

Bowenoid Papulosis in a Patient with AIDS Treated with Imiquimod: Case Report

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SUMMARY A 53-year-old male patient with acquired immunodeficiency syndrome (AIDS) was treated with topical immunomodulator imiquimod for bowenoid papular. Clinically the lesions presented as condilomatous and papulous changes with color varying from skin color to grayish. The lesions were located in the glans and in the dorsum of the penis. Clinical diagnosis was confirmed by histopathological examination, and the polymerase chain reaction (PCR) demonstrated the presence of human papilloma virus (HPV) 16. It was decided to apply a topical treatment with imiquimod 5% cream three times a week for 16 weeks. Almost complete regression was obtained; the residual lesions were treated with a combined chemical cauterization by using 50% trichloroacetic acid followed by 25% podophylin. Although it is not a definitive treatment, the use of topical immunomodulator is one more therapeutic option in the selected HPV cases.

KEY WORDS *adjuvants, immunologic; Bowen's disease; condylomata acuminata; human papilloma virus; penile neoplasms*

INTRODUCTION

Human papilloma virus (HPV) has been associated with several types of benign and malignant lesions of both skin and mucous membranes. In the genital area, HPV infection may cause the development of condyloma acuminatum (genital wart), bowenoid papulosis, or squamous cell carcinoma (SCC) (1). In men, some types of HPV have been implied as possible agents that trigger the induction of dysplasia, anal and penile carcinoma. Most cases of condylomata acuminata in the male anogenital tract contain HPV types 6 and 11, of "low malignancy risk", while pre-malignant lesions or inva-

sive tumors frequently contain HPV types 16 and 18, which are of "high malignancy risk" (2).

Bowenoid papulosis presents, in most cases, with pigmented papules in the genitalia. It has been associated with HPV infection involving virus types 16, 18, 31-34, 39, 42, 48, and 51-54, with HPV 16 being more common than other types. Histopathologically, it produces an SCC *in situ* picture, with viral cytopathic alterations. Its evolution is normally benign, but may progress to invasive SCC, mainly in immunodepressed patients, who also have a dif-

ficult response to conventional treatments and greater number of recurrences (3-7).

Imiquimod is an immunomodulator with antiviral and indirect antitumor activities. It acts by cytokine induction, primarily interferon- α , resulting in an increase of immune response through cell mediation (6,8). In this way, besides destroying visible lesions, it combats the latent infection, reducing the number of recurrences (7).

CASE REPORT

A 53-year-old black man, previously treated for syphilis and known to be HIV-positive for seven years, presented with asymptomatic genital lesions that developed over 18 months. He had systemic arterial hypertension controlled with atenolol, asymptomatic hepatitis C, and was hospitalized for dysphagia, fever, and postprandial vomiting. Digestive endoscopy revealed esophagitis caused by herpes simplex virus (HSV), with associated candidiasis. The patient stated that he used illicit drugs (inhaled cocaine) and had had multiple sexual partners of both sexes in the last several years. A dermatological consultation was requested for evaluation of the genital lesions.

At physical examination, the patient presented with a good general condition. A hyperchromic maculopapular lesion was found in the balanopreputial groove (Fig. 1), whereas grayish, flat, confluent papular vegetating lesions were located on the dorsum of the penis and scrotum (Fig. 2). There was also an exulcerated and painful lesion on the glans compatible with ulcer caused by HSV, which improved with parenteral acyclovir administered for the treatment of the esophagitis.

Due to the clinical suspicion of infection with HPV, biopsies of lesions on the glans and dorsum of the penis were performed. Histopathological examination of biopsy material revealed vacuolation of the keratinocytes and nuclear hyperchromasia; acanthosis with papillomatosis, pigmentary incontinence, and melanin in the upper layers of the epidermis; hyperplasia of the keratinocytes at the base of the lesion with disordered epithelial architecture, nuclear piling up, and mild atypia. Such histological alterations were compatible with bowenoid papulosis. The polymerase chain reaction to detect the



Figure 1. Bowenoid lesions in the balanopreputial groove.



