Topical Imiquimod Therapy for Chronic Giant Molluscum Contagiosum in a Patient With Advanced Human Immunodeficiency Virus 1 Disease

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF A CASE

A 32-year-old African American woman with human immunodeficiency virus 1 (HIV-1) and a 3-year history of extensive facial molluscum contagiosum (MCV) presented to the dermatology clinic for treatment. The patient had been treated with multiple therapies, including liquid nitrogen, topical 0.05% liquid tretinoin, and 0.5% topical podofilox, with no improvement and some secondary irritation to the latter 2 therapies.

At her initial appointment, she was taking nelfinavir mesylate (Viracept), 750 mg 3 times daily; stavudine (Zerit), 40 mg twice daily; didanosine (Videx), 200 mg twice daily; trimethoprim-sulfamethoxazole (Bactrim DS), 800 mg/160 mg every day; and fluconazole (Diflucan), 100 mg every day. She had been receiving nelfinavir, stavudine, and didanosine for 5 months and trimethoprim-sulfamethoxazole and fluconazole since shortly after her diagnosis 3 years earlier. Her CD4 T-cell count was 0.004 \times 10^9/L (38/mm^3) and the viral load (Roche Amplicor HIV-1 RNA–polymerase chain reaction [RNA-PCR]) was at 2900 RNA copies/mL. This represented an approximately 1.5 log reduction in her initial viral load and had remained relatively stable during the past few months.

On examination, there were papules and large nodules and plaques predominantly on the face. They ranged in size from 3 to 20 mm, with areas of depressed scarring and postinflammatory hyperpigmentation (Figure 1).

THERAPEUTIC CHALLENGE

Our goal was to find a therapy for this severely immunosuppressed patient with disfiguring MCV lesions. Although she had shown a marked decrease in her viral load with multidrug antiviral therapy, her CD4 T-cell count remained low, and she showed no improvement in her MCV lesions.

SOLUTION

The patient was started on imiquimod (Aldara), 5% cream, 25-mg single-use packets. She applied 2.5 packages of the imiquimod cream 3 times per week at bedtime. She left the medication on her face for 6 to 10 hours, washing it off later with mild soap and water. At the 1-month follow-up, most of the lesions showed mild erythema and some superficial erosions with stable but continued postinflammatory hyperpigmentation. All of the lesions had flattened and were reduced in diameter by approximately 25% to 50%. For the second month, she used 2 packages of imiquimod to the residual lesions as previously described. By the end of the second month, the lesions nearly were resolved clinically with stable postinflammatory hyperpigmentation. For the third and last month of therapy, the patient used only 1 packet of the imiquimod to the residual lesions. By the end of the third month, the lesions appeared cleared with minimal erythema, some residual depressed scarring, and residual postinflammatory hyperpigmentation. The patient was given 4% hydroquinone cream to be applied daily for the hyperpigmentation. The hyperpigmentation showed progressive improvement during the next few months. Following her last month of therapy, her CD4 T-cell count was 0.007 \times 10^9/L (70/mm^3) and the viral load was at 4000 RNA copies/mL.

The patient was seen 5 months after therapy, with no evidence of recurrent lesions (Figure 2). Her CD4 T-cell count was 0.006 \times 10^9/L (60/mm^3) and the viral load was at 3600 RNA copies/mL.

COMMENT

Molluscum contagiosum virus is a large double-stranded DNA virus that is either considered a member of the Orthopoxvirus genus of the family Poxviridae or an unclassified poxvirus. It has a worldwide distribution, and, with the eradication of smallpox (variola virus), MCV is the most common pox viral pathogen for humans.1,7 Lesions of MCV occur in skin, with only rare reports of mucous membrane involvement.1,3 The MCV in-
Infections occur in young children, sexually active adults, and in some immunosuppressed patient populations. Although widespread lesions do occur in patients with HIV-1, head and neck lesions are most common, followed by genital involvement. In addition to the typical umbilicated papules, patients with HIV-1 may also present with verrucous, warty papules of MCV that may become giant lesions greater than 1 cm in diameter. In patients without severe immune suppression, lesions produced by MCV typically regress spontaneously, usually within months. However, with persistent immunosuppression associated with HIV-1 infection, MCV lesions may be persistent and deforming. After beginning multidrug antiviral therapy, including protease inhibitors, some patients with HIV-1 and chronic MCV lesions have shown clearing of their lesions. The dramatic decrease in viral loads seen in some patients following these regimens, with or without increases in peripheral CD4+