Acquired epidermodysplasia verruciformis in a renal transplant recipient - Case report*

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Abstract: A 24-year-old male patient, who underwent kidney transplant six years ago due to Lupus nephritis, for the last two years presented asymptomatic erythematous scaly plaques on the abdomen and areas exposed to light. Post-transplantation immunosuppressive medications included prednisone, mycophenolate sodium and sirolimus. The histopathologic features were typical for epidermodysplasia verruciformis. Epidermodysplasia verruciformis is a rare autosomal recessive genodermatosis with increased susceptibility to specific strains of cutaneous human papilloma virus. The term "acquired epidermodysplasia verruciformis" was recently introduced to the literature and describes epidermodysplasia verruciformis occurring in patients with impaired cell-mediated immunity. We report an additional case associated to immunosuppression after kidney transplantation.
Keywords: Epidermodysplasia verruciformis; Immunosuppression; Kidney transplantation

INTRODUCTION

Epidermodysplasia verruciformis (EV), initially described by Lewandowski and Lutz in 1922, is a rare genodermatosis, autosomal recessive or linked to the X chromosome, characterized by susceptibility to chronic infection and disseminated by specific strains of human papilloma virus (HPV), secondary to defect in cellular immunity. Its onset is usually in early childhood, with the appearance of hypo or hyperpigmented macules, pityriasis versicolor-like lesions, flat warts and early development of skin carcinomas.[1,2] There are at least 20 types of HPVs associated with EV, which include types 3, 5, 8, 9, 10, 12, 14, 15, 17, 19-25, 38, 29, 36, 46, 47, 49 and 50.[3] These viruses have oncogenic potential in these patients and around 30 to 60% of affected patients may develop squamous cell carcinoma, usually in areas exposed to sunlight and in the fourth decade of life.[3] The term acquired EV was recently introduced in the literature to describe EV developing in the immunocompromised host, like carriers of acquired immunodeficiency virus, Hodgkin disease and systemic lupus erythematosus.[3-6] Reports of acquired EV in kidney transplanted patients are rare, with few cases described in the worldwide literature to date.[7-9]

CASE REPORT

A 24-year-old male patient, student, presented for two years asymptomatic lesions in areas exposed to light, which increased progressively in number. He used oral and topical antifungals without improvement. He had history of systemic lupus erythematosus for 11 years and kidney transplant due to renal failure secondary to lupus nephritis for the last 6 years and, for this reason, he is undergoing immunosuppressant treatment with sirolimus 1mg 2x/day, mycophenolate sodium 360mg/day and prednisone 10mg/day. There was no history of consanguinity and affected relatives. On examination, he had numerous erythematous papules and macules (pityriasis versicolor-like) on his face, neck, V-shaped neckline, forearms and abdomen (Figure 1). Histologic examination of the skin biopsy from abdomen revealed vacuolated cells in the upper epidermis with a bubbly, bluish cytoplasm, thickened granular layer and mild perivascular infiltrate in the superficial dermis, consistent with EV (Figure 2).

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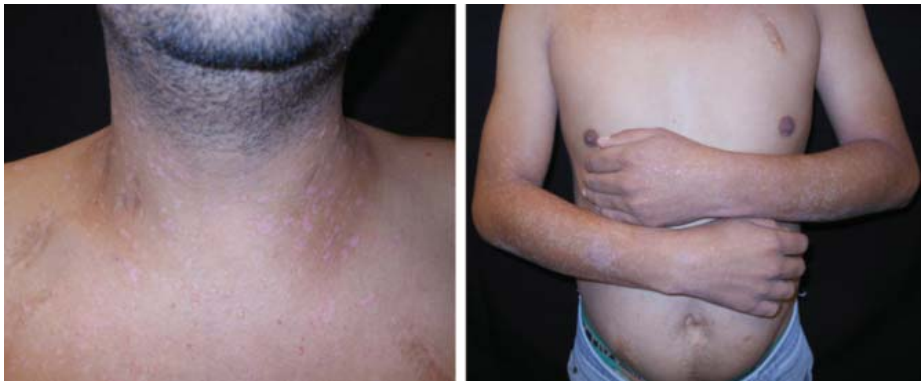

