphyria. This condition is mostly secondary to drugs such as sulphonamides, tetracycline, non-steroidal anti-inflammatory drugs, dapsone, furosemide, and nalidixic acid. Our first two cases were diagnosed with pseudoporphyria, one due to doxycycline use and the cause could not be established in the other patient.

Well documented porphyrin profiles in both patients refuting the diagnosis of PCT are strength of our study. Further, all the cases have final diagnosis determined with adequate follow up available data. Small sample size of only two cases, however, is a limitation.

In summary, our case series describes two cases with skin histology changes in PCT, and highlights the need for obtaining the urine and plasma porphyrin profile to confirm the diagnosis, before initiating any specific therapy for PCT.

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None.

Conflicts of interest

Authors declare that there are no conflicts of interest.

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