Case 15

Whitish spots on a boy's forehead

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Patient: A 10-year-old boy from Nakhonsawan

Chief complaint: Multiple whitish spots on forehead for 1 year

Present illness:

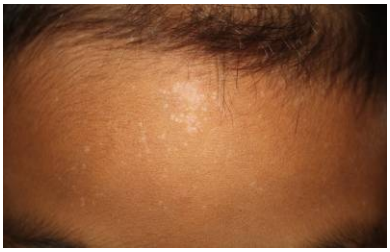
The patient is healthy child with multiple asymptomatic whitish spots, which his mother noticed developing since infancy. Over the years, the lesions are gradually increased, but in the past year the lesions rapidly proliferate.

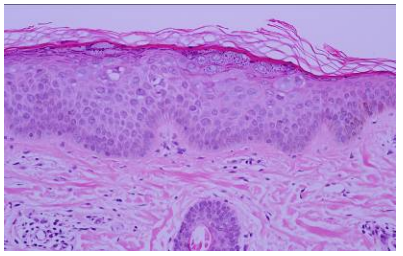
Past history: No underlying disease

Family history: No other family member has similar symptom. No history of consanguineous marriage in his family.

Skin examination:

- Multiple symmetrical tiny hypopigmented macules and patches with wrinkly surface on forehead
- No lesion on trunk and extremities





Histopathology: (S14-8273, forehead)

There is hypergranulosis and mild epidermal hyperplasia composed of large keratinocytes with pale vesicular nuclei with basophilic abundant cytoplasm in the epidermis.

Diagnosis: Epidermodysplasia verruciformis

Treatment:

- Advice about the natural history and prognosis of disease
- 0.05% Tretinoin cream apply lesion at bedtime

Discussion:

Epidermodysplasia verruciformis (EV) is a rare skin disorder, characterized by susceptibility to HPV infection.[1,2] It can be classified into inherited and acquired form. In most instances of inherited cases, autosomal

recessive mutation in the EVER1 or EVER2 genes is responsible for most of the cases. The mutation in either EVER1 or EVER2 genes causes an abnormal susceptibility to be infected by a specific group of HPV genotypes known as EV-HPV, which are not typical subtype of warts in normal population. More than 30 EV-HPV types have been described (e.g., 4, 5a, 5b, 8, 9, 12, 14, 15, 17, 19–25, 36–38, 47).[3] In EV-HPV types have oncogenic potential, and over time, 30% to 60% of affected individuals will develop squamous cell carcinoma (SCC). More than 90% of EV-associated SCC are related to HPV-5 and HPV-8.[3]

An acquired form of EV has been described in immunocompromised hosts such as patients with HIV infection, SLE and renal allograft transplant recipients.[4] The nature of the acquired EV, however, seem to be similar to inherited EV, and patients with acquired EV are likely at increased risk for development of SCC.[1]

Clinically, EV has highly polymorphic cutaneous lesions, including hypopigmented and red–brown pityriasis versicolor-like macules and flat wart-like papules, usually appear on the trunk, neck, arms, and face during childhood. A pseudo-Koebner's phenomenon is frequently observed in affected patients, with multiple flat warts appearing in excoriated areas as a result of inoculation of HPV.[3] Notably, the EV lesions, especially in sun-exposed area can have malignant transformation to SCC. These malignancies are primarily Bowen's type carcinoma in situ and non-metastasize SCC. This usually develops during the fourth and fifth decade of life.[2] However, nowadays, malignant conversion is seen over shorter periods of time, possibly due to increase of time to sun exposure, altitude or outdoor occupations.[5]

The classic histologic features of EV are a verruca plana-type lesion with minimal hyperkeratosis and acanthotic areas where the clumps of nests of large cells, especially in the spinous and granular layers contain perinuclear halos and distinctive blue–gray pallor.[6]

The clinical differentiated diagnosis of EV includes multiple verruca plana, acrokeratosis verruciformis of Hopf and keratotic papules in Darier's disease. Less commonly, epidermal nevus and WHIM syndrome can mimic EV. All of these conditions can be distinguished by history, histologic findings and HPV testing.

The treatment of EV is not standardized, and a wide range of therapies has been tried in congenital and acquired EV. Various medical, physical and surgical treatments have been implicated.[5]

The use of vitamin A derivatives has been recommended especially for patients with early premalignant lesions, because of their antiproliferative and differentiation-inducing effects. But there are significant side effects and relapses commonly occur after discontinuation of therapy. Other medical treatment e.g. immunotherapy, cimetidine[7,8] and imiquimod[9] have been regarded as a possible therapeutic alternative. But all of those treatments had variable outcomes.

Other physical therapy such as photodynamic therapy (PDT),[10] cryotherapy and surgical intervention[5] also had inconsistent outcomes.

In conclusion, there is currently no definitive treatment for the congenital or acquired EV. Patients need to be closely surveyed for malignant transformation. Preventive strategies are also important, including restoration of the immune system where possible and patient education about the importance of daily sunscreen use and regular dermatologic follow-up.

Our patient is another classic case of congenital EV. The patient is a 10-

year-old boy presented with multiple hypopigmented macules and patches on his face. He is immunocompetent and has no family history of EV. The clinical and histopathological findings recover the diagnosis of epidermodysplasia verruciformis. He is treated with topical retinoids and sunscreen use. Long-term dermatologic follow-up is important for early detection of malignant transformation.

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References:

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