LETTER TO THE EDITOR

A distinct variant of Epidermodysplasia verruciformis in a Turkish family lacking EVER1 and EVER2 mutations

Epidermodysplasia verruciformis (EV) is a rare genodermatosis associated with a high risk of skin cancer. This condition is characterized by an abnormal susceptibility to human papillomavirus genotypes from the genus beta. The cutaneous lesions of EV first appear in childhood and are highly polymorphic. Multiple squamous cell carcinomas (SCC) of the skin develop subsequently on sun-exposed skin. 

Fig. 1  (a) Hyperpigmented SK-like lesions on the boy’s face and forehead. (b) Brown, scaly PV-like macules on the neck and trunk. (c) Successful treatment of SK-like lesions by cryosurgery. (d) Multiple brownish plaques and SK-like lesions on face, neck and trunk of the female. (e) PV-like lesions on the hands.

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sites in about half of the patients. Benign cutaneous lesions are associated with polymorphic lesions such as pityriasis versicolor-like (PV-like) macules, flat warts and red macules. EV is believed to be an autosomal recessive disease (reviewed in ref. [1]). Two susceptibility loci, EV1 and EV2, have been mapped with EV1 containing the characterized EVER1 and EVER2 genes [2].

In this report, we present a 22-year-old Turkish male and his 45-year-old mother with extensive seborrheic keratosis-like (SK-like) viral warts with no family history of EV. Initial facial lesions developed aged 8 years and disseminated with time. PV-like brown scaly macules resembling pityriasis versicolor were observed on the trunk and neck (Fig. 1b and d). The patients showed SK-like viral warts characterized by dark brown or black pigmented proliferative lesions with hyperkeratotic surfaces. Facial SK-like lesions were dark and plaque-like (Fig. 1a and d). All lesions disappeared following liquid nitrogen cryosurgery (Fig. 1c). Blood profile (son) including full blood count, erythrocyte sedimentation rate, C-reactive protein, liver and renal function tests, serum lipid and cholesterol level, levels of immunoglobulins, complement components and circulating immune complexes were normal. The patient showed no decrease in the number of CD8+ T-cells as described previously for EV [10]. The patient was HIV-negative.

Skin biopsies were taken from a SK-like wart and histopathologic evaluation of a warty lesion revealed hyperkeratosis and hypergranulosis with vacuolation and koilocytes consistent with HPV infection. The lesion showed mild to moderate dysplasia in the epidermis (Fig. 2). The dermatopathological findings were pathognomic for EV.

HPV DNA analysis was performed on a formalin-fixed, paraffin-embedded hyperkeratotic lesion from the face. The sample was tested positive for oncogenic HPV type 8 using a multiple nested degenerated PCR method with the capacity to detect a broad spectrum of cutaneous, alpha- and beta-HPV types [3]. No other HPV types were detected.

Genetic analysis of the genes EVER1 and EVER2, two known genes to be associated with this disease, did not detect any loss of function mutations by sequencing the coding exons from genomic DNA with previously described primers [2]. We found only a non-synonymous single nucleotide polymorphism in the intron between exon 10 and exon 11 (cacgtgcc[c/g]ctggggaggcag) of EVER1.

This phenotype of EV, dominated by SK-like lesions, has previously been reported in a subset of African EV patients [4–6]. This is the first report of this EV phenotype in a Caucasian family. The diagnosis of EV is supported by the characteristic histology and the presence of the EV-associated HPV8. Both patients showed PV-like scaly macules in addition to the clinically dominant SK-like warts. To our knowledge, EVER mutations have previously been described in few reports [2,7–9], with only one publication reporting the lack of EVER mutation [10]. Our analysis shows also lack of EVER1 and EVER2 mutations and represents a distinct clinical and genetic variant of EV underlining the probable involvement of other genetic loci in the development of this disease.

![Fig. 2](image_url)  
Histology of SK-like viral wart from the boy (a and b) and his mother (c and d) showing typical EV changes. (a and c) 50-fold magnification; (b and d) 200-fold magnification.
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