Acquired epidermodysplasia verruciformis in an HIV positive child. Report of a case

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ABSTRACT

Epidermodysplasia verruciformis (EV) is a rare genodermatosis whose main feature is a genetic predisposition to persistent skin infection by different serotypes of human papillomavirus (HPV). In recent years, an EV-like syndrome has been described in patients with impaired cell-mediated immunity, including patients with HIV. We report the case of a teenage female patient with congenital infection with the human immunodeficiency virus (HIV), which has similar lesions to classical EV.

Keywords: Epidermodysplasia verruciformis; human papilloma virus; human immunodeficiency virus

INTRODUCTION

Epidermodysplasia verruciformis (EV) is a rare autosomal recessive genetic disorder, characterized by persistent skin infection by the human papillomavirus (HPV), because there is a greater genetic susceptibility to infection with certain oncogenic HPV subtypes [1,2]. The clinical appearance in patients with inherited and acquired immunodeficiencies is similar to those of classical EV symptoms.

It is proposed to call these acquired EV [1].

CASE REPORT

A 10-year-old female diagnosed at age 7 with human immunodeficiency virus (HIV), CD4 count = 765 cells/mm3 and viral load (VL) of 58,842 copies at the time of diagnosis; initiation of antiretroviral therapy, aged 9, with CD4 count = 545 cells/mm3 and CV = 132,589 copies.

Presented to the consult with white spots on neck progressively increasing in number and extending to arms, some of them tend to rise. Mycological study is negative. At that time a clinical diagnosis of flat warts is made, and receives several treatments including topical 20% urea and 35% trichloroacetic acid (TCA); imiquimod 7.5% 3 times/week; 0.025% retinoic acid 1 time/day; there was no improvement in the lesions.

At 13 years old returns to the consultation with the same lesions described above, to which are added warts on knees and toes. The patient reported no family history of consanguinity. On physical examination she presented numerous hypopigmented papules and plaques, with irregular and well defined borders, between 0.5-2 cm in diameter on forehead, neck, V-shaped neck line, back and upper limbs (Fig. 1). On knees and toes presented skin colored flat papules that were treated with electrocoagulation (Fig. 2).

Given several persistent treatments, it was decided to perform a skin biopsy.

Histopathology reports: epidermis with acanthosis with bulbous elongation of rete ridges, hyperkeratosis over acanthosis, absence of papillomatosis. Vacuolization of epidermal keratinocytes of superior layers. They show gray cytoplasm, enlarged nuclei, nuclear irregularity.
These findings of enlarged cells in granular layer of grayish granular cytoplasm, enlarged and irregular nuclei, are indirect signs of HPV-EV infection in the skin (flat wart in the context of an EV) (Fig. 3).

With these data, the diagnosis of acquired epidermodysplasia verruciformis in a patient with vertical HIV transmission is made.

Prior to the study, patient agreed to the examination and biopsy and a legal representant signed the written consent after been informed about the procedure.

**DISCUSSION**

Epidermodysplasia verruciformis is a disease in which there is an increased genetic susceptibility to infection by certain subtypes of human papillomavirus (HPV-EV) viruses, such as subtypes 5 and 8 [2,3].

This disease can occur in all races, there is no sex predilection and is most common during childhood and puberty; age of onset is usually between 5 and 8 years old [4].

Initially the lesions are localized being only hypochromic scaly patches on the face and neck, similar to tinea versicolor. Over time they increase in number and tend to evolve to papules resembling flat warts from pink to brownish, sized a few millimeters, with a smooth surface. Subsequently they extend to the dorsum of the hands, forearms, knees, legs and feet. Mucous membranes are not affected [4,5].

In highest sun exposed areas such as the face, especially the forehead, V neckline and back of hands erythematous plaques arise, become keratotic and prone to erosion and in the third decade of life can evolve into Bowen’s disease or squamous epithelioma [4].

The EV has a pathognomonic histological and ultrastructural features. Hypergranulosis, acanthosis and hyperkeratosis, and large clear cell nests extending from one level to the granulosa suprabasal layer, mainly at the level of the rete ridges. Cells have large, clear and lumpy cytoplasm, thick cytoplasmic membrane without intercellular bridges and a core with a central vacuole. These cells are the result of viral cytopathic effects and were described by Rueda, in 1967, who called them epidermodisplastic cells [6].

In the last decade there have been some cases of acquired EV associated with immunosuppression states such as renal transplantation, graft versus host disease, systemic lupus erythematosus and HIV infection [1,7].

In the HIV carrier population, men and women are affected in the same proportion. It has been observed that it is more frequent in younger patients with
congenital HIV infection because they were probably infected with HPV before developing a good state of cellular immunity [7].

Classical EV results from a deficiency in cell-mediated immunity and genetic susceptibility to HPV-EV. This results in a natural inhibition of cytotoxic mechanisms against infection by HPV keratinocytes, leading to the development of skin lesions.

It is likely that patients infected with HIV have an acquired deficiency of the secondary cell mediated immunity to chronic infection and untreated HIV.

Patients with vertical HIV transmission probably have their first HPV infection in early childhood when their cell mediated immune system has already been infected with HIV, while adults who have been infected with HIV have strengthened immune mechanisms against HPV infection, which develops in childhood while their immune system is still intact. This could explain why EV is not as common in HIV-infected adults as it is in HIV MTCT adults [3,8].

According to the literature, the progression of skin lesions appears to be influenced by the immune status of the patient, by the viral phenotype and sun exposure, and its evolution to malignancy, particularly squamous cell carcinoma, is described in up to 30-60% of patients. [3,7]. On EV lesions carcinomas may appear, mainly epidermoid, Bowen’s disease (squamous cell carcinoma in situ), basal and some premalignant lesions such as actinic keratoses [9].

Currently there is no specific or effective treatment for EV, the management of patients includes preventive measures such as genetic counseling, photoprotection and monitoring of symptoms for proper identification of premalignant and malignant lesions. Sunscreens are recommended to avoid direct exposure to UV radiation, since constant exposure tends to increase the risk of malignancy. Topical and systemic retinoids, in combination with with vitamin D analogs (calcipotriol) and alpha interferon are used. 5-fluorouracil has also been used for the treatment of precancerous lesions. Other treatments options include photodynamic therapy, immunotherapy and surgical treatment of premalignant and malignant lesions [10].

CONCLUSIONS

1. The absence of affected family members or history of consanguinity in the case presented, and the fact that it appears in the context of a state of immunodeficiency leads to the diagnosis of Acquired Epidermodysplasia Verruciformis.
2. It is important to establish a proper diagnosis in patients with lesions resembling flat warts and that are refractory to treatment.
3. The gold standard for diagnosis is histopathology, although in this case no HPV serotypes have been identified, there were indirect histological signs of HPV-EV serotypes infection that all dermatopathologists should know.
4. This patients should undergone lifetime monitoring due the high risk of developing premalignant and malignant lesions.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. A legal representant signed the written consent for the publication of this article and any accompanying images.

REFERENCES