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## Case Report

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# A Case of Epidermodysplasia Verruciformis with Squamous Cell Carcinomas on Non-Sun-Exposed Areas of Skin

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**Epidermodysplasia verruciformis is an inherited disorder, characterized by multiple plane warts, pityriasis versicolor-like lesions, defects of cell-mediated immunity, and tendency to develop skin malignancies, primarily on sun-exposed areas. In this article, we present a case of epidermodysplasia verruciformis with multiple plane warts, pityriasis versicolor-like lesions, and squamous cell carcinomas on non-sun-exposed areas of skin. After acitretin prescription, significant improvement was found in plane warts, but not in pityriasis versicolor-like lesions.**

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### Introduction

**E**pidermodysplasia verruciformis (EV) is an inherited disorder, in which there is widespread and persistent infection with human papillomaviruses (HPVs). It presents with a characteristic combination of plane warts, pityriasis versicolor-like lesions, and red plaques.<sup>1</sup> Impairment of cell-mediated immunity, notably T-helper cells is commonly found.<sup>2</sup> Malignant skin changes are common and occur on sun-exposed areas of skin.<sup>3-5</sup>

In the present article, we describe a typical case of EV with multiple squamous cell carcinomas on non-sun-exposed areas of skin

### Case Report

A 25-year-old Iranian man (from Tehran) presented to the dermatology department because of two ulcerative plaques on his right knee and left ankle. The lesions had six months duration and a slowly progressive course. Physical examination of

the skin revealed two ulcerated plaques on the right knee (Figure 1) and the left lateral malleolus, multiple plane wart-like lesions on the upper and lower extremities (Figure 2), diffuse hyperpigmented macules and patches (Figure 3) on the whole body skin, and a small red scaly plaque on the left calf. The distribution of plane wart-like lesions was limited to the extremities and no wart was seen on the face and trunk. He had noticed the dyspigmented lesions when he was five years old, and plane wart-like lesions from 14<sup>th</sup> year of life. The dimensions of the ulcerative plaques were 4 x 2 cm on the right knee and 2.5 x 2 cm on the left ankle.

Four skin biopsies were obtained: from ulcerative plaques, a plane wart-like lesion, and the



**Figure 1.** Ulcerative plaque of squamous cell carcinoma on the right knee.

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**Figure 2.** Plane warts on the right lower extremity.

plaque on the left calf. The report of histopathological examination of the ulcerative plaques was squamous cell carcinoma (Figure 4) and of the left calf plaque was moderate dysplasia. The diagnosis of plane wart was confirmed with skin biopsy.

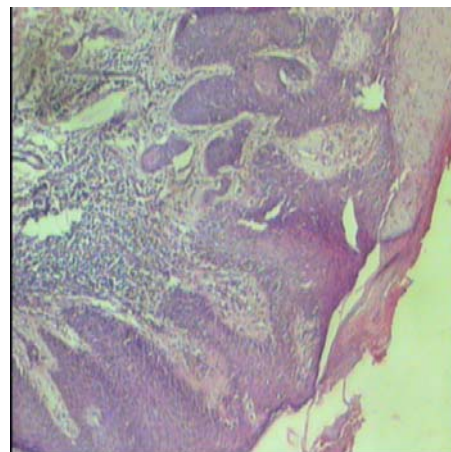
According to the above findings, the diagnosis of EV was made. The patient had no positive family history of EV or malignant skin lesions. Squamous cell carcinomas and dysplastic plaques were excised with free margins. Acitretin was prescribed for the patient with the dose of 1 mg/kg daily. After about two months, significant regression of plane warts were seen, but skin dyspigmentation had no change.