Figure 1: Erythematous papules, pityriasis versicolor-like plaques, on areas exposed to light

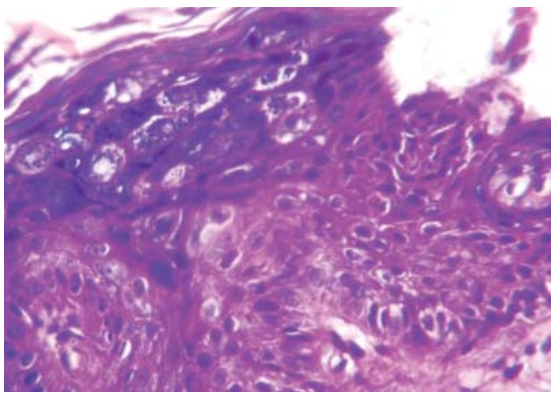

Figure 2: A biopsy from the abdomen shows bubbly bluish cytoplasm and thickened granular layer consistent with epidermodysplasia verruciformis

DISCUSSION

The pathogenesis of congenital EV remains unknown. On familial cases were found mutations of EVER1/TMC6 and EVER2/TMC8 genes, present in chromosome 17q25. These mutations could negatively regulate cell-mediated immunity, by diminishing the capability of presenting peptides derived from HPV to T lymphocytes. Immunosuppressed patients acquire susceptibility to HPV that cause EV, innocuous to the general population, highlighting the role of cell-mediated immunity in resistance to the HPVs that cause the syndrome. Similar to inherited EV, HPVs 5 and 8 are the most common subtypes found in acquired EV.[3] Although these are associated with the development of squamous cell carcinoma in inherited EV, the potential for malignancy in acquired forms is uncertain.[3] Our patient was on immunosuppressing treatment with sirolimus, prednisone and mycophenolate sodium. Sirolimus acts on cell immunity by T lymphocytes activation and proliferation inhibition. On cells, sirolimus links itself to immunophilin, binding protein FK 12 (FKBP-12), in order to form an immunosuppressant complex. The sirolimus/FKBP-12 complex does not have effects over calcineurin activity. This complex links itself to mTOR, an important regulatory kinase, inhibiting its activity. This inhibition suppresses cytokine-induced T cell proliferation, inhibiting the progression of phase G_1 to phase S of the cell cycle.[10] Mycophenolate sodium is a competitive and reversible inhibitor of inosine monophosphate dehydrogenase and, therefore, inhibits the *de novo* synthesis of guanosine nucleotides, with no DNA incorporation. Mycophenolate sodium has potent cytostatic effects over lymphocytes, since B and T lymphocytes are critically dependent on purines for their proliferation, whereas other types of cells can use alternative pathways. Prednisone acts on growth, differentiation and maturation of the lymphocyte, inhibiting proliferation of germinal centers of lymph nodes and spleen. The clinical and histopathological manifestations of EV are similar in the two clinical forms. The histopathological exam of lesions shows hyperkeratosis, acanthosis, keratinocytes with ample cytoplasm and picnotic nuclei, located in the granular layer. The main objective of EV treatment is to avoid the malignant transformation of lesions, for up to this moment there is no effective therapy for the congenital and acquired forms. The use of sunscreen is recommended for all patients at the time of diagnosis. Among the therapeutic options are topical and systemic retinoids with antiproliferative action, imiquimod, cryotherapy, 5-fluorouracil and topical cidofovir, none of them with proven effectiveness.[1] Interferon can be utilized due to its antiviral action mechanism, besides stimulating T cells. With prolonged life expectancy of immunosuppressed patients it is fundamental that patients undergo complete dermatological exams periodically, to detect skin alterations resulting from cell immunity defects, among which EV stands out due to probable risk of carcinoma development. ❑

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