

Dramatic Clearance of HIV-Associated Bowenoid Papulosis Using Combined Oral Acitretin and Topical 5% Imiquimod

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Bowenoid papulosis (BP) is an uncommon squamous intraepithelial neoplasia, which manifests as an eruption of flesh colored or hyperpigmented verrucous papules that may become confluent plaques, involving the genitalia and anogenital regions.

A 39-year-old Chinese gentleman with a past medical history of Human Immunodeficiency Virus (HIV) infection on antiretroviral therapy, presented to our center with a one-year history of biopsy proven BP. Physical examination revealed widespread disease with multiple hyperpigmented verrucous papules, patches and confluent plaques over the perianal area (Figure 1).

Given the extent of his disease, conventional therapy with liquid nitrogen and topical 5% imiquimod would necessitate multiple treatments; the patient was commenced on oral acitretin 25 mg daily (0.38 mg/kg/day) in combination with topical 5% imiquimod, to be applied every alternate day. His BP regressed after eight weeks of treatment to flattened pigmented patches. No adverse effects were reported. His medication was tapered with continued clinical response to a maintenance regime of oral acitretin 25 mg three times a week and topical 5% imiquimod twice a week. After 6 months of treatment, the lesions had cleared with post-inflammatory depigmentation (Figure 2).

Bowenoid papulosis is associated with infection by oncogenic human papillomaviruses (HPV),¹ which spread by skin-to-skin contact during coitus. BP typically runs an indolent course with the risk of malignancy reported to be at 1%.² Histologically, BP is characterised by acanthosis with full-thickness dysplasia, making it challenging to distinguish from other variants of squamous carcinoma in-situ. Hence, the diagnosis is clinched by establishing a clinicopathological correlation.

The treatment for BP is conservative as it usually regresses spontaneously. For persistent, extensive or symptomatic lesions, therapy is similar to the options for condylomata acuminata, which is directed at local destruction via keratolysis

FIGURE 1. Hyperpigmented, condylomatous papules, patches, and plaques resembling seborrheic warts over the perianal region, prior to commencement of treatment.



FIGURE 2. After 6 months of treatment, lesions have cleared with post-inflammatory depigmentation.



(eg, podophyllotoxin), immunomodulation (eg, topical 5% imiquimod and 5% 5-fluorouracil), cryotherapy ablation, photodynamic therapy (PDT) or other surgical methods (eg, laser or electrocurettage).

BP's link to HIV infection is two-fold; patients with HIV infection are at higher risk for developing BP from exposure during sexual contact; there is a greater risk of malignant transformation of BP due to their concurrent immunocompromised state. In light of the latter, BP in HIV patients need to be managed with urgency through regular post-treatment checks monitor for disease recurrence. Our patient's CD4 count at therapy initiation was 178 cells/mm³ (reference interval 500 – 1000 cells/mm³) indicating immunodeficiency.

Therapeutic options for our patient were limited as he was not keen for surgery. Sole application of topical therapies, though proven to be effective in BP in HIV patients,^{3,4} may cause discomfort owing to the development of ulcerations at the sensitive anatomical area of affliction. Moreover, an immunosuppressed constitution may engender treatment failure when imiquimod⁵ is used to achieve immunomodulation. PDT is a viable option

but can be painful and was left as final line treatment. As such, a novel combination of oral acitretin 25 mg daily and topical 5% imiquimod every alternate day was commenced. Resolution of BP lesions can take up to 18 months⁶ in patients with HIV.

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Acitretin is a second-generation anti-psoriatic retinoid that induces keratinocyte differentiation and leads to the retardation of cellular turnover. It is via this mechanism that we postulate the combination regime was able to achieve good clinical results expediently. Review at 7 months post-treatment revealed sustained remission of disease.

In conclusion, we would like to underscore the association of HIV with BP and the need to treat it to prevent malignant transformation, which is potentiated in view of the former. We would also like to highlight the effectiveness of acitretin used with topical imiquimod in the treatment of HIV-associated BP.

Disclosure

The authors have not declared any relevant conflicts.

References

1. Cardoso JC, Calonje E. Cutaneous manifestations of human papillomaviruses: a review. *Acta Dermatovenerol Alp Panonica Adriat.* 2011; 20(3):145-54.
2. Von Krogh G, Horenblas S. Diagnosis and clinical presentation of premalignant lesions of the penis. *Scand J Urol Nephrol. Suppl* 2000; (205):201-14.
3. JM Ricart, J Cordoba, M Hernandez, I Esplugues. Extensive genital bowenoid papulosis responding to imiquimod. *J Eur Acad Dermatol Venereol.* 2007; 21(1):113-5.
4. Redondo P, Lloret P. Topical imiquimod for bowenoid papulosis in an HIV-positive woman. *Acta Derm Venereol.* 2002; 82(3):212-3.
5. Van der Meiden W.I., Van,t Hof A.T. One-year experience with imiquimod cream in the treatment of large or widespread ano-genital warts in patients seen at the Erasmus MC STD clinic. Abstracts of the 12th Congress of the European Academy of Dermatology and Venerology, 15-18 October 2003, Barcelona, Spain. *J Eur Acad Dermatol Venereol.* 17; Nov 2003, 4158.
6. James C. Godfrey, Mary C. Vaughan and Judith V. Williams. Successful treatment of bowenoid papulosis in a 9-Year-Old girl with vertically acquired human immunodeficiency virus. *Pediatrics.* 2003; 112:e73

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