Epidermodysplasia verruciformis: clinical presentation with varied forms of lesions

Epidermodisplasia verruciforme: apresentação clínica com variadas formas de lesões

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Abstract: Epidermodysplasia verruciformis is a rare inherited skin disorder spread by HPV, with cases linked to chromosome X. It is characterized by hypo- or hyper-pigmented macular lesions, pityriasis versicolor-like lesions and an early tendency to develop skin malignancies. We present a case of epidermodysplasia verruciformis with a variety of lesions such as multiple plane warts, pityriasis versicolor-like lesions and aggressive squamous cell carcinoma on the face.
Keywords: Carcinoma, squamous cell; Keratosis, actinic; Epidermodysplasia verruciformis; Warts

Resumo: Epidermodisplasia verruciforme é uma genodermatose rara caracterizada por infecção disseminada por HPV, de caráter recessivo, com casos ligados ao cromossoma X. É caracterizada clinicamente por lesões maculares hipo ou hiperpigmentadas, lesões pitiríase versicolor like, verrugas planas e desenvolvimento precoce de carcinomas cutâneos. Descreve-se um caso de paciente com quadro clínico exuberante, apresentando todas as formas de lesões desta doença, inclusive presença de carcinoma espinocelular agressivo na face.
Palavras-chave: Carcinoma de células escamosas; Ceratose actínica; Epidermodisplasia verruciforme; Verrugas

INTRODUCTION

Epidermodysplasia verruciformis is a rare disease, first described by Lewandowski and Lutz in 1922, characterized by susceptibility to infections caused by human papillomavirus (HPV), beta-papillomavirus (HPV 5, 8, 9, 12, 14, 15, 17 and 19 - 25). It is a rare autosomal recessive genodermatosis, with cases linked to chromosome X.[1,2] It is believed that susceptibility to the disease is due to a defect in cellular immunity. [3,4]

Histopathologic examination shows keratinocytes with wide layers of grayish cytoplasm and pyknotic nuclei. [2]

The disease indicates abnormal susceptibility to infection by various HPV types, which normally does not occur in immunocompetent individuals. It is believed that it arises from the selective inhibition of T-lymphocyte immune response against HPV infection, probably due to the defective presentation of viral antigens on the surface of keratinocytes. [2,5,6]

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The clinical symptoms generally manifest in childhood or at puberty, with flat wart-like lesions, erythematous macules or papules and/or hypopigmented or pityriasis versicolor-like lesions and even acninic-like keratosis, affecting the entire skin surface and the perineum. [4]

The lesions may become malignant in approximately 30% of cases, most commonly between the third and fourth decades of life, especially in areas exposed to sunlight. Squamous cell carcinoma is the most common type and can be aggressive, including with metastases. [1, 2, 4, 5]

We describe a case of epidermodysplasia verruciformis in a 35-year-old female patient with clinically exuberant, polymorphic lesions and the presence of squamous cell carcinoma on the face.

