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Photo Vignette

Pigmented Bowen's disease of the penis and scrotum in a patient with AIDS

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Introduction

Patients with HIV have higher risk of developing squamous cell carcinoma of the skin given the increased risk of HPV infection, which alters cell proliferation and apoptosis [1]. Pigmented Bowen's disease is an uncommon form of squamous cell carcinoma in-situ characterized by pigmented lesions that can clinically mimic superficial spreading melanoma, pigmented basal cell carcinoma, melanocytic nevus, Bowenoid papulosis, and seborrheic keratosis [2,3,4].

Key words: Bowen's disease; AIDS; Melanoma; squamous cell carcinoma in-situ

Case synopsis

A 42-year-old, Fitzpatrick skin type V, circumcised Middle Eastern male with AIDS (CD4 count =30, viral load=142 copies/ml) was evaluated for a three-year history of two gradually enlarging lesions of the penis and scrotum. The lesions were asymptomatic and the patient did not consider seeking medical attention until he was admitted to the hospital with Candida esophagitis. The admitting physician noticed both lesions while performing a full physical exam. He is not a smoker. There was no history of exposure to radiation, tar or arsenic. He was not complaint to his antiretroviral treatment and denied any personal or family history of skin cancer. On physical examination of the left half of scrotum, there was a dark brown plaque with irregular borders and a few whitish speckles at the center measuring approximately 2 cm in the widest diameter (Fig. 1). On the ventral aspect of the penis, there was a brown flat-topped plaque with few white speckles at one edge measuring approximately 1.5 cm in the widest diameter (Fig. 2).

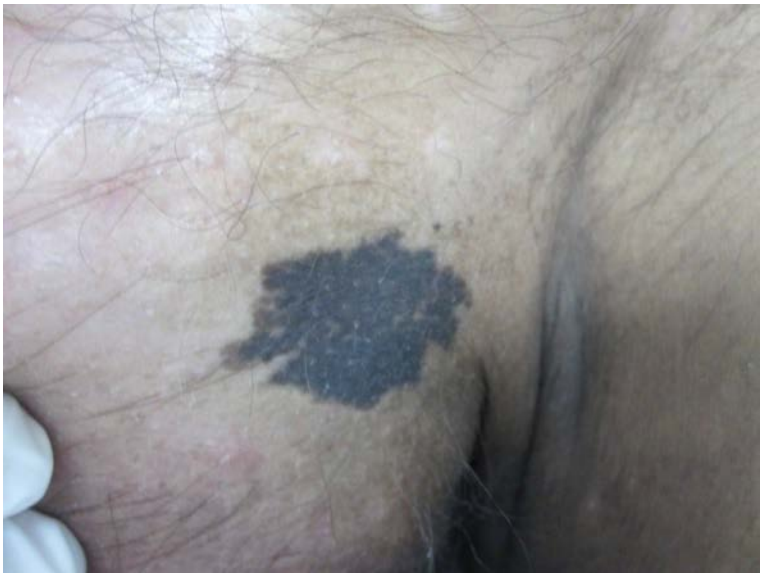

Figure 1. Penile skin showing brown non-scaly plaque with areas of white speckles and irregular borders.

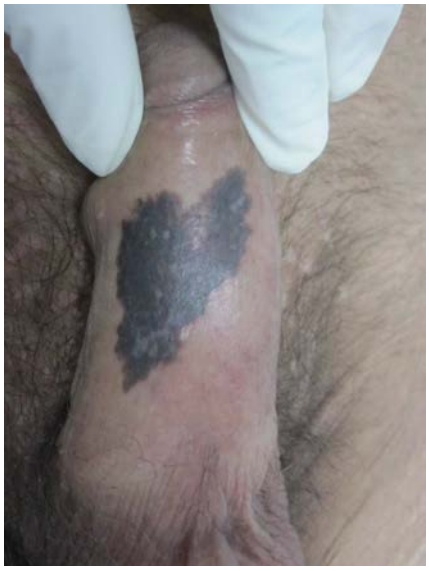

Figure 2. Scrotal skin showing dark brown flat non-scaly plaque with irregular borders.

The clinical differential diagnosis included pigmented basal cell carcinoma, melanocytic nevi, superficial spreading melanoma and fungal infection. Histopathology of both lesions showed epidermal thickening with complete loss of polarity and atypical/dysplastic keratinocytes, occasional atypical mitotic figures, many dyskeratotic cells and increased melanin pigment throughout the epidermis. Scattered melanophages were present in the superficial dermis (Figs 3-5). The dysplastic keratinocytes were negative for Melan-A (a melanocytic differentiation antigen) and positive for Ki-67 (a cellular proliferation marker) by immunohistochemistry (Figs 4-5). HPV studies were not available at our center.

