Treatment of Recalcitrant Herpes Simplex Virus With Topical Imiquimod

Dawn Hirokawa, MD, MPH; Adam Woldow, MD; Susanne Nussen Lee, MD; Faramarz Samie, MD, PhD

Herpes simplex virus (HSV) is a common, easily transmissible virus. There is growing awareness of acyclovir-resistant HSV, particularly among immunocompromised patients, which may be due to protracted treatments with guanosine analogues. Given the considerable morbidity associated with other classes of antiherpetic medications such as foscarnet (renal impairment, seizures) and cidofovir (renal impairment, neutropenia), imiquimod, a toll-like receptor agonist that enhances the innate immunologic responses against the virus, has been utilized in treating acyclovir-resistant HSV. We present a case of a human immunodeficiency virus (HIV)–positive patient who was successfully treated with topical imiquimod after treatment failures with other oral antivirals.

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Herpes simplex virus (HSV) is a common, easily transmissible virus. Infections with both HSV type 1 and HSV type 2 (HHV-2) are causes of considerable morbidity. Although most herpetic lesions are easily recognized clinically as vesicles, pustules, or ulcers, HSV infections in the immunocompromised setting may have an atypical presentation, such as hypertrophic or verrucous plaques.[1,2] There is growing awareness of acyclovir-resistant HSV, particularly among immunocompromised patients, which may be due to protracted treatments with guanosine analogues.[3] Given the considerable morbidity associated with other classes of antiherpetic medications such as foscarnet (renal impairment, seizures) and cidofovir (renal impairment, neutropenia), imiquimod, a toll-like receptor agonist that enhances the innate immunologic responses against the virus, has been utilized in treating acyclovir-resistant HSV.[3-6]

We present a case of a human immunodeficiency virus (HIV)–positive patient who was successfully treated with topical imiquimod after treatment failures with other oral antivirals.

Case Report

Our patient is a 41-year-old HIV-positive man with recurrent genital HSV infection of 17 years' duration. Upon presentation, the patient was taking highly active antiretroviral therapy with a CD4 count of

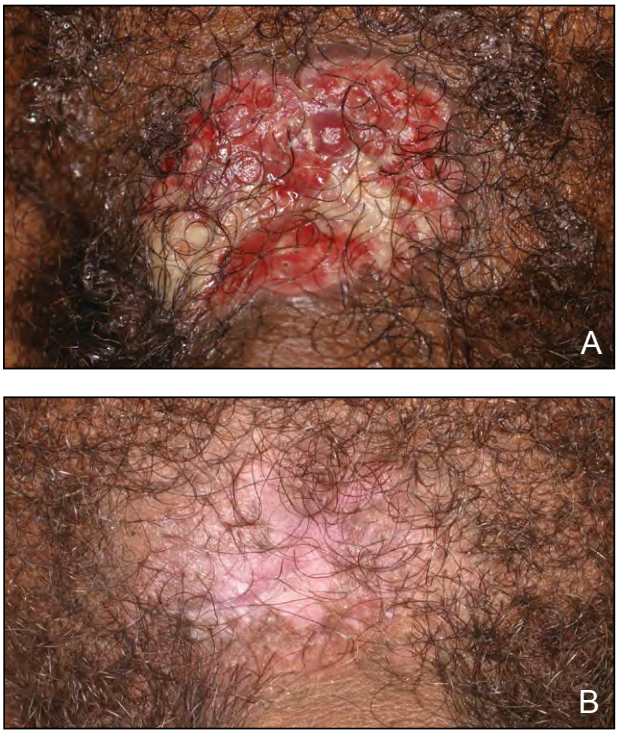

Figure 1. Persistent ulcerovegetative plaque at the base of the penis in a human immunodeficiency virus–positive patient with a history of genital herpes simplex virus on chronic suppressive therapy before (A) and after imiquimod therapy with complete resolution of the lesion (B).

Drs. Hirokawa, Woldow, and Samie are from the Department of Dermatology, Jefferson University Hospital, Philadelphia, Pennsylvania. Dr. Lee is from Dermpath Diagnostics, Newtown Square, Pennsylvania.

The authors report no conflict of interest.

