An interdigital case of pediatric pigmented Bowen's disease associated with human papillomavirus antibodies: A location not previously reported in this age group

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Key words: Bowen's disease; human papillomavirus; pediatric; squamous cell carcinoma in situ.

INTRODUCTION

Bowen's disease (BD), also known as squamous cell carcinoma in situ, is a keratinocytic neoplasm that is limited to the epidermis. This entity usually develops in elderly people, although 4 cases in healthy pediatric patients have been described. Kim et al[1] reported a 4-year-old girl, the youngest patient documented, with a hyperpigmented periungual plaque on the right thumb that showed slow growth over 3 years without any other symptom. The plaque was removed surgically and the histologic analysis was compatible with BD; in situ hybridization analysis was negative for human papillomavirus (HPV) DNA subtypes 6, 11, 16, 18, 21, 33, and 51. Firooz et al[2] described a 20-year-old woman who presented with a lesion that closely mimicked malignant melanoma that was finally diagnosed as BD, with negative results for antibodies against HPV in the histologic analysis. Hyun et al[3] reported case of a healthy 12-year-old boy with a periungual hyperpigmented plaque on the right index finger that was compatible with BD; in this case, in situ hybridization result for HPV was positive for subtype 34. He was treated with photodynamic therapy and had an uneventful recovery. Finally, Hudson et al[4] described the case of an 11-year-old girl with a periungual hyperpigmented plaque located on the third finger of her left hand that was also positive for HPV (high-risk subtypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) in the in situ hybridization analysis. Acral BD lesions tend to show hyperkeratosis and pigmentation. Despite the fact that 2 of the previous cases did not show the presence of HPV, the authors did not discount a role of this pathogen in the oncogenesis process because of its well-known role in the development of acral BD. A summary of the literature review is presented in Table I.

Abbreviations used:

BD: Bowen's disease
HPV: human papillomavirus

The objective of the following study is to report the finding of BD in an unusual location not previously described in pediatric-aged patients.

CASE REPORT

A previously healthy 16-year-old female with no family or personal history of cancer, no use of medications, no history of sexual intercourse, and no HPV vaccination presented to the dermatology clinic with a 2-year history of 2 asymptomatic, hyperpigmented, verrucous papules located in the web space between the second and third toes of her left foot. The larger one measured 9 × 8 × 2 mm and the smaller one 2 × 2 × 1 mm; both had well-defined borders, a brownish appearance, and a rough surface (Fig 1).

A dermoscopic examination was performed with a DermLite DL200 (Capistrano, CA) Hybrid at polarized light mode. Whitish digitiform irregular

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Table I. Literature review of pediatric BD

Case	Sex/age, years	Location	Evolution, years	Presentation	HPV status	Treatment
Firooz, 2007	Woman/20	Pulp of fourth finger of left hand	4	Hyperpigmented patch	Negative	Surgery
Kim, 2014	Girl/4	Right thumb	3	Hyperpigmented periungual plaque	Negative	Surgery
Hyun, 2016	Boy/12	Right index finger	3	Hyperpigmented periungual plaque	HPV 34	Photodynamic therapy
Hudson, 2018	Girl/11	Third finger of left hand	4	Hyperpigmented periungual plaque	High-risk HPV	Surgery

BD, Bowen's disease; *HPV*, human papillomavirus.

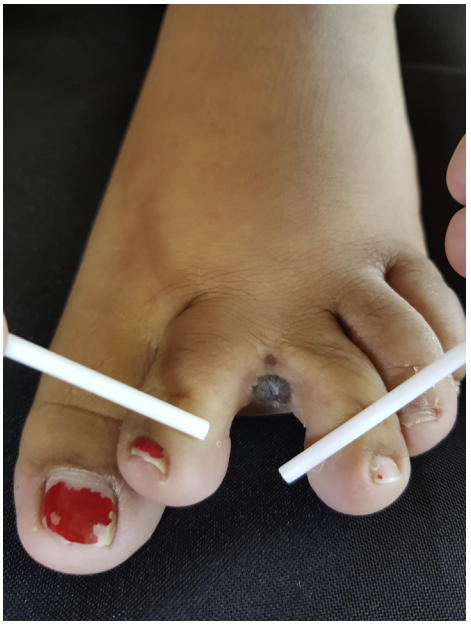

Fig 1. Pigmented BD. *BD*, Bowen's disease.

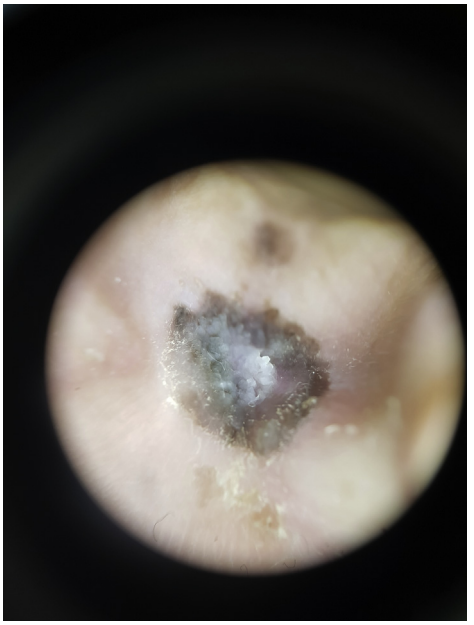

Fig 2. Dermoscopy findings. Whitish projections over the surface, pigmented dots at the periphery, and a milky-red base were observed.

projections on a milky-red base with peripheral pigmented dots were observed (Fig 2).