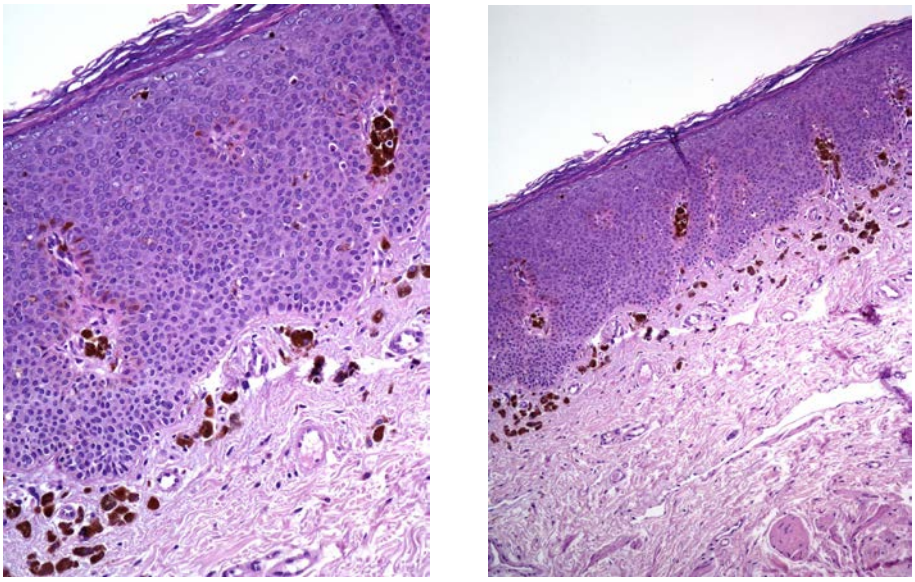

Figure 3. Penile skin tissue exhibiting a full thickness dysplasia with mild to moderate nuclear pleomorphism , multifocal absence of the granular layer, scattered mitosis and many melanophages. (hematoxylin-eosin, 10 X)

Figure 4. Scrotal skin tissue showing similar features as penile lesion. (hematoxylin-eosin, 4 X)

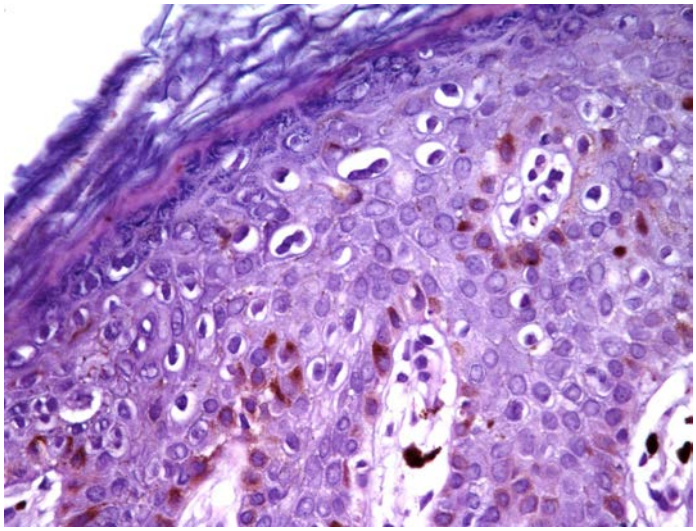

Figure 5. Scrotal skin tissue showing melanin pigmentation of keratinocytes (hematoxylin- eosin, 40 X)