Correspondence: Dawn Hirokawa, MD, MPH, 833 Chestnut St, Ste 740, Philadelphia, PA 19107 (dawn.hirokawa@hotmail.com).

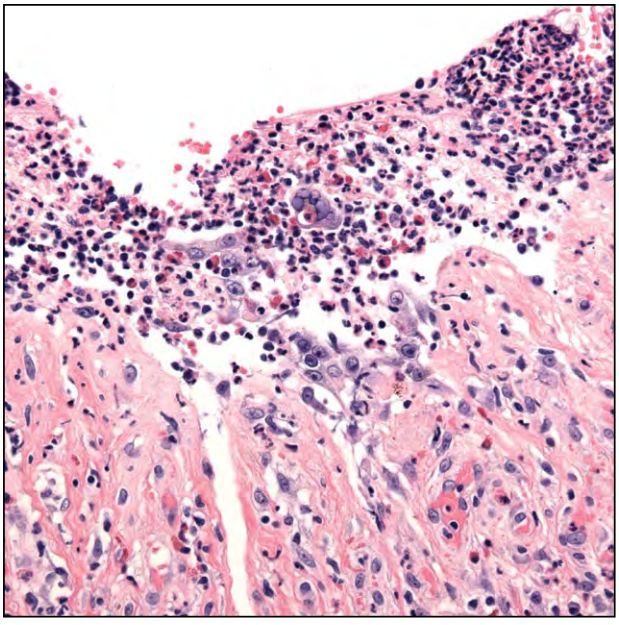

Figure 2. A light micrograph revealed multinucleated giant cells with nuclear molding and margination of chromatin underneath an ulcer (H&E, original magnification ×400).

approximately 260 cells/mm^3 and an undetectable viral load. He had been treated for 4 years with valacyclovir hydrochloride (1 g orally daily) with the intention of suppressing HSV outbreaks. His regimen had successfully maintained herpetic eruptions to less than 4 per year. He presented to our office with a growing ulcerovegetative plaque at the base of the penis of 4 months' duration (Figure 1A). Prior to presentation, he was treated with a valacyclovir pulse (3 g daily) as well as doxycycline and amoxicillin.

A punch biopsy demonstrated an ulcer with multinucleated giant cells and features of nuclear molding and margination of chromatin; these results were consistent with an active HSV infection (Figure 2). Given the persistence of the lesion despite high-dose valacyclovir, the patient was treated with imiquimod cream 5% 3 times weekly for 2 months. The patient was followed monthly. At the first visit, a marked reduction in the size of the ulcer was noted, while no adverse effects were encountered. At 2 months, imiquimod was discontinued and the patient was advised to apply petroleum jelly to the area twice daily. At 3 months, the involved area had completely reepithelialized and no clinical evidence of active HSV infection was evident (Figure 1B).

Comment

We report the successful treatment of valacyclovir-resistant genital herpes with imiquimod cream 5% applied 3 times weekly for 8 weeks in an HIV-positive patient.

Gilbert et al[5] are credited with the pilot case report of treating guanosine analogue–resistant penile HHV-2 infection in an HIV-infected patient with topical imiquimod. In their study, imiquimod was used for 1 week and no recurrence was noted at 1 month.[5] Since then, multiple other encouraging case reports and case series have been published; however, it should be noted that these studies vary considerably in the length of therapy that the patients received. Martinez et al[6] presented 2 immunocompromised patients—one with genital HHV-2 and the other with HSV type 1 lesions of the mouth, lips, and fingers—who both showed clinical resolution of lesions after 2 to 4 weeks of therapy, with no recurrence at 10- and 12-month follow-up visits, respectively. Danielsen et al[7] presented an HIV-infected patient with HSV lesions that resolved within 10 weeks of imiquimod 3 times weekly combined with oral antiviral therapy. Finally, Yudin and Kaul[1] more recently reported a case of hypertrophic HHV-2 lesions in an HIV-infected female who showed clinical response to topical imiquimod therapy within 8 weeks.

Conclusion

The positive outcome observed in our patient supports topical imiquimod as a promising treatment of acyclovir-resistant HSV lesions. Additional studies should be performed to further qualify and quantify this therapy.

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