

## Topical Imiquimod for Bowenoid Papulosis in an HIV-positive Woman

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Sir,

Bowenoid papulosis consists clinically of multiple verrucoid papules, usually situated in the anogenital region of young men and women. Histologically, it is an *in situ* squamous cell carcinoma (1) and is most commonly associated with high-risk oncogenic genotypes of human papillomavirus (HPV) types 16, 18, 33 and 39 (2, 3). Bowenoid papulosis usually follows a benign course and may spontaneously resolve in immunocompetent patients. In older women and immunocompromised patients it generally persists and may progress to an invasive squamous cell carcinoma. Conventional treatments include local excision, electrocoagulation, electrodesiccation, cryosurgery, laser removal and topical 5-fluorouracil. Imiquimod, an imidazoquinoline amine, is an immune response modifier recently approved for the topical treatment of external genitalia and perianal warts (4). Imiquimod exhibits antiviral and antitumour effects *in vivo* through induction of cytokines and enhancement of cell-mediated cytolytic antiviral activity. In the following, topical imiquimod was used in a human immunodeficiency virus (HIV) infected woman with perianal and perivulvar bowenoid papulosis.

### CASE REPORT

A 36-year-old woman presented with perianal and genital skin lesions of 6 years' duration. The patient's HIV-1 infection had been diagnosed approximately 10 years earlier, and had been well controlled during most of that time with antiviral therapy. The patient's viral load and CD4 levels were 50 copies/ml and 750/mm<sup>3</sup>, respectively. She had received previous treatment with cryotherapy and local excision with electrocoagulation, with relapses. Physical examination revealed perianal and perivulvar red plaques covered with warty papules (Fig. 1A). Histological specimens confirmed the clinical diagnosis of bowenoid papulosis. Topical treatment with imiquimod 5% cream was proposed. The patient applied the cream at bedtime on the affected areas. Tolerance was good, with initial irritation and burning during the first 2 weeks. After one month of treatment, spectacular improvement was achieved, vulvar affection disappeared and perianal lesion accomplished remarkable clinical remission (Fig. 1B). The patient refused a further biopsy to confirm the absence of histological lesions. At that moment, the patient discontinued treatment. Two



Fig. 1. Confluent plaques of bowenoid papulosis. Perianal involvement with pigmented area and labia majora effect before (A) and after one month treatment with imiquimod (B). Labia majora affectation disappeared and perianal lesion decreased in size significantly.

months later, she was examined because of fever of unknown origin, and improvement persisted despite discontinuation of treatment.

## DISCUSSION

The exact mechanism of imiquimod's antiviral activity is unknown; however, its effects are likely to be related to its immunomodulating properties. Imiquimod stimulates the innate immune response through induction of cytokine, and the cellular arm of acquired immunity through induction of interferon-alpha (IFN- $\alpha$ ), IFN- $\gamma$  and interleukin-12. By inducing cells, including keratinocytes, to produce cytokines, imiquimod may cure genital warts (5). Furthermore, imiquimod has recently been shown to enhance the functional maturation of Langerhans' cells, as well as their migration to regional lymph nodes (6, 7). Functional maturation and migration of Langerhans' cells are necessary for antigen presentation in the development of adoptive immune responses. When given orally to mice, imiquimod has antitumour activity and has been shown to inhibit the growth of MC-26 colon carcinoma, Lewis lung carcinoma, RIF-1 sarcoma and B16-F10 melanoma (8). In patients, oral imiquimod treatment was associated with an increase of IFN- $\alpha$  (9). Several authors have used topical imiquimod to treat basal cell carcinoma (10), Bowen disease (11), viral vulvar intraepithelial neoplasia (12) and cutaneous melanoma metastasis (13).

HIV causes disease by infecting lymphocytes and progressively destroying critical regulatory and effector cells of the immune system, leaving patients vulnerable to bacterial, fungal and viral infections. Recently, Pehoushek & Smith (14) treated an HIV-1-positive man affected by a perianal squamous cell carcinoma with topical imiquimod and topical 5% fluorouracil therapy. Previous topical application of imiquimod has also induced clearing of chronic giant molluscum contagiosum in a patient with HIV-1 disease (15).

In short, treatment with imiquimod seems to be effective in controlling bowenoid papulosis in immunocompromised patients. Controlled trials with a long-term clinical and histopathological follow-up for HPV in patients infected with HIV are needed.

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