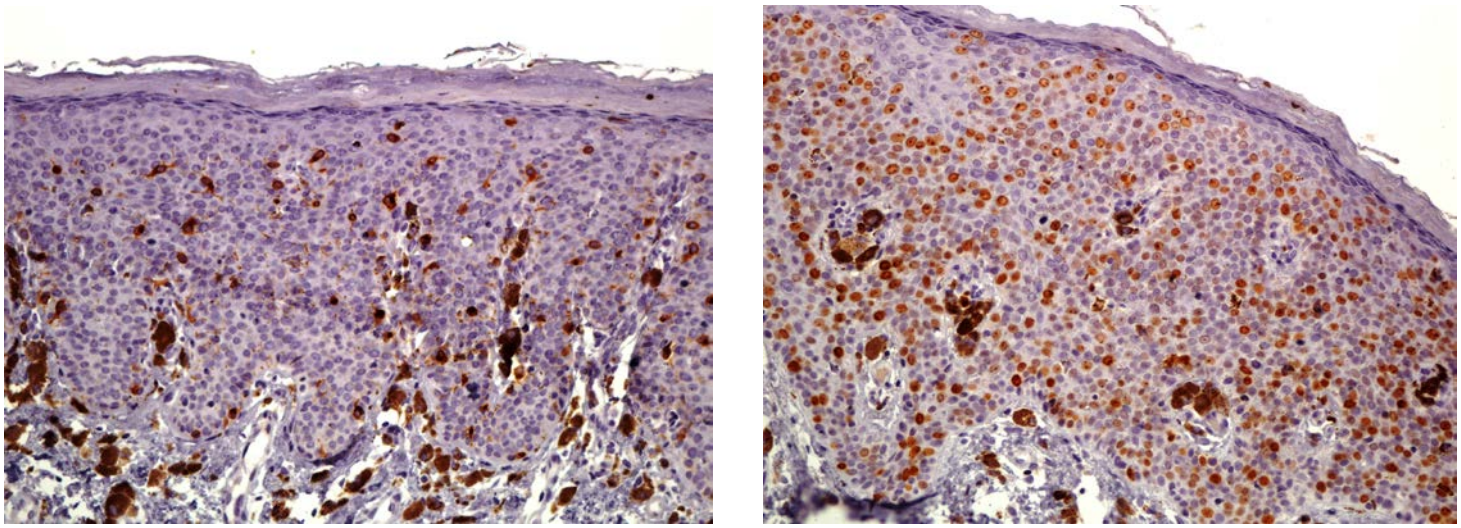

Figure 6. Melan-A immunoperoxidase stain: Positive immunoreactivity of normal melanocytes at the epidermal-dermal junction. The dysplastic mucosal keratinocytes are negative. Pigmented melanophages are seen in the superficial dermis. (10 X)

Figure 7. Ki-67 immunoperoxidase stain: Very high proliferation index of dysplastic keratinocytes involving the entire epidermal thickness. (10 X)

Both lesions were treated with imiquimod 5% cream 5 days per week for 10 weeks. The response to imiquimod 5% cream could not be assessed because of the pigmented nature of the lesions and the patient refusal of a repeated biopsy for response assessment. Complete excisions of both lesions were performed. Histopathological examination of the excised lesions showed residual pigmented Bowen's disease and free margins were confirmed. One-year follow-up showed no recurrence.

Discussion

Pigmented Bowen's disease is an uncommon presentation of squamous cell carcinoma in-situ. In one study pigmented Bowen's presented 7 % of the squamous cell carcinoma in- situ cases. Clinically the lesion usually present as a sharply demarcated, flat sometimes ulcerated pigmented plaque. Pigmented Bowen's disease can clinically mimic several skin lesions, including superficial spreading melanoma, Bowenoid papulosis, pigmented basal cell carcinoma, melanocytic nevus and seborrheic keratosis [2,3,4].

The solitary presence of both lesions in each area involved, the size and the full thickness atypia present on histopathology, helped in excluding Bowenoid papulosis [5].

Oncogenic human papillomaviruses (mainly HPV 16, 18, 31 and 33) are implicated in many cases of anogenital squamous cell carcinoma, particularly in immunocompromised patients with HIV [1]. It was found that HIV-1 Tat protein enhances the replicative potential of cells infected with HPV 16 and increases the expression of the E6 and E7 oncogenes [6]. To date, there are no standardized dermatoscopic features for pigmented Bowen's disease; however atypical vascular structures, homogeneous areas of grayish-brown dots arranged in a linear pattern and patchy globules are common findings [7,8]. Histologically pigmented Bowen's disease shows acanthosis with full thickness epidermal dysplasia, abnormal keratinization, abundance of melanin rich cells and mitotic figures. There is lack of dermal invasion. The deposition of pigment is explained by the increased uptake of melanin by the differentiated keratinocytes. The melanin is produced by enlarged melanocytes within the tumor [9].

Treatment options for HIV-infected patients with Bowen's disease include 5- Fluorouracil 5% cream, imiquimod 5% cream, radiation or excision [10,11,12]. Excision margins within few millimeters of the tumor edge provides oncological control with a 4 % recurrence rate in invasive penile squamous cell carcinomas stages T1-T3 [14]. Mohs micrographic surgery is indicated for genital Bowen's disease because of its tissue sparing properties and low recurrence rate [13]. In a retrospective study published by Shindel et al, 1 of 7 patients with SCCIS of the penis developed recurrence following Mohs micrographic surgery at a mean follow up of 58+/- 63 months [14].

Although imiquimod 5 % cream was found to be effective for treatment of genital Bowen's disease lesions, the lack of response to in our patient could be related to the reduced dendritic cell activity and the drop in the levels of circulating INF inhibitors caused by active the HIV infection. Both of which are important for imiquimod's antiviral and antitumor activity [16,17,18,19].

Conclusion

The diagnosis of pigmented Bowen’s disease should be considered in the differential diagnosis of pigmented lesions in non-sun exposed skin and malignant melanoma needs to be excluded.

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