Case 6
A Thai 26-year-old woman
Chief complaint: Multiple fluid filled blisters on face and hands for 6 months

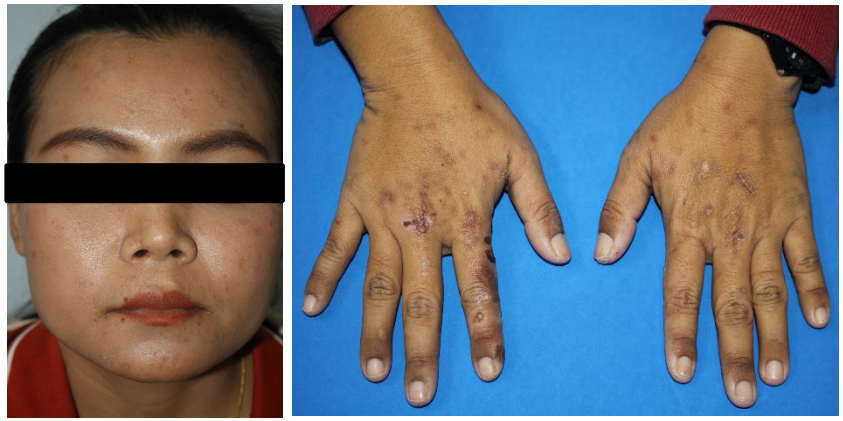

Fig.6.1

Present illness: The patient presented with a 6-month history of fluid filled blisters, recurrent rash, and increasingly fragile skin on her face and dorsum of both hands. Her symptoms aggravated by sunlight. No history of topical products used before the development of rash. Oral contraceptive pills have been used for one year
Underlying disease: Hb H disease without current treatment
Family history: no history of autoimmune disease or similar lesion in her family members
Dermatologic examination: (Fig. 6.1)
Multiple brownish and atrophic macules on face
Multiple hemorrhagic crusts, erosions, vesicles, bullae, milia, brownish and atrophic macules on dorsal hands

Physical examination:
-HEENT: Mildly pale conjunctivae, anicteric sclerae, no oral ulcer, no hair loss
-Other systemic examination revealed no abnormality
Lab investigations:

- **CBC**
  - WBC 7740/mm^3 (N 75, L 16, Mo 8, Eo 1%)
  - Hb 8 g/dl, Hct 27.9%, MCV 69.6 fL
  - platelet 351,000/mm^3
- **Iron study:** Reticulocyte count 5.6%, ferritin 599 ng/mL, serum iron 35 ug/dL, TIBC 140 ug/dL
- **Liver function test:** AST/ALT 52/100 U/L, ALP 48 U/L, TP/Alb 78.5/34 g/L, TB/DB 1.2/0.5 mg/dl
- **Renal function:** BUN/Cr 7/0.44 mg/dl
- **Immunology/biological chemistry:**

- ANA: Positive fine speckled 1:320
- Anti-BP 180/230, anti-DsG1/DsG3 antibody: All negative
- Urine uroporphyrin (24 hours): 12,465.60 ug/day
- Indirect/direct coombs test: All negative
- HBsAg, anti-HCV, anti-HIV: All negative

Histopathology (S17-040461, skin, right dorsal hand) (Fig. 6.2)

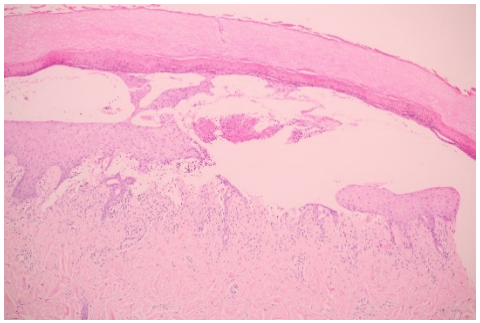

Fig. 6.2

- Subepidermal blister associated with superficial perivascular infiltration, mainly lymphoctyes. Mild fibrosis

Direct immunofluorescence (S17-040391, skin, right dorsal hand) (Fig. 6.3)

