Epidermodysplasia verruciformis: a rare disease

Iran J Dermatol 2021; 24: 252-253

DOI: 10.22034/ijd.2020.253555.1247

Dear Editor,

Epidermodysplasia verruciformis (EV), also known as tree man syndrome, is a very rare autosomal recessive disease characterized by increased susceptibility to certain types of the human papillomavirus (HPV) [1,2]. Many different types of HPV have been shown to be responsible for cutaneous lesions of EV including types 3, 5, 8, 10, 9, 12, 14, 15, 17, 19-25, 28, 29, 36, 38, 46, 47, 49, and 50 [3]. In EV, there are mutations in the EVER1/TMC6 and EVER2/TMC8 genes located on chromosome 17q25 that lead to cell-mediated immunity defects and an unusual susceptibility to certain types of HPV [2-4].

EV manifests as verrucose cutaneous lesions that may develop into squamous cell carcinoma (SCC). The most common HPV types in EV-related cancer are HPV 5 and 8. According to studies, malignant transformation is seen in about 35-50% of patients in their forties or fifties [3,5]. Also, EV can present with pityriasis versicolor-like scaly macules and flat wart-like papules and plaques [4]. In more than half of patients, symptoms first appear between the ages of 5 and 11, and symptoms initiate during puberty in nearly a quarter of cases. The lesions are mainly on sun-exposed areas like the face, neck, trunk, and extremities [4].

Acquired EV has also been described in immunosuppressed patients [4]. Diagnosis is based on clinical and histological findings. The skin biopsy reveals flat wart-like lesions with mild hyperkeratosis, hypergranulosis, and acanthosis of the epidermis. Keratinocytes of the upper epidermis are enlarged with perinuclear vacuolization and a typical blue-gray pallor. HPV can be detected in keratinocytes using in situ hybridization or immunohistochemistry with anti-HPV antibodies.

Although any therapy cannot achieve the permanent cure of EV, treatment modalities include cryotherapy, topical imiquimod and 5-fluorouracil, systemic retinoids, interferon-alpha, and 5-aminolevulinic acid photodynamic therapy. Surgical excision is the treatment of choice for SCC. Sun exposure avoidance and photoprotection are crucial in EV patients [6].

A 49-year-old man came to the Shahid Faghihi Hospital (Shiraz, Iran) with gray-black papules on the forehead, verrucose plaques on the right forearm, and erythematous papules and plaques on the trunk since 30 years ago (Figures 1 and 2) that had worsened since about 2-3 years ago. He had no family history of similar lesions. Some of the lesions were previously treated with cryotherapy with the diagnosis of warts, but treatment was not effective. A skin biopsy was taken, showing hyperkeratosis, acanthosis, hypergranulosis, and enlarged keratinocytes with perinuclear vacuolization in the upper epidermal layer (Figure 3). EV was diagnosed according to the history, physical exam, and histopathological findings. Some of the biopsied verrucose lesions also had the differential diagnosis of SCC. Those lesions for which SCC was confirmed were excised completely. We started acitretin 25 mg daily for the patient and advised photoprotection.

According to the rarity of EV, a review of the literature performed by Imahorn *et al.* in 2017 found about 500 patients with this disease worldwide [7]. Added to the rarity, the absence of

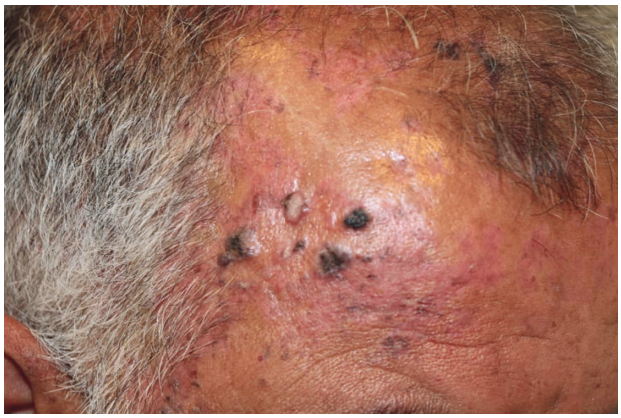

Figure 1. Verrucose plaques on the forehead.

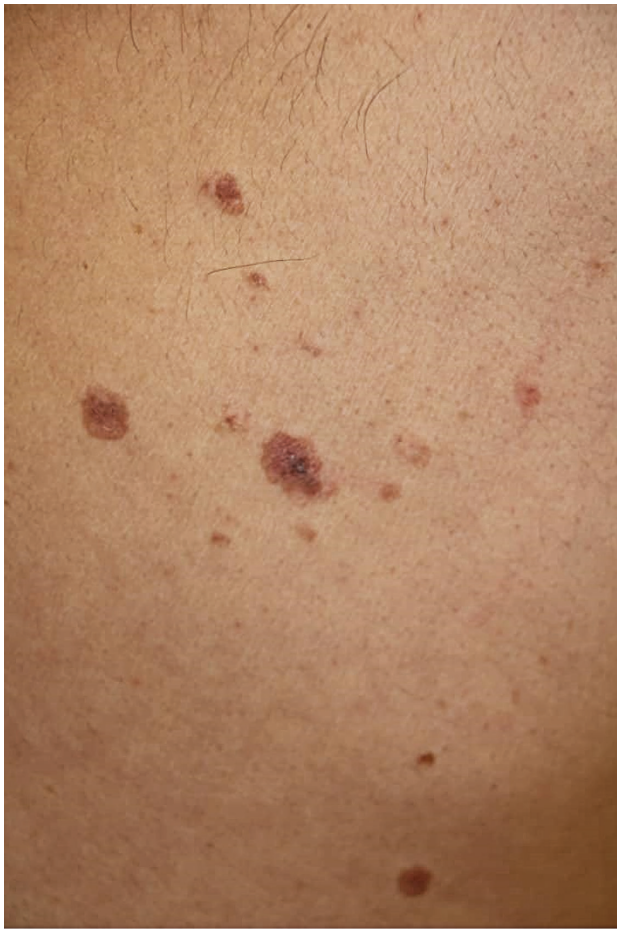

Figure 2. Erythematous papules and plaques on the trunk.

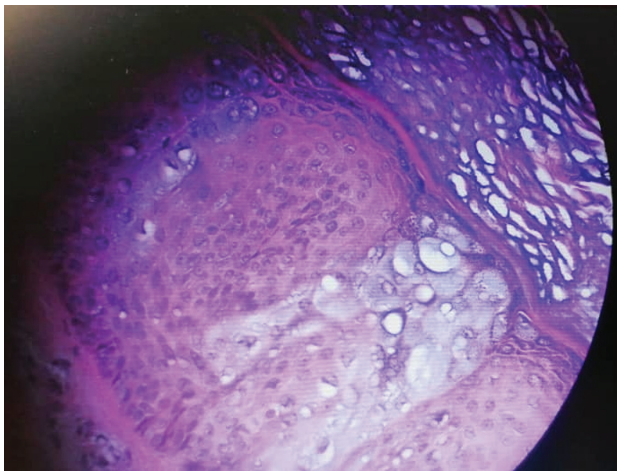

Figure 3. Hyperkeratosis, acanthosis, hypergranulosis, and enlarged keratinocytes with perinuclear vacuolization (H&E staining, ×400).

positive family history in this patient also makes it a notable case. There is no permanent cure for EV, but photoprotection and regular follow-up for monitoring malignancy is recommended.

Acknowledgment

The authors would like to thank the Shiraz Molecular Dermatology Research Center.

Conflict of interest: None declared.

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Received: 19 October 2020
Accepted: 20 October 2020

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