Facial hyperpigmentation and crusted papules on the hands

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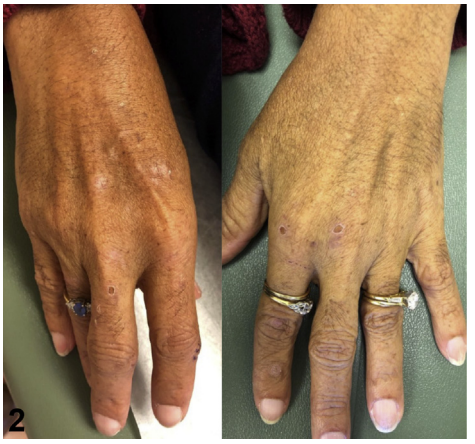

A 69-year-old woman with a history notable for lichen planus, breast cancer status post chemotherapy 7 years previously, and fibroid-related menorrhagia status post hysterectomy and bilateral oophorectomy 20 years previously presented with a 6-year history of facial hyperpigmentation and new painful, nonpruritic, blisters, erosions, and scabbing lesions on the backs of both of her hands. She had been taking ferrous sulfate 325 mg 3 times daily since her menorrhagia diagnosis 25 years previously. Exam revealed diffuse hyperpigmented patches on the face with hypertrichosis of the temporal region (Fig 1) and fragile skin with crusted papules on the dorsal aspect of both hands (Fig 2).

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Question 1: Which is the most likely diagnosis?

A. Epidermolysis bullosa acquisita

B. Porphyria cutanea tarda (PCT)

C. Airborne contact dermatitis

D. Bullous lupus erythematosus

E. Lichen planus pigmentosus

Answers:

A. Epidermolysis bullosa acquisita — Incorrect. Although noninflammatory bullae on acral sites are common in epidermolysis bullosa acquisita, facial hyperpigmentation is not characteristic.

B. PCT — Correct. A photo-distributed bullous eruption accompanied by facial discoloration and hypertrichosis is characteristic of PCT. In this case, hyperpigmentation and blistering of the dorsal aspect of the hands in the setting of elevated porphyrins and iron levels is most consistent with a diagnosis of PCT due to acquired hemochromatosis from oral iron supplementation. The patient reported lightening of her face and improvement of her hand lesions after treatment with serial phlebotomy and hydroxychloroquine 100 mg twice weekly, further supporting the diagnosis. While chemotherapy was considered as a cause of her facial hyperpigmentation, the lack of improvement over time since stopping her chemotherapeutic regimen argues against medication-induced hyperpigmentation.

C. Airborne contact dermatitis — Incorrect. Although chronic exposure to an airborne allergen or irritant could lead to vesicobullae and/or post-inflammatory hyperpigmentation, this patient's lack of erythema and pruritus argues against this diagnosis.

D. Bullous lupus erythematosus — Incorrect. Noninflammatory vesicobullae are not characteristic of lupus, and this patient lacks other features suggestive of connective tissue disease.

E. Lichen planus pigmentosus — Incorrect. Lichen planus pigmentosus may cause facial hyperpigmentation but would not exhibit associated hypertrichosis or result in crusted papules on the hands.

Question 2: Decreased activity in which enzyme plays a role in most cases of this patient's condition?

A. Aminolevulinic acid dehydratase

B. Ferrochelatase

C. Porphobilinogen deaminase

D. Uroporphyrinogen III decarboxylase (UROD)

E. Protoporphyrinogen oxidase

Answers:

A. Aminolevulinic acid dehydratase — Incorrect. Inherited or acquired aminolevulinic acid dehydratase deficiency causes acute porphyria.[1]

B. Ferrochelatase — Incorrect. Inherited deficiency of ferrochelatase causes protoporphyria. Acquired deficiencies in ferrochelatase are due to lead poisoning and may cause acute porphyria.[1]

C. Porphobilinogen deaminase — Incorrect. Deficiency in this enzyme results in acute intermittent porphyria.[1]

D. UROD — Correct. PCT is caused by UROD deficiency, which may be inherited or acquired in the setting of hepatic dysfunction.[1] In this case, excess oral iron supplementation led to UROD inhibition.[2] Iron promotes the formation of non-porphyrin products that directly inhibit UROD, increase the formation of reactive oxygen species that oxidize uroporphyrinogen to uroporphyrin, and induce the synthesis of uroporphyrinogen precursors, leading to increased porphyrin production.[3,4] Increased circulating porphyrins deposit in the skin, resulting in tissue damage after exposure to sunlight.

E. Protoporphyrinogen oxidase — Incorrect. Deficiencies in this enzyme are inherited in an autosomal dominant fashion and cause variegate porphyria.[1]

Question 3: What is the first-line diagnostic test for this patient's condition?

A. Ferritin level

B. Histopathologic exam

C. Hemochromatosis gene (*HFE*) mutation analysis

D. Direct immunofluorescence

E. Plasma and urinary total porphyrins

Answers:

A. Ferritin level — Incorrect. Ferritin levels will be elevated in iron-overload PCT, but this will not establish the diagnosis.

B. Histopathologic exam — Incorrect. Histopathologic exam may reveal subepidermal split with

minimal inflammation, basement membrane trapping in the epidermis (caterpillar bodies), festooning of dermis, and hyalinization of vessels; however, these findings are not specific for PCT.

C. *HFE* mutation analysis — Incorrect. *HFE* mutations may predispose to PCT, and more than 50% of patients with PCT carry a mutation for hemochromatosis.[4] Patients with PCT should undergo testing for *HFE* mutations, but it is not required for diagnosis.

D. Direct immunofluorescence — Incorrect. Although direct immunofluorescence would be expected to show immunoglobulin and complement deposition along the basement membrane zone and perivascular space, this does not distinguish PCT from other porphyrias or pseudoporphyrias.

E. Plasma and urinary total porphyrins — Correct. Porphyrin analysis is necessary to diagnose PCT, as normal levels exclude all cutaneous porphyrias. Testing will reveal increased plasma and urine porphyrins with a predominance of uroporphyrin and heptacarboxyporphyrin.[5]

Abbreviations used:

HFE: Hemochromatosis gene
PCT: porphyria cutanea tarda
UROD: uroporphyrinogen III decarboxylase

Conflicts of interest

None disclosed.

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