Figure 2. Lesions on the dorsum of the penis and scrotum.

presence of HPV types 6-11 and 16-18 revealed HPV 16 in both lesions.

The immunological profile, performed only three months after the first dermatological consultation (when the patient had already been using regular anti-retroviral therapy), showed a viral load of less than 80 copies/mL and a CD4 T-lymphocyte count of 198 cells/mm³.

The patient was instructed to apply imiquimod 5% cream on the lesions three times a week, leaving it over night for eight hours. He completed 16

weeks of treatment without any side effect. After 12 weeks of therapy, there was already a complete regression of the lesion in the balanopreputial area and partial regression of the lesions on the penis. At the end of the 16 weeks, only about six papular residual lesions remained on the dorsum of the penis (Fig. 3 and 4). The treatment was complemented with combined chemical cauterization by use of 50% trichloroacetic acid, followed by application of 25% podophylin every three weeks. The patient also applied imiquimod 5% cream on lesions of molluscum contagiosum in the beard area, with com-



Figure 3. Balanopreputial groove after 16 weeks of treatment with imiquimod.



Figure 4. Dorsum of the penis and scrotum after 16 weeks of treatment with imiquimod.

plete regression after four weeks. Antiretroviral treatment was started concomitantly with 600 mg/day of zidovudine, lamivudine 300 mg/day, and nevirapine 400 mg/day.

DISCUSSION

Immunodepressed patients represent a distinct group among patients with HPV infections. They are frequently infected with types of high risk HPV, usually uncommon in immunocompetent patients, and are prone to more aggressive forms of disease, with greater incidence of oncogenic transformation (2). HIV infection can also promote the persistence or reactivation of the HPV in the genital tract, favoring its progression to cancer besides facilitating the primary HPV infection (1). Therefore, as in our patient, immunodepressed patients with high risk HPV lesions that already show intraepithelial neoplastic changes should have their treatment optimized to avoid the development of invasive disease.

There are several treatment modalities for the lesions caused by HPV, including topical application of chemotherapeutic agents, such as podophilotoxin, 5-fluouracil 5%, and etretinate; chemical cauterization with 30% or 50% trichloroacetic acid and 25% podophylin; and surgical extirpation by electrocoagulation, cryosurgery, surgical removal or Mohs' micrographic surgery (6). However, these modalities only destroy the lesion, whereas the virus remains in latency in the surrounding cells, causing frequent recurrences. Immunomodulatory treatment is the only that can destroy the virus, imiquimod 5% cream being one of the current therapeutic options. Recent reports of its use in the treatment of mollusca contagiosa, viral cutaneous infections associated with HIV, and recalcitrant facial warts are promising (9-11).

However, traditionally effective treatments for HPV infections in immunocompetent patients are frequently less effective in immunocompromized individuals. A study by Gilson *et al* (12) demonstrated that the cream with imiquimod was not significantly better than placebo in obtaining a complete response in HIV-positive patients, but it caused a significant decrease in the area attacked by the warts, allowing the combined treatment with other medications. The same results were obtained in our patient, with almost complete regression of the lesions

after the use of cream with imiquimod, making the end of the treatment with chemical cauterization viable. Godfrey *et al* (13), on the other hand, reported on a case of a nine-year-old HIV-positive girl with bowenoid papulosis, who showed little response to the use of the cream applied every other day for two months. A monthly chemical cauterization with 25% podophylin was then started with complete regression of the lesions after one year (13).

Our patient's improvement could be questioned regarding its relationship with the beginning of the antiretroviral therapy, which coincided with the beginning of the use of the imiquimod 5% cream. However, after three months of the specific treatment, the patient still had a CD4 count below 200 cells/mm³. In any way, one cannot avoid considering that a global improvement of the patient's immunological status could have contributed to the therapeutic success.

CONCLUSION

The imiquimod 5% cream was an excellent option in the treatment of the lesions of bowenoid papulosis in our patient with AIDS regardless of his low CD4 count, allowing complementation of the treatment with chemical cauterization. The regression of the lesions of mollusca contagiosa on the patient's face was also obtained. The treatment was practical (could be performed at home) and there were no side effects.

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