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Case Report

Epidermodysplasia verruciformis associated with cutaneous malignancy: a rare inherited genodermatosis in a mother and daughter

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ABSTRACT

Epidermodysplasia verruciformis (EV) is an autosomal recessive genodermatosis marked by a heightened risk of developing non-melanoma skin cancers due to a unique vulnerability to specific HPV genotypes. This susceptibility is often due to mutations in the EVER-1 or EVER-2 genes located on chromosome 17q25. Individuals with EV typically present with plane warts and pityriasis versicolor-like lesions early in life, which may evolve into malignant lesions such as Bowen's disease, squamous cell carcinoma (SCC), and basal cell carcinoma after decades of sun exposure. EV is predominantly inherited as an autosomal recessive pattern, and several reports of EV occur in siblings. However, autosomal dominant and X-linked patterns have been sporadically recorded. This report details the rare occurrence of EV in a mother and daughter, both of whom developed cutaneous malignancies in sun-exposed areas.

Keywords: Epidermodysplasia verruciformis, Cutaneous malignancies, HPV

INTRODUCTION

Epidermodysplasia verruciformis (EV) is an autosomal recessive genodermatosis marked by a heightened risk of developing non-melanoma skin cancers due to a unique vulnerability to specific HPV genotypes.[2] This susceptibility is often due to mutations in the EVER-1 or EVER-2 genes located on chromosome 17q25.[2,3] Individuals with EV typically present with plane warts and pityriasis versicolor-like lesions early in life, which may evolve into malignant lesions such as Bowen's disease, squamous cell carcinoma (SCC), and basal cell carcinoma after decades of sun exposure.

EV is predominantly inherited as an autosomal recessive pattern, and several reports of EV occur in siblings. However, autosomal dominant and X-linked patterns have been sporadically recorded. This report details the rare occurrence of EV in a mother and daughter, both of whom developed cutaneous malignancies in sun-exposed areas.

CASE REPORTS

Case 1-Daughter

A 29-year-old female from rural northern India presented to a tertiary care center with multiple, non-itchy, raised, and some flat discolored lesions since 3 years of age. In her 28th year of age, she noticed an ulcerative lesion developing on the right side of her forehead, which bled upon contact. The patient reported long-term treatment with both systemic and topical therapies. Her family history was notable for similar dermatological complaints and skin cancer in her mother. There was no history of similar disease among her siblings. On examination, she had hyperpigmented, warty papules and hypopigmented macules present on her face and other sun exposed parts

of her body. On the right side of her forehead, an ulcerative plaque measuring 3×4 cm with crusted, everted edges was present. Diagnostic biopsies were performed on a warty papule on the right forearm and from the edge of the forehead lesion.

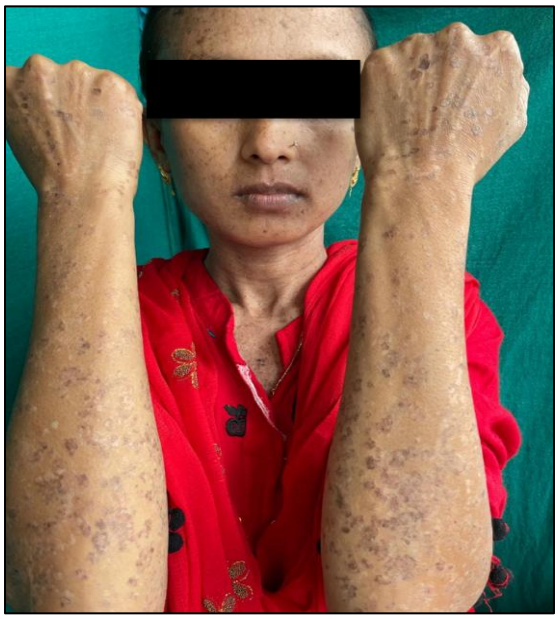

Figure 1: Hyperpigmented macules and plane warts over the forearms and legs.