## Discussion

EV is a rare inherited disorder, characterized by an abnormal susceptibility to HPV infection, leading to a combination of plane warts and pityriasis versicolor-like lesions from an early age.<sup>5-7</sup> Its inheritance is usually autosomal recessive,



**Figure 3.** Pityriasis versicolor-like lesions on the right upper extremity.



**Figure 4.** Histopathological examination of the right knee ulcer: squamous cell carcinoma (Hematoxylin and eosin stain,  $\times 100$ ).

although autosomal dominant and X-linked dominant patterns have been reported.<sup>3</sup> EV was first described in 1922, but its specific genetic defect has not been identified yet.<sup>4,8</sup> In addition to genetic factors, extrinsic factors (solar radiation and some types of HPVs) and immunological disturbances play roles in the pathogenicity of EV.<sup>4</sup>

In early childhood, scaly macules appear on the trunk, shoulders, neck, arms, and face. They may, however, be more widely distributed. The lesions are brown red or white and in darkly pigmented skin they may appear black. The appearance and distribution of these lesions have been similar to tinea versicolor.<sup>4</sup>

Papular lesions, which resemble flat warts often appear on the skin.<sup>4</sup> Warts in EV are usually widespread and most numerous on the face, neck, and dorsa of the hands and feet, although there are some patients with only a few classic lesions limited to one extremity.<sup>1,5</sup> The involvement of large areas of the body with warts or failure to eradicate the lesions despite adequate treatment is the typical sign to consider this diagnosis. Mucosal warts of the cervix and oropharynx are rare, but can occur. Despite treatment, warts in EV always recur.<sup>5</sup>

At least 15 types of HPVs have been recognized in EV benign lesions. HPV types 3, 5, 8 – 10, 12, 14, 15, 17, 19 – 25, 26, 37, 38, and 47 have been found in EV lesions.<sup>3,4</sup> There is a tendency for HPV-3 and HPV-10 to be found in plane warts in EV.<sup>1,3</sup>

Patients with EV may have defects in cell-mediated immunity. T-cells and natural killer cells in these patients may have a decreased response to specific HPVs. As a result, they have diminished

resistance to infection with HPVs. Interestingly, these patients do not appear to be at increased risk for developing other viral or bacterial infections and may also have cutaneous anergy to contact sensitizers.<sup>4,9</sup>

One of the most important aspects of EV is developing nonmelanoma type skin cancers. In EV, malignant skin changes primarily occur on sun-exposed skin, suggesting that UV radiation is an important factor. UV radiation impairs the skin resistance to infections.<sup>8-10</sup> In these patients, skin cancers usually occur later in the life, in comparison with benign lesions.<sup>3, 4</sup> Another co-factor in developing malignant skin changes in EV is infection with HPVs. HPV-5 and HPV-8 are regularly found in EV malignant lesions. These viruses interact with UV-induced apoptosis.<sup>6</sup> Defect of cell-mediated immunity plays a role in developing skin malignancy in EV too. Most of these malignant tumors remain local.<sup>5</sup>

Treatment of EV is limited and aimed mainly at preventing the progression of benign lesions to malignant ones. Protection from UV light in early childhood is encouraged.<sup>4</sup>

Oral retinoids have been used in the treatment of EV, but their effects are often reversible after discontinuation of the treatment. These drugs can exert multiple beneficial effects including antiviral action, and antiproliferative effect through the control of epithelial cell differentiation.<sup>2</sup>

Interferons for their antiviral activities and capacity to inhibit malignant cell growth and the ability to stimulate natural killer and T-cells have been used effectively for treating warts in EV.<sup>2</sup> Immunomodulators have not been helpful in treating patients with EV.<sup>4,8</sup>

In the present case, the typical findings of EV such as pityriasis versicolor-like lesions, plane warts, and malignant skin changes were found. The appearance of benign lesions was in childhood and that of malignant skin changes in adulthood.

The interesting finding in this case was the distribution of squamous cell carcinomas and epidermal dysplasia, which were located on non-sun-exposed areas of skin. This suggests that UV radiation is important for developing skin

malignancy in EV, but is not critical and other factors like HPVs and defects of cell-mediated immunity can cause malignant skin changes without UV radiation.

We prescribed acitretin (1 mg/kg/day), and after about two months we found significant improvement in plane warts, but pityriasis versicolor-like lesions did not change.

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