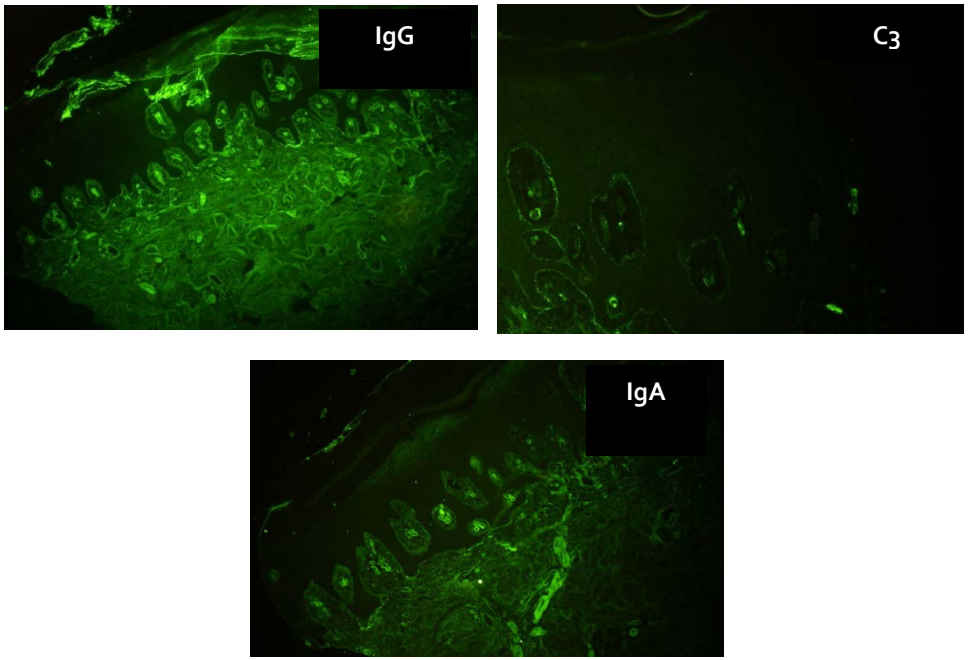

Fig.6.3

- Homogenous deposition of IgG, C3, IgA at superficial blood vessel wall
- Focal granular deposition of IgG, IgM at dermo-epidermal junction (DEJ)
- Few cytoid body of IgM
- Homogenous granular deposition of C3 along DEJ

Diagnosis: Porphyria Cutanea Tarda

Treatment

- Advice discontinuation of oral contraceptive pills
- Hydroxychloroquine (200) 1 tab po twice weekly
- Sunscreen apply face and dorsal hands in the morning
- 2% hydroquinone cream apply hyperpigmented lesion bid

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Discussion:

The porphyrias are disorders of heme synthesis, which has eight steps. Each type of porphyria involves a defect, either inherited or acquired. It results in overproduction of pathway precursors preceding the defective step. The diseases have been grouped as acute hepatic porphyrias and photocutaneous porphyrias. The acute porphyrias are due to hepatic overproduction of the porphyrin precursors, and the symptoms are caused by injury primarily to the nervous system. Cutaneous porphyria is due to overproduction of photosensitizing porphyrins by the liver or bone marrow.[1]

Porphyria cutanea tarda (PCT) is the most common porphyria, with prevalence of 40 per 1,000,000 in population.[2] PCT is a chronic form of hepatic porphyrias that may occur either as sporadic (type 1, acquired) or familial (type 2, hereditary). Acquired (type 1) PCT is found in 75% of cases.[3]

Pathogenesis of PCT is a defect in UROD, which catalyzes the fifth step in heme synthesis. Porphyrins in skin absorb ultraviolet A, generating peroxides that cause oxidative damage and inflammation.[4] The major precipitating factors of PCT include

excess alcohol intake, cigarette smoking, iron overload, estrogen use, hepatitis C virus (HCV) infection, and human immunodeficiency virus (HIV) infection.[5]

Clinical manifestations of PCT include bullae, blisters or vesicular lesions restricted to sun-exposed areas such as the dorsum of hands, face and neck. In women, the legs and dorsum of the feet can also be affected. Skin fragility is a specific feature. Hypertrichosis is often observed on the upper cheeks, ears and arms. Increased pigmentation of sun-exposed areas is common.[6]

Biological diagnosis of PCT is essential to confirm diagnosis. A presumptive clinical diagnosis of PCT should followed by urine, plasma, and stool porphyrin profile.[1] The porphyrin excretion pattern of PCT has three main features: (1) increased urinary excretion of uroporphyrin and other acetate-substituted porphyrins; (2) a distinctive pattern of excretion of isomer series I and III porphyrins; and (3) increased excretion of fecal isocoproporphyrin. The ratio of urine URO to COPRO is often helpful in differentiating PCT (ratio usually exceeds 3:1) and VP (ratio typically less than 1:1).[7]

Histopathology of a blister shows subepidermal bullae with little or no inflammation and an upward projection of papilla into the bullae (festooning). Chronic lesions show thickened dermal vessels with PAS-positive diastase resistant glycoprotein material in and around the vessels near the dermal–epidermal junction. Direct immunofluorescence shows IgG, IgM, fibrinogen, and complement deposition in the basement membrane and around vessels of the upper dermis.

Differential diagnosis of PCT includes pseudoporphyria, epidermolysis bullosa acquisita, addison's disease paraneoplastic hypertrichosis lanuginose acquisita, and chronic hand eczema.[4]

Treatment of choice for PCT is phlebotomy, which depletes hepatic iron. Identification and restriction of risk factors such as alcohol, tobacco, and estrogen use, may result in improvement. The initial end point of treatment is a serum ferritin level at the low end of the normal range (approximately 20 ng/mm), which is typically achieved with three to eight phlebotomies. An alternative to iron depletion is low-dose hydroxychloroquine (100 mg) or chloroquine (125 mg), twice weekly (both used on an off-label basis). They act within hepatocytes to mobilize porphyrins, which then undergo urinary excretion.[1] Not only the drugs are comparably effective with phlebotomy, they are also more convenient and less costly.Treatment should be continued until urinary porphyrin excretion normal. Clinical remission is usually achieved several months before biochemical remission.[2] Moreover, sun avoidance and good care of vulnerable skin are also very important.[8]

In all patients, an annual check of urine or plasma uroporphyrin levels is recommended for early detection of recurrence and for retreatment.[1]

In our patient, the diagnosis of PCT has been confirmed by her typical clinical manifestations, histopathology, DIF, and positive urine uroporphyrin. Oral contraceptive pills seem to be the precipitating factor, so we suggested her to stop taking this medication. Alternative treatment with hydroxychloroquine 200 mg twice weekly was prescribed because she has anemia from her underlying thalassemia. She has responded well to treatment.

References:

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