

Case 27

A 76 year-old Thai man from Chainart

Chief complaint: Generalized hypopigmented papules on face, trunk, and extremities for 20 years



Present illness: The patient has had numerous asymptomatic hypopigmented papules on face, trunk, and extremities, which were increasing in number for 20 years.

Past history:

He was otherwise in good health.

Deny history of herbal medicine uses.

Family history:

None of his family members has similar skin lesions.

Skin examination:

Numerous discrete mildly erythematous and hypopigmented flat-topped papules and plaques on face, scalp, arms and dorsal side of both hands. Koebner phenomenon was also presented.

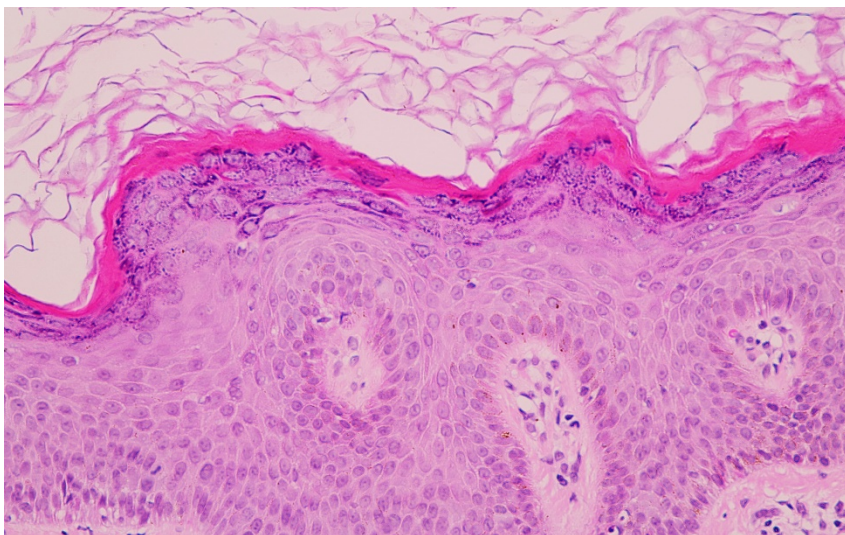
Physical examination:

Systemic examination other than skin lesions revealed no abnormality.

Investigation:

- Anti-HIV: Negative
- Hb 13.6 g/dl, Hct 43.1%, WBC 7280(N53, L34, M5, E7, B1%), Plt 207,000
- CD4 and CD8 level: Normal.

Histopathology: (S16-23007A, left arm)



- Mild hyperkeratosis and papillated epidermal hyperplasia
- Hypergranulosis with coarse keratohyaline granules and perinuclear vacuoles

Diagnosis: Generalized verruca plana

Treatment:

- Contact immunotherapy with diphencyprone (DCP)
- Acitretin (0.2 mg/kg/day) 10 mg oral once daily
- Zinc sulphate (8mg/kg/day) 220 mg twice daily

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Discussion:

Warts are common benign skin infection, caused by human papillomavirus (HPV). HPV, a non-enveloped, double-stranded DNA virus, spread from one to another through direct skin-to-skin contact or indirectly through contaminated surfaces and objects¹. Cutaneous warts are classified by morphology, histology and anatomic location, for example; common wart (verruca vulgaris), palmar and plantar wart (verruca palmaris/ plantaris), flat wart (verruca plana) and butcher's wart¹. Warts most often occur in children and young adults, but can occur at any age².

Verruca plana is characterized by 1-4 mm, skin-colored or pinkish to brown, smooth-surfaced or minimal scaly, slightly elevated, flat-topped papules that are most commonly located on the face, hands, arms, and lower legs. Verrucae plana are usually caused by HPV types 3 or 10, and less often by HPV type 28 and 29^{1,2}.

The diagnosis of warts is made from clinical examination if typical features are shown. Occasionally, histopathology may be required for confirmation.

Histopathology of verruca plana usually shows basket-weave appearance in the stratum corneum layer, epidermal hyperkeratosis and acanthosis, with no or minimal papillomatosis. Hypergranulosis and vacuolization of cells in the granular and upper Malpighian layers (koilocytes) are also presented¹.

