Case 6

Blistering in a photodistribution

Ploychompoo Srisuwanwattana, M.D.
Natta Rajatanavin, M.D.

Patient: A 36-year-old woman from Chanthaburi

Chief complaint:
Blistering lesions the on face, dorsum of hands and feet for 2 months

Present illness:
The patient presented with a 2-month history of recurrent pruritic vesicles on the face, neck, dorsum of hands, forearms and feet followed by erosions and scar. She denied the history of trauma and sun exposure aggravation of lesions.

Personal history: No history of alcohol consumption, oral contraceptive pills or use of herbal medicine

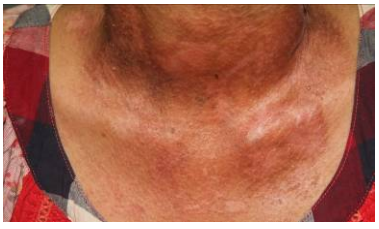
Past history:
AIDs was diagnosed for 7 months, last CD4 count was 150 cells/ul

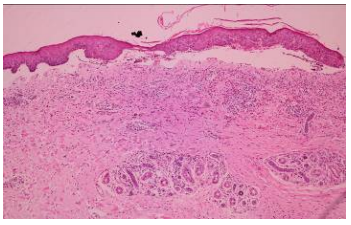
Current medications: Didanosine 250 mg/d, Nevirapine 400 mg/d, Lamivudine 300 mg/d

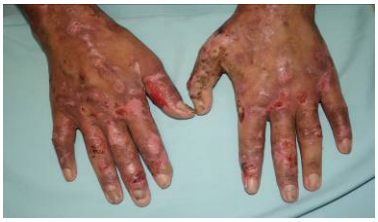
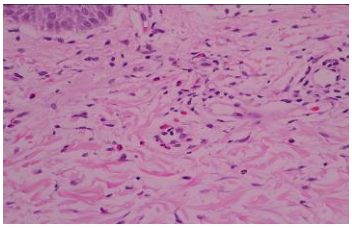
Physical examination:
GA: A middle-aged woman, not pale, no jaundice
HEENT: No pale conjunctiva, anicteric sclera, no conjunctival injection, no oral ulcer
Heart & lungs: Within normal limit
GI: No hepatosplenomegaly

Skin examination:
- Few vesicles and multiple crusted erosions with atrophic scars on face, V-shape of neck, dorsum of hands, forearms and feet

Histopathology: (S14-16392, right hand)
- Subepidermal vesicles in association with inflammatory cell infiltrate of mostly lymphocytes and eosinophils in the upper dermis
- Special stain: PAS stain failed to demonstrate abnormal deposition around blood vessel walls





Investigation:

CBC: WBC 5,090 cells/mm^3 (N 62%, L 21%, M 5% **E 12%**),
Hct 36.7%, Platelet 259,000 cells/mm^3
BUN 9 mg/dL, Cr 0.93 mg/dL
LFT: AST 49 U/L, ALT 40 U/L, ALP 206 U/L, GGT 47 U/L,
TP 93.1 g/L, **Alb 20.5 g/L**, TB 0.9 mg/dL, DB 0.5 mg/dL
Serum iron 79 ug/dL (35-150 ug/dL)
TIBC 454 ug/dL (250-450 ug/dL)
Ferritin 99.6 ng/ml (10-130 ng/ml)
HBsAg: Negative
Anti HCV: Negative
CD4 14%, 150 cells/ul
24-hour urine uroporphyrin 265.9 ug/day (0-50 ug/day)

Diagnosis: Porphyria cutanea tarda

Treatment:

- Sun protection and board spectrum sunscreen
- Hydroxychloroquine 200 mg/day

Discussion:

The patient presented with blistering lesions, which followed by erosions and atrophic scars on sun-exposed areas in the fourth decade of life. The differential diagnosis of this patient includes Porphyria cutanea tarda (PCT), Pseudoporphyria, Bullous lupus erythematosus and Epidermolysis bullosa aquisita. Increased urinary excretion of uroporphyrin confirmed a diagnosis of PCT even the histopathology did not show a typical finding of PCT.

Porphyrias result from dysfunction of specific enzymes involved in heme biosynthesis. Porphyrias were classified into either non-acute versus acute or cutaneous versus non-cutaneous forms. PCT is one of subtypes of non-acute porphyria and it is the most common type of porphyrias[1]. It's can occurs sporadic (type I)[2], hereditary (type II)[2], inherited in autosomal dominant pattern or sporadic nature with familial history (type III). The pathogenesis is deficiency of uroporphyrinogen decarboxylase, the fifth enzyme in heme biosynthesis.