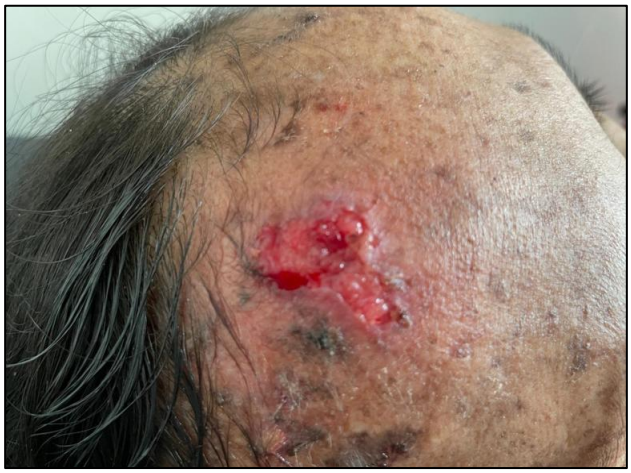

Figure 2: Ulcerative growth measuring 3×4 cm over the right side of the forehead with areas of induration and irregular borders.

Case 2-Mother

A 55-year-old female exhibited numerous wart-like lesions with crusting and pigmentation variations over her entire body since adolescence. She was of consanguineous marriage. On examination, it was found that she had a plaque with crusting, irregular borders, and raised edges measuring about 4×5 cm on her right clavicle. She had consulted several doctors and had undergone several treatments. Biopsies taken from various sites in both cases showed histopathological evidence such as hyperkeratosis, moderate acanthosis, and vacuolated keratinocytes with bluish-gray cytoplasm suggestive of EV.

Figure 3: Multiple hyper and hypopigmented macules and some plaques with pityriasis versicolor like lesions, present over the face and forearms.

Figure 4: Brownish warty macules and plaques over the legs.

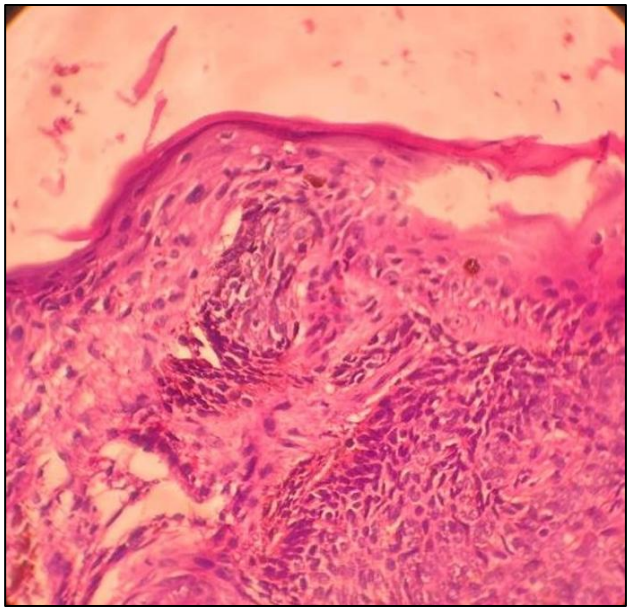

Figure 5: Features of basal cell carcinoma-nests of basaloid cells under the epidermis with large oval nuclei.

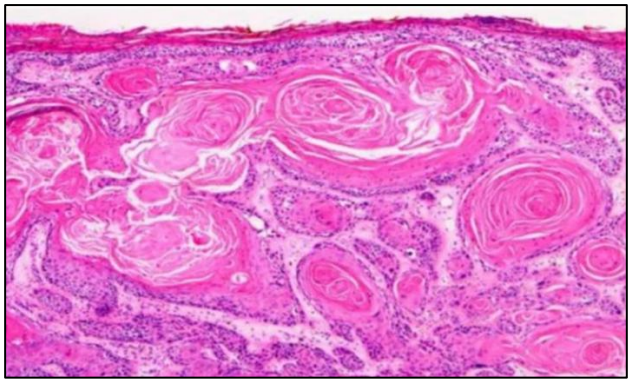

Figure 6: Features of squamous cell carcinoma-downgrowth of epidermis into dermis and subcutis. cells are large, polymorphic; dyskeratotic-appear pink.