Individuals with impaired cell-mediated immunity, such as after organ or bone marrow transplant or severe combined immune deficiency, are associated with extensive and recalcitrant HPV infection^{1,2}. Warts may also be the presenting feature of milder immunosuppressed states such as lymphoma, idiopathic CD4 lymphocytopenia or HIV infection². The extensive involvement of verruca plana in our case led us to further investigate to determine the immune status of the patient. Complete blood count did not reveal any abnormality. The result of enzyme-linked

immunosorbent assay (ELISA) for HIV was negative. Immunologic screening revealed a normal level of CD4 and CD8.

Although in children, spontaneous clearance of warts can occur in about two-thirds of patients in 2 years, warts in adults can be much slower to clear, and persistent for 5–10 years².

Treatment of cutaneous warts should be considered based on number, morphology and distribution of warts, patient goals, immune status and pain tolerance¹. According to British association of dermatologists' guidelines for the management of cutaneous warts 2014, recommendations for flat warts are 2–10% salicylic acid cream/ointment or cautious use of 12–17% salicylic acid paint, cryotherapy of milder freeze, topical retinoid². Other recommended treatments include acupuncture, cantharidin, 5-FU cream, formaldehyde gel, 10% glutaraldehyde solution, 15% glycolic acid, imiquimod, PDT, topical immunotherapy, zinc oxide, and 10% zinc sulfate solution².

Retinoids are capable of affecting epidermal proliferation and differentiation, and may inhibit the replication and assembly of HPV within the affected cells³. Isotretinoin 30 mg/day or placebo was administered to 16 and 15 patients with recalcitrant facial flat warts, respectively, for 12 weeks³. In the isotretinoin group, 87.5% of patients had a complete clearance, while none in the placebo group showed any improvement³. Al-Hamamy reported a complete clearance in 72.3% of the patients with facial flat warts after 2 months treatment with isotretinoin 0.5 mg/kg/day⁴. Acitretin 0.3–1 mg/kg/day for 2-3 months showed a marked improvement of resistant common warts, but with a high risk of recurrence on discontinuation of therapy^{5,6}.

Zinc is important for immune regulation and mediates the role of leucocytes and NK cells, but the mechanism of action in the treatment of warts is uncertain². Although a double-blinded RCT showed no difference between 2-month duration of oral zinc sulfate (10 mg/kg/day) and placebo in patients with resistant

cutaneous warts, a single-blinded RCT showed 87% response in patients treated with oral zinc sulfate at a dose of 10 mg/kg/day up to 600 mg per day, compared with no response in the placebo group^{7,8}. Yaghoobi et al. also reported a 59.3% and 78% complete response after 1 and 2 months of treatment, respectively, with oral zinc sulfate (10 mg/kg to a maximum dose of 600 mg/day) in recalcitrant cutaneous warts⁹.

Contact immunotherapy with diphencyprone (DCP) induces a local delayed hypersensitivity reaction at the wart site and triggers a local immune response¹⁰. Buckley et al. reported 88% complete clearance of recalcitrant palmoplantar warts treated with DCP in 48 patients¹¹. Patients were initially sensitized by using 2% DCP, then initial concentration of 0.1% for digital warts and 2% for plantar warts was applied at 1-4 weekly intervals. The median treatment time to clearance was 5 months, and no recurrences were observed in a 2-year follow-up period. Uptis et al. reported 87.7% complete clearance of recalcitrant palmoplantar or periungual warts treated with DCP in 154 patients¹². Moreover, contact immunotherapy has been reported a clearance effect not only on treated lesions but also on distant untreated lesions.

Given the extensive involvement of skin lesions in our patient, systemic therapy and immunotherapy are preferred. Retinoids, zinc sulfate, and contact immunotherapy with diphencyprone (DCP) are available in our setting. Thus, the combination regimen with oral zinc sulfate and DCP was initiated, but he failed sensitization with 2% DCP. Oral acitretin was subsequently in place. The treatment outcome remains to be seen since he is undergoing treatment.

References

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