Numerous factors contribute to development of PCT type I including alcohol, estrogens, iron overload, polychlorinated hydrocarbons, viral infections included hepatitis C virus (HCV)[3-4] and human immune deficiency virus (HIV)[2].

The pathogenesis of porphyria cutanea tarda in HIV infection is unclear. HIV infection may altered porphyrins metabolism, direct hepatic damage, impaired cytochrome oxidase or increased estrogen levels.

Diagnosis of PCT is made from increased urinary excretion of uroporphyrins with an elevated uroporphyrin I/ uroporphyrin III ratio. The urine must be protected from light for an accurate result. The urine fluorescence shows bright pink under Wood's lamp. Serum iron, ferritin, transaminase and gamma-glutamyltranspeptidase level often elevated.

Histopathology shows subepidermal blister, corrugated and undulating base of bullae, little or no inflammatory cell infiltration. Direct immunofluorescence reveals deposition of C3, C5b-9 and IgG in granular pattern at dermal-epidermal junction and in and around vessel walls.

Management included sun avoidance, sunscreens which mainly against ultraviolet A (UVA) and visible light, protective clothes, avoidance of skin trauma and exogenous exacerbating factors. First line treatment included antimalarial, phlebotomy, combined low-dose chloroquine and phlebotomy (level IIa evidence) and erythropoietin in end-stage renal disease (level III evidence). Phlebotomy is definitive treatment if no contraindication. Withdrawal of blood reduces iron stores and liver iron content. The guideline suggest removal of 7 ml of blood per kg body weight, not to exceed 550 ml in one session, once or twice-weekly until serum ferritin reach lower normal limit then once biweekly or monthly to maintenance appropriate hemoglobin[5] Low dose of chloroquine 125 mg twice weekly[6] or hydroxychloroquine 100 mg twice weekly[7], is a useful alternative if phlebotomy is not recommended e.g. anemia, cardiopulmonary disorders or HIV. Antimalarials administration usually starts at lower dosage to avoid hepatotoxicity and gradually increase to regular dosage if no respose[8]. Effects of chloroquine and hydroxychloroquine included immunomodulatory, anti-inflammatory and complex formation with porphyrins result in increase porphyrin excretion[9]. Low dose of both of chloroquine and hydroxychloroquine were found to be effective in treatment of porphyria cutanea tarda with lower hepatotoxicity[9]. Second line treatment included desferrioxamine, deferiprone and cimetidine (level III evidence).

References:

1. Horner ME, Alikhan A, Tintle S, Tortorelli S, Davis DM , Hand JL. Cutaneous porphyrias part I: epidemiology, pathogenesis, presentation, diagnosis, and histopathology. Int J Dermatol. 2013; 52: 1464-80.
2. Mendez M, Rossetti MV, Del CBAM , Parera VE. The role of inherited and acquired factors in the development of porphyria cutanea tarda in the Argentinean population. J Am Acad Dermatol. 2005; 52: 417-24.
3. Gisbert JP, Garcia-Buey L, Pajares JM , Moreno-Otero R. Prevalence of hepatitis C virus infection in porphyria cutanea tarda: systematic review and meta-analysis. J Hepatol. 2003; 39: 620-7.
4. Ryan Caballes F, Sendi H , Bonkovsky HL. Hepatitis C, porphyria cutanea tarda and liver iron: an update. Liver Int. 2012; 32: 880-93.
5. Brissot P, Troadec MB, Bardou-Jacquet E, Le Lan C, Jouanolle AM, Deugnier Y et al. Current approach to hemochromatosis. Blood Rev. 2008; 22: 195-210.
6. Tintle S, Alikhan A, Horner ME, Hand JL , Davis DM. Cutaneous porphyrias part II: treatment strategies. Int J Dermatol. 2014; 53: 3-24.
7. Singal AK, Kormos-Hallberg C, Lee C, Sadagoparamanujam VM, Grady JJ, Freeman DH, Jr. et al. Low-dose hydroxychloroquine is as effective as phlebotomy in treatment of patients with porphyria cutanea tarda. Clin Gastroenterol Hepatol. 2012; 10: 1402-9.
8. Kalia S , Dutz JP. New concepts in antimalarial use and mode of action in dermatology. Dermatol Ther. 2007; 20: 160-74.
9. Ochsendorf FR. Use of antimalarials in dermatology. J Dtsch Dermatol Ges. 2010; 8: 829-44.