A wedge biopsy from the edge of the ulcer in the daughter's forehead revealed features consistent with basal cell carcinoma (Figure 5), while the biopsy from the right clavicle of the mother suggested a diagnosis of basaloid squamous cell carcinoma. The diagnosis of EV in both these cases was confirmed by their typical clinical features, family history, and histopathological findings. Both patients showed characteristic EV features, such as early-onset, persistent skin lesions and cutaneous malignancies in sun-exposed areas.

Histologically, hyperkeratosis, acanthosis, and vacuolated keratinocytes with bluish-gray cytoplasm were present in the warty lesions, while the ulcerated lesions showed evidence of malignant transformation. The familial pattern of similar symptoms, the typical clinical appearance, and the cutaneous malignancies confirmed the diagnosis of EV.

DISCUSSION

EV is a rare genodermatosis with a multifactorial pathogenesis such as defective cell-mediated immunity, genetic and extrinsic (actinic) factors with an abnormal susceptibility to a specific group of Human Papillomavirus (HPV). The disease phenotype is characterized by chronic infection with HPV characterized by widespread skin eruptions of flat-to-papillomatous, wartlike lesions and reddish-brown pigmented plaques on the trunk, the hands, and the upper and lower extremities. Various types of HPV, such as HPV 3,5,8,9,10,12,14,17,19-25 and 29, have been associated with EV along with HPV 5 & 8, which have an oncogenic potential.[4]

Usually, EV occurs as an autosomal recessive condition in which the EVER 1 and 2 genes located on chromosome 17q25 become mutated, resulting in defective cell-mediated immunity for HPV.[5] In an autosomal recessive pattern of inheritance, the siblings exhibit phenotypic manifestations that are absent in their parents. In our report, both the mother and daughter manifested the disease, suggesting the possibility of an autosomal dominant mode of inheritance, which has been rarely reported.[6]

EV can also present in acquired patterns in individuals who are immunocompromised without a familial pattern of inheritance called acquired epidermodysplasia verruciformis (AEV). The impaired cell-mediated immunity in AEV can be caused by conditions such as HIV, lepromatous leprosy, Hodgkins's lymphoma, or medications.[7]

The familial history, typical clinical features and histopathology confirmation established the rare diagnosis of EV with cutaneous malignancies in our patients. This report highlights the rare occurrence of a possible autosomal dominant mode of inheritance and the presence of nonmelanoma skin cancers in both the parent and offspring. Despite their age difference, the presence of skin cancer in mother and daughter reveals the carcinogenic potential of solar exposure in the susceptible background of oncogenic HPV virus in EV.

CONCLUSION

Positive familial history, clinical findings, and histological evidence helps us understand that malignant conversion depends on the type of HPV and longstanding cutaneous EV lesions over sun-exposed areas. This highlights the importance of patient education regarding sun protection, early reporting for surgical excision of cutaneous malignancies and genetic counselling.

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REFERENCES

1. Patel T, Morrison LK, Rady P, Tyring S. Epidermodysplasia verruciformis and susceptibility to HPV. Dis Markers. 2010;29(4):199-206.
2. Gober MD, Rady PL, He Q, Tucker SB, Tyring SK, Gaspari AA. Novel homozygous frameshift mutation of EVER1 gene in an epidermodysplasia verruciformis patient. J Invest Dermatol. 2007;127(4):817-20.
3. Sun XK, Chen JF, Xu AE. A homozygous nonsense mutation in the EVER2 gene leads to epidermodysplasia verruciformis. Clin Exp Dermatol. 2005;30(5):573-4.
4. Silva C, Oliveira LL, Sotto WRP. Epidermodysplasia verruciformis: revision of a model of carcinogenic disease. Surg Exp Pathol. 2019;2:679.
5. Agrawal PG, Mahajan SA, Khopkar US, Kharkar VD. Epidermodysplasia verruciformis: an unusual malignant transformation. Indian J Dermatol Venereol Leprol. 2013;79(1):97-9.
6. Gaspari A, Garg V, Epidermodysplasia Verruciformis, published on Medscape. 2019.
7. Agrawal PG, Mahajan SA, Khopkar US, Kharkar VD. Epidermodysplasia verruciformis: an unusual malignant transformation. Indian J Dermatol Venereol Leprol. 2013;79(1):97-9.

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