A Rare Cause of Squamous Cell Carcinoma which Develops at an Early Age: Epidermodysplasia Verruciformis

Seyda Guray Evin, Ahmet Bilirer, Osman Akdag, Mehtap Karamese
Department of Plastic, Reconstructive and Aesthetic Surgery, Selcuk University, Konya, Turkey

Abstract

Epidermodysplasia verruciformis (EV) (Lewandowsky–Lutz syndrome) is a genodermatosis that accommodates premalignant skin lesions extensively infected with human papillomavirus with underlying cellular and humoral immune disorders. Localized especially in regions extensively exposed to the sun such as the forehead, these skin lesions may turn into malignant lesions with the mutation-inducing effect of ultraviolet lights. The skin lesions that may emerge as a result of this transformation include actinic keratosis, Bowen’s disease, squamous cell carcinoma (SCC), and more rarely basal cell carcinoma. The SCC that develops in patients with EV may act aggressively and can become locally invasive. This article aims at presenting the underlying EV as a rare etiological cause in patients with SCC at an early age.

Keywords: Hepatitis B, HIV, skin neoplasms, squamous cell carcinoma

Introduction

Epidermodysplasia verruciformis (EV) (Lewandowsky–Lutz syndrome) is a genodermatosis that creates susceptibility to human papillomavirus (HPV) infection due to an abnormality in cell-mediated and humoral immunity.[1,2] As a result of being infected by HPV, generalized flat warts, hypo- or hyperpigmentation, and other macular lesions may appear in skin. These lesions have the potential to turn into a malignancy in time, particularly which exposed to the sun light.[3] This article aims at underlying EV as a rare etiological cause of squamous cell carcinoma (SCC) that develops at an early age.

Case Report

A 19-year-old male patient presented with lesions approximately 2 cm × 3 cm in size, localized in the left temporal region, having ulcerated appearance in the center and involving sporadic dry and bleeding areas [Figure 1]. Patients family history revealed that his parents had consanguineous marriage and his sister had similar symptoms. The patient was engaged in farming and open-air workmanship, but did not use any sunscreen and stated that the lesion first appeared 2 years ago and grew in the last 3 months with occasional bleeding. His whole blood count, chemistry, and tumor markers were found normal. In his hepatic panel and enzyme-linked immunosorbent assay assessment, the patient was found to be a hepatitis B carrier only. His physical examination showed that he had a large number of hypopigmented, round, smoothly contoured, and not raised lesions in his neck and back and flat warts on his dorsum of the hand bilaterally. Red macules localized in his frontal trunk were also visible [Figure 2]. The pathological results of the multiple incisional biopsies taken from these lesions were reported as EV. The result of the incisional biopsies taken from the lesion in the temporal region was reported as SCC. Surgical excision and reconstruction was planned for the patient. The SCC was excised, leaving 1 cm of intact surgical margin. Taking into consideration the local aggressive prognosis and recurrence possibility of SCC in patients with EV, the defect was closed with a skin graft of partial thickness [Figure 3]. A reconstruction was planned with esthetically more appropriate options after ensuring the absence of recurrence. The patient is still under follow-up.

Address for correspondence: Dr. Seyda Guray Evin, Department of Plastic, Reconstructive and Aesthetic Surgery, Selcuk University, Faculty of Medicine, Konya, Turkey.
E-mail: sydguray@gmail.com

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**DISCUSSION**

EV was described by Lewandowsky–Lutz in 1922. It has both genetic and acquired forms. In its genetic form, besides autosomal recessive and X-associated inheritance, it has been shown that the mutations in EVER 1 and EVER 2 genes also lead to autosomal dominant inheritance. In a way to evidence genetic inheritance, 10% of the EV patients are born as a result of inbreeding and more than one child is affected in 10% of the families with EV. Our patient had a family history similar to those in the literature. The acquired forms of EV develop due to secondary HPV infections occurring after susceptibility to immunosuppression in patients with lymphoma, leukemia, myelodysplastic syndrome, leprosy, organ transplantation, systemic lupus erythematosus, bone marrow transplantation, atopic eczema, and graft versus host disease. The skin lesions occurring in these patients cannot be distinguished from genetic EV clinically or histologically and are referred to with the same name. More than 30 HPV types are responsible for the occurrence of the disease, but it is often linked to HPV 5 and 8 due to their higher oncogenic potential. These two types have been isolated from 90% of the patients developing SCC. It is agreed that EV lesions are infected by HPV without exception. Since the results of the biopsies taken from the skin of our patient were also supporting classical EV, no laboratory tests were done to show the presence of HPV DNA. In the study conducted by Shayanfar et al., hepatitis B and HIV infections were shown to create single-nucleotide polymorphism in some exons of various genes. They argued that this genetic change increased susceptibility to EV. As our patient did not have active hepatitis B infection, the relationship between the presence of hepatitis B and the development of EV could not be demonstrated as a scientific fact.

EV clinically appears in two main forms: benign and malignant. At the early stages of the disease, wart-like lesions are seen in the hands, feet, and face, lesions resembling pityriasis versicolor in proximal sites of the trunk, neck, and extremities or hyperpigmented macular lesions at the skin level. The differentiation between benignity and malignancy is made according to the lesions. While flat wart lesions similar to those seen in the normal population generally appear in the benign form, the lesions are more polymorphic in the malignant form. After the age of thirty, 30%–50% of these undergo a malignant transformation. Our patient had also flat warts on the dorsa of his hands, red macules in his trunk, and lesions resembling pityriasis versicolor in his neck in a way to support polymorphism in the malignant form. These lesions have been persistent since the age of 5. Malignant transformation is more common in the lesions that are in regions frequently exposed to UV lights such as the face and forehead. Actinic keratosis, Bowen’s disease, invasive SCC, and more rarely basal cell carcinoma occur as a result of this transformation. A combination of topical aminolevulinic acid and photodynamic therapy, CO laser, and imiquimod are used for the treatment of superficial skin cancers such as basal cell carcinoma, Bowen’s disease, and actinic keratosis. However, it is not possible to obtain a firm surgical margin with these therapies and local recurrences are frequent. The SCC
that develops in EV patients may progress quite aggressively and follow an invasive biological course. For this reason, when detected, surgical excision with a sufficient margin or excision with the Mohs micrographic surgical method can be used to achieve a complete cure.

Conclusions

If flat warts, red macules, and lesions resembling pityriasis versicolor are present, particularly in those parts of the body exposed to the sun in patients who present with nonmelanotic skin cancers, EV should definitely be considered as an initial diagnosis. The relatives of these patients should be screened for genetic predisposition. In this way, there can be a chance to intervene before the lesions turn malignant. If the histology of the nonmelanotic skin cancer developed in the patient is compatible with SCC, considering the possibility of a local invasion, it is essential to perform excision with a firm surgical margin and to closely monitor the patient for recurrences.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References