Skin erosions and abnormal liver function

Yuan-Jessica Zhuang, Andrew Awad, Ashok S Raj, Gayle Ross

CASE

A man, aged 50 years, was referred to a dermatology outpatient clinic with 12 months of skin fragility on the dorsum of his hands. He described intense pruritus, blistering and erosions, which were slow to heal. He often wore short sleeves and spent time outdoors. His past medical history included cerebral palsy, epilepsy, legal blindness since childhood and Tetralogy of Fallot, which was surgically repaired in infancy. Regular medications included carbamazepine, clobazam, perampanel, sodium valproate and vitamin B. He denied drinking alcohol or smoking. On examination, multiple superficial erosions were seen on the dorsum of the hands along with postinflammatory hyperpigmentation and scarring. There were small milia on the dorsum aspect of his left hand (Figure 1).

QUESTION 1

What are the main differential diagnoses for a localised blistering skin condition?

QUESTION 2

What investigations should you consider for this patient?

ANSWER 1

The main differential diagnoses for a localised blistering skin condition include bullous pemphigoid, contact dermatitis, bullous systemic lupus erythematosus, porphyria and epidermolysis bullosa acquisita.

ANSWER 2

The main investigations healthcare practitioners should consider in this case include blood tests (ie full blood examination, electrolytes and liver function tests), as well as a porphyria screen (ie plasma, urine and faecal porphyrins). Other investigations should include an autoimmune screen, skin autoantibodies, iron studies, hepatitis B/C serology, human immunodeficiency virus (HIV) serology and haemochromatosis genotyping. Skin biopsy to exclude other blistering skin conditions such as bullous pemphigoid or epidermolysis bullosa acquisita should also be performed.

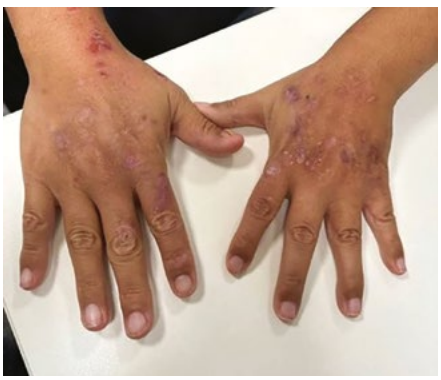

Figure 1. Bilateral dorsum of the patient hands demonstrating several superficial erosions, postinflammatory hyperpigmentation and scarring. Small milia are present on the dorsum of the left hand.

CASE CONTINUED

Following the dermatology consultation, a plasma, urine and faecal porphyrin screen was sent for biochemistry. Returned results indicated globally elevated porphyrins across all three samples (Table 1). Full blood examination results were normal, and the autoimmune screen was negative. The liver function test indicated a mixed picture derangement for liver enzymes (Table 2). The ferritin level was 247 µg/L (normal range [N]=30–300 µg/L) and the haemochromatosis genotype was normal. Notably, hepatitis C antibodies were detected and quantitative polymerase chain reaction (PCR) for it was high (16,300,000 IU/mL). Hepatitis B core antibody was positive, but testing for the surface antigen was negative, which is consistent with prior exposure but no current infection. A liver ultrasound demonstrated hepatic steatosis, and a fibroscan revealed an elevated liver stiffness of 12.0 kPa, which is suggestive of a high likelihood of cirrhosis.

QUESTION 3

Given the above, what is the most likely diagnosis and most common causes?

ANSWER 3

The most likely diagnosis is porphyria cutanea tarda (PCT). It is acquired in 80% of cases, of which common causes are related to alcohol and drug use, high oestrogen levels,

as well as hepatitis C virus (HCV) infection in particular.[1] A genetic predisposition because of a deficient uroporphyrinogen decarboxylase (UROD) enzyme level with low clinical penetrance is present in approximately one-third of cases.[2]

CASE CONTINUED

The patient was diagnosed with PCT secondary to chronic HCV infection, which was reported to the Victorian Department of Health. A skin biopsy was not performed as he demonstrated both clinical and biochemical evidence of PCT. The patient was advised to wear sun-protective clothing and reapply tinted sunscreen every two hours to block visible light. Monthly 500 mL venesections were commenced, aiming for a ferritin level of 50 µg/L. Iron supplements could worsen the condition, hence were to be avoided; however, it was not necessary to omit dietary iron.