Because of the nonspecific morphology of the lesion, an incisional biopsy was performed. Hematoxylin-eosin staining exhibited full-thickness keratinocytic atypia, hyperchromatic nuclei, and atypical mitotic figures with koilocytes. Immunohistochemical analysis performed on a formalin-fixed, paraffin-embedded tissue section had a positive result for antibodies against HPV 16 and 18 in less than 10% of epidermal cells (Figs 3 and 4).

The diagnosis of BD with associated HPV antibodies was made. The patient underwent a digital syndactylization and remains free of recurrence without sequelae after 1 year of follow-up.

DISCUSSION

This case highlights the importance of considering BD as part of the differential diagnoses when evaluating pigmented and hyperkeratotic acral lesions because they are usually misdiagnosed as viral warts.

Among the identified risks factors that explain the appearance of BD are chronic ultraviolet light exposure, arsenic exposure, ionizing radiation, burns, chronic ulcers, and HPV infection. The latter is mostly related to BD in an acral location, especially HPV subtype 16.[5]

Alam et al[6] analyzed 23 BD cases positive for HPV in finger lesions. They reported that the most commonly affected finger was the index in 42% of individuals, followed by the third finger in 29%. HPV

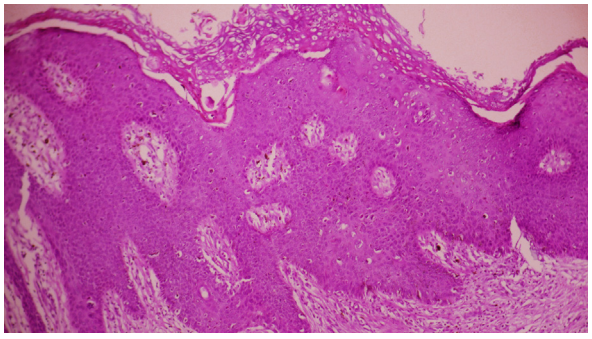

Fig 3. Hyperkeratosis, papillomatosis, and atypical keratinocytes on all levels of the epidermis, as well as hyperchromatic nuclei and koilocytes. (Hematoxylin-eosin stain; original magnification: ×10.)

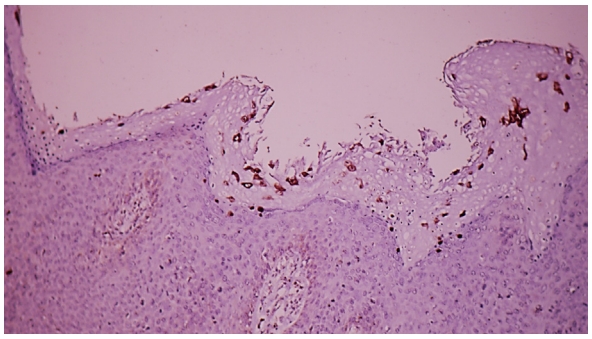

Fig 4. Immunostaining for HPV 16 and 18 subtypes was positive in less than 10% of epidermal cells. (Hematoxylin-eosin stain; original magnification: ×10). *HPV*, Human papillomavirus.

subtype 16 was most frequently identified (89%), followed by subtypes 31 and 35. During a 2-year follow-up, disease recurrences were identified in 26% of cases and 1 case of metastatic disease was recorded. Among the 23 patients, 4 had a history of genital warts or cervical dysplasia. Additionally, Shimizu et al[7] suggested that the nail matrix could serve as a reservoir for HPV infection because the absence of Langerhans cells would make this anatomic location particularly vulnerable to infection.

It is not feasible to detect HPV in all cases of acral BD. Such infection promotes acquisition of mutations, including those within tumor suppressor genes, as in the *p53* gene. Over time, there is an increasing mutational burden leading to selection of clones with proliferative advantage, culminating in a full-thickness dysplasia. While mutational burden increases, there is a loss of HPV episomes, which is called a "hit and run" mechanism of transformation.[8] This could explain the absence of HPV viral genome in some cases of acral BD.

Diagnosis is challenging and is usually based on clinical-histopathologic correlation. Cameron et al[9] found that pigmented points with a gray to dark-brown hue that were arranged linearly, as well as the presence of glomerular vessels at the periphery of the lesions, were findings most strongly associated with the histopathologic diagnosis of BD in a series of 52 patients. In our study, we observed brown dots at the periphery of the lesion but without a specific arrangement; therefore, the clinical-histopathologic correlation was invaluable for final diagnosis.

Several options are available for treatment: topical 5-fluorouracil, imiquimod, photodynamic therapy, cryosurgery, curettage, and surgical excision. The latter is the treatment of choice for BD with an acral location because of anatomic peculiarities. Mohs micrographic surgery is recommended because preservation of the greatest amount of healthy tissue for reconstruction is essential.[5] Our patient underwent excision and digital syndactylization, with good results; this technique was previously reported as an option for interdigital BD with interdigital location.[10]

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