

# Development of Squamous Cell Carcinoma on an Inflammatory Linear Verrucous Epidermal Nevus in the Genital Area

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*Inflammatory linear verrucous epidermal nevus is a rare cutaneous disorder characterized by pruritic, erythematous, and verrucous papules and plaques along the lines of Blaschko. Histopathologically, there is a benign verrucous proliferation of keratinocytes together with alternating parakeratosis and orthokeratosis as well as inflammatory changes. We report a patient who developed squamous cell carcinoma (SCC) on an inflammatory linear verrucous epidermal nevus and we discuss the importance of regular follow-up of patients with epidermal nevi.*

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**D**evelopment of squamous cell carcinoma (SCC) on epidermal nevi has been rarely reported.<sup>1-4</sup> We report a case of a patient who developed SCC on an inflammatory linear verrucous epidermal nevus in the genital area.

## Case Report

A 28-year-old woman presented with congenital, pruritic, brown, verrucous, linear lesions on the left side of her body, as well as a mass on her left groin. The lesions had been present at birth. At 7 years of age, genital verrucous plaques had grown in size and had become a vegetative tumor. There was no

history of genital warts. Six months before admission, a mass had been palpated on her left groin. On dermatologic examination, verrucous linear plaques with erythema along the lines of Blaschko on the left side of her trunk, upper extremity, and left lower extremity were observed (Figure 1). A vegetative tumor measuring 10 to 20 cm in diameter arose on her left labium majus and extended to the anal region with an infiltrated area on the left edge (Figure 2). Enlarged nontender groin lymph nodes were palpated bilaterally.

Laboratory tests including a complete blood cell count, erythrocyte sedimentation rate, kidney and liver function tests, and urinalysis were within reference range. Ultrasonography of the groin lymph nodes revealed conglomerated lymphadenopathies. Histopathologic examination of the lesions on the left arm revealed columnar alteration of orthokeratotic hyperkeratosis/hypergranulosis as well as parakeratotic hyperkeratosis/hypogranulosis or agranulosis with papillomatosis in the epidermis and lymphohistiocytic infiltration in the dermis. The vegetative genital mucosal lesions also revealed columnar alteration of orthokeratotic hyperkeratosis/hypergranulosis as well as parakeratotic hyperkeratosis/hypogranulosis or agranulosis with papillomatosis and prominent koilocytosis at the site of parakeratosis. However, there were dysplastic changes in the basal cell layers followed by the development of invasive SCC on histopathology of the infiltrated area (Figure 3). Results from the excised material were positive for human papillomavirus (HPV) types 6, 35, 38, and 42. Histopathologic examination

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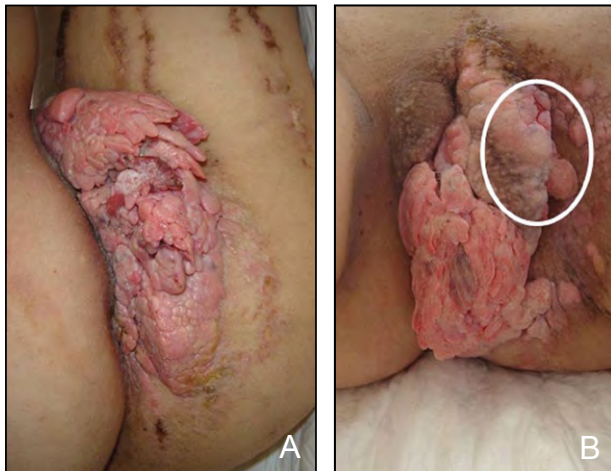
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The authors report no conflict of interest.

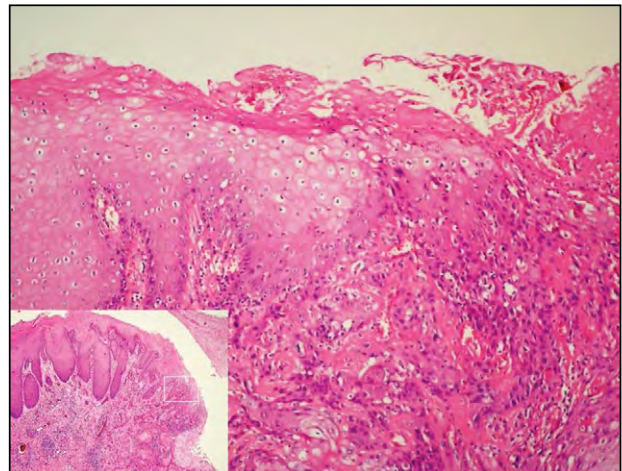
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**Figure 1.** Verrucous linear plaques with erythema along the lines of Blaschko on the left side of the trunk (A and B) and extremities (B and C).



**Figure 2.** A vegetative tumor on the left labium majus (A) extending to the ipsilateral inguinal and anal regions. Squamous cell carcinoma was determined in the infiltrated area (white circle)(B).



**Figure 3.** Hyperplasia and dysplasia in the squamous epithelium (H&E, original magnification  $\times 4$  [inset]). Dysplasia was present in the basal cell layers on the left side and invasive squamous cell carcinoma on the right side (H&E, original magnification  $\times 40$ ).

from the lymphadenopathy also confirmed metastasis of SCC.

Cranial magnetic resonance imaging and full-body positron emission tomography revealed no distant metastasis. The patient was treated with the chemotherapeutic agent cisplatin  $100 \text{ mg/m}^2$  and 5-fluorouracil  $500 \text{ mg/m}^2$  for 6 cycles followed by surgery and radiotherapy, respectively. The

patient is still on follow-up without recurrence or metastasis for 5 years.

### Comment

Development of SCC on an inflammatory linear verrucous epidermal nevus is rare. Squamous cell carcinoma has been reported on another type of inflammatory epidermal nevus, CHILD (congenital

hemidysplasia with ichthyosiform nevus and limb defects) syndrome.<sup>4</sup> Unfortunately, the etiology of malignant transformation has not been discussed in these reports.<sup>1-4</sup> Human papillomaviruses are small double-stranded DNA viruses that may induce a wide variety of cutaneous and mucosal lesions. High-risk HPVs (ie, types 16, 18, 31, 33, 35, 58) are associated with the development of cervical cancer. Although the role of HPV in the pathogenesis of nonmelanoma skin cancer in epidermodysplasia verruciformis and immunosuppressed patients is known, its role in the general population is unclear. Human papillomavirus types 5 and 8 are the most common types found in SCC of epidermodysplasia verruciformis patients, whereas HPV types 5, 15, 24, 36, 38, and 80 often are associated with nonmelanoma skin cancer in the general population.<sup>5</sup> In our patient, HPV types 6, 35, 38, and 42 were detected in SCC.

Of 44 formalin-fixed paraffin-embedded samples of nevus sebaceus (NS) in a study conducted in 2008, HPV DNA was detected in 36 of 44 patients comprising 82%.<sup>6</sup> The authors of the study also showed that NS with secondary tumors such as trichilemmoma or trichoblastoma had a higher frequency of HPV DNA than NS without secondary tumors. They concluded that those findings might suggest the role of HPV in the pathogenesis of epidermal nevi by triggering the development of mosaic cell lines and also in the process of malignant transformation.<sup>6</sup> Determination of different HPV types in

our patient also supported the possible role of HPV in tumorigenesis.

### Conclusion

Human papillomavirus should be considered as a risk factor for malignant transformation of epidermal nevi and regular follow-up should be carried out in patients with epidermal nevi.

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