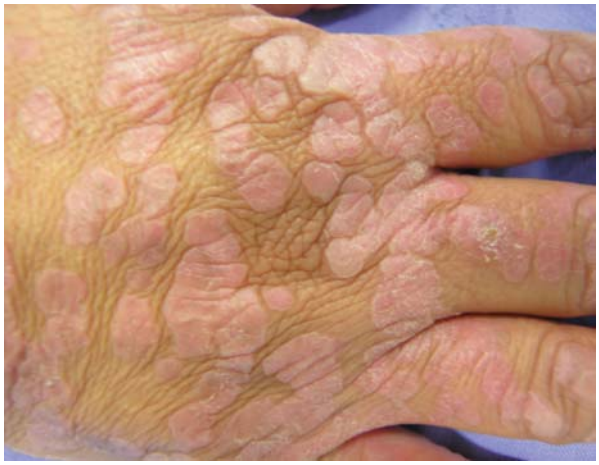

Figure 2: Flat warts on the hands

CASE REPORT

35-year-old female patient complaining of skin lesions present since childhood. Several surgeries were performed over the past 10 years to remove squamous cell carcinomas on the face and upper limbs. 3 years ago a tumor appeared in the right mandibular region. This increased in size and the patient presented at the Head and Neck Department where squamous cell carcinoma was diagnosed by biopsy. Left maxillectomy exision performed. History of consanguinity revealed between the parents (first cousins) and a mother with similar clinical symptoms. The dermatological examination showed multiple disseminated lesions, some in slightly scaling hypopigmented plaques on the back, flat normochromic plaques on the backs of hands, erythematous plaques with sharp edges on the neck and abdomen and actinic keratosis lesions on the face (Figures 1, 2, 3 and 4). Negative HIV serology. Biopsy from two different skin lesions (plaques on hand and back), showing acanthotic epidermis with hyperkeratosis and, across the entire thickness of the epidermis, areas permeated by cellular nuclei of moderate size and with small amphophilic citopolasma granules (Figures 5 and 6). Dermis preserved. Clinical and histological picture compatible with epidermodysplasia verruciformis. Patient is receiving oral retinoids, sunscreen and monitoring at the Dermatology Outpatients Clinic.

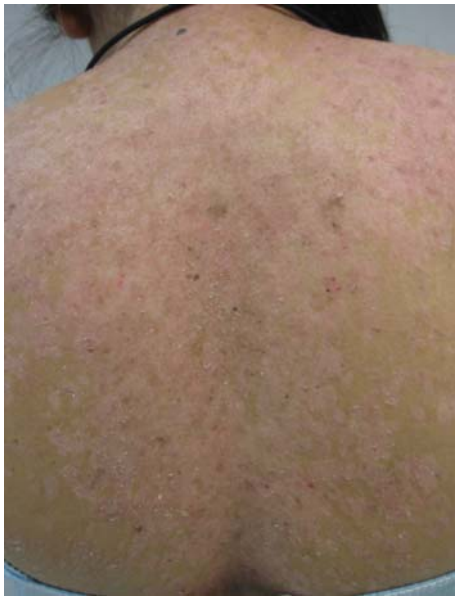

Figure 1: Erythematous scaly, pityriasis versicolor-like lesions on the back

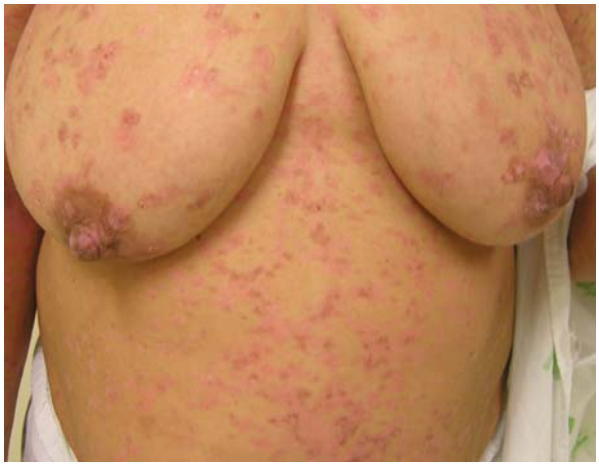

Figure 3: Erythematous plaques with little scaling, some brown patches on the trunk and upper limbs

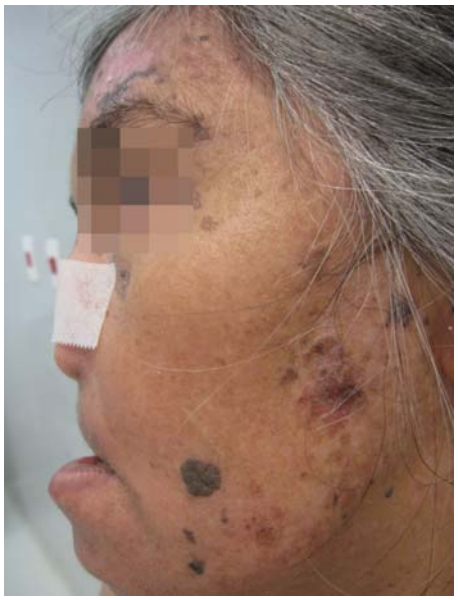

Figure 4: Actinic keratosis lesions on the face

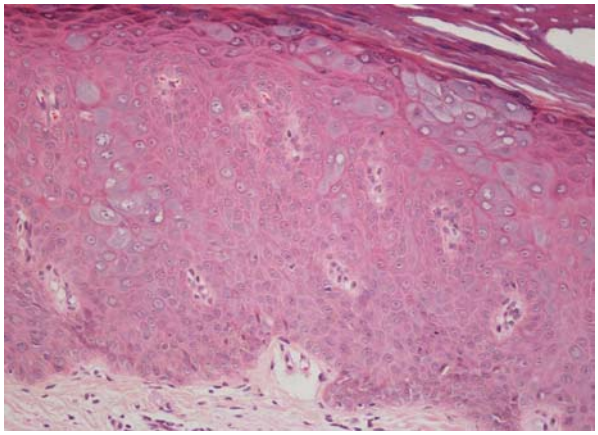

Figure 5: Biopsy of lesion on hand – acanthotic epidermis showing keratinocytes with bluish cytoplasm related to HPV infection, typical of epidermodysplasia verruciformis. Hematoxylin-eosin stain at 200X magnification