A gastroenterology opinion concluded liver cirrhosis secondary to chronic hepatitis C and hepatic steatosis. Antiviral therapy was recommended to cure HCV (and therefore treat PCT) and prevent hepatic decompensation. The patient was commenced on lifelong hepatocellular cancer surveillance with six-monthly ultrasound and alpha-fetoprotein. A 12-week course of glecaprevir/pibrentasvir was proposed (a slightly longer duration given the potential for a carbamazepine-induced reduction in antiviral efficacy). The patient continues to be followed-up for both dermatology and gastroenterology conditions.

Table 1. Porphyrin results from plasma, urine and stool samples of a case study patient. The elevated porphyrins levels are consistent with a diagnosis of porphyria cutanea tarda

Investigation	Sample	Result	Reference values
Porphyrin	Plasma	123 (H)	<10 nmol/L
Total porphyrin RBC	Plasma	0.9	<1.8 µmol/L RBC
Porphobilinogen screen	Urine	Negative	NR
Total porphyrin	Urine	4018 (H)	<300 nmol/L
Porphyrin/creatinine ratio	Urine	264.3 (H)	<35.0
Uroporphyrin	Urine	3294 (H)	<40 nmol/L
Coproporphyrin	Urine	465 (H)	<150 nmol/L
T porphyrin	Stool	346 (H)	<200 µmol/kg
T coproporphyrin	Stool	48	<180 µmol/kg
Isocoproporphyrin	Stool	107 (H)	<2 µmol/kg
Protoporphyrin	Stool	35	<180 µmol/kg
C3/C1 ratio	Stool	0.4	<1.5

H, high; NR, no reference; RBC, red blood cell.

Table 2. Liver function test results for the case study patient

Investigation	Result	Reference values
AST	53 (H)	<35 IU/L
ALT	49 (H)	5–40 IU/L
ALP	66	30–110 IU/L
GGT	207 (H)	<65 IU/L
Albumin	35	35–50 g/L
Bilirubin	9	<21 µmol/L

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyl transferase; H, high.

Discussion

Porphyrias are a constellation of disorders caused by congenital or acquired enzymatic defects in the haem–biosynthetic pathway. PCT is the most common porphyria stemming from the inhibition of uroporphyrinogen III decarboxylase enzyme activity.[3] Here, we present a case of PCT, which led to the diagnosis of chronic HCV infection, highlighting the importance of cutaneous findings as a prompt to investigate and manage reversible medical conditions.

The patient presents with typical clinical manifestations of PCT. During the bullae healing process, small keratin-filled milia can form on sun-exposed areas.[4] Mottled hyper- or hypopigmentation and facial hypertrichosis on the malar cheeks occur in some cases.[3]

HCV is one of the most common predisposing factors for PCT in Australians.[5] The detection of HCV in this patient was unexpected as he did not have typical risk factors (eg intravenous drug use, tattoos or unprotected sex with multiple partners), so presumptively he acquired this from blood products prior to 1990, during childhood repair of his Tetralogy of Fallot. No prior hepatitis serology was available.

An imbalance in iron homeostasis can be induced by excess dietary supplementation or oxidative stress associated with HCV. High ferritin levels result in increased UROD inhibitor concentrations and exacerbates clinical disease. First-line treatment thus involves iron depletion in addition to management of HCV infection and reduction or cessation of precipitating factors.

Key points

- PCT is a form of blistering photodermatosis that should prompt early investigation and treatment of any reversible causes.
- Patients should be screened for high alcohol consumption, hepatitis C, haemochromatosis genotyping and use of an oral contraceptive pill or hormone replacement therapy.
- Hepatitis C treatment plus venesection should result in complete resolution of this patient's skin changes.

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