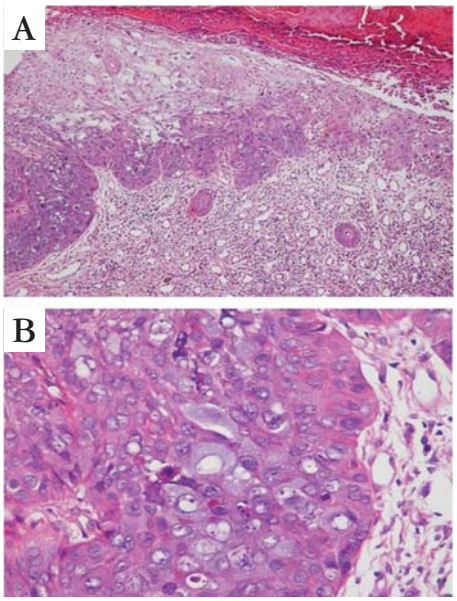

Figure 6: **A**. Biopsy of CEC of the face: the picture on the left shows ulcerated epidermis with intensely expressed keratinocytes & nbsp; atypical and disceratose throughout its thickness, and invading the superficial dermis. Hematoxylin-eos at 200X magnification.
B. Detail of the lesion showing keratinocytes with blue cytoplasm typical of epidermodysplasia verruciformis with cellular pleomorphism & nbsp; Hematoxylin-eosin stain at 400X magnification

DISCUSSION

Epidermodysplasia Verruciformis is a genodermatosis characterized by disseminated HPV infection and is considered to be the first model of virus-induced carcinogenesis in humans. [2,4]

Immunological changes occur in patients with this disease, especially in their cellular immunity. [1,6,7] This deficiency appears to be local and specific, which causes the generation of several cytokines which prevent the immune system recognizing HPV. [2,3,7]

The disease has no preference for gender or race and can be sporadic or familial. [3] It is regarded as an autosomal recessive hereditary disease, although there are reports of possible links with chromosome X [2,4] The patient reported on has a history of consanguinity between the parents, and the mother carries the same disease.

The disease usually begins in childhood. The presentations are polymorphic, usually starting with flat wart-like lesions on the back of hands. [4,7,8] Macules and hypochromic plaques may also be present, resembling pityriasis versicolor and actinic keratosis lesions. [2,7]

Epidermodysplasia Verruciformis may present only with flat warts, associated with “benign” non-oncogenic HPV 3 and/or 10, or appear as polymorphic lesions with a tendency toward malignancy (the "malignant form") associated with multiple HPV (some oncogenic, most commonly 5 and 8). [2,6,9] The initial presence of flat warts, followed by the appearance of polymorphism characteristic of malignant form, are known as the "mixed form". [2,9]

This patient presented clinical symptoms of intense polymorphism, with the presence of all the types of lesions described above which suggested epidermodysplasia verruciformis, including malignant transformation into poorly differentiated squamous cell carcinoma on the face, typical of the “malignant form”of the disease.

Epidermodysplasia verruciformis is considered a pre-neoplastic condition given that in 30-50% of

cases malignant transformation of the lesions occurs (generally on areas exposed to sunlight). [2,5,7-10]

Treatment options of epidermodysplasia verruciformis are limited, and to date no specific treatment exists. Treatment aims primarily to prevent the progression of benign lesions to malignancy. Patients need to be advised to use sunscreen from childhood. The use of derivatives of vitamin A has been described and recommended. [1,2,4] The use of cimetidine has produced good results and few side effects. [1,11] Oral retinoids have also been used in the treatment of EV, but their effects in the majority of cases are reversible after discontinuation of treatment. These drugs can however have several beneficial effects, including antiviral and antiproliferative action of tumor cells. [6,9,11-15] Interferons have been used effectively for the treatment of warts in EV, with their antiviral action and ability to inhibit malignant cell growth and stimulate natural killer cells and T cells. [6,12,13] Genetic counseling and frequent dermatologic monitoring of patients should be undertaken. [1,2,4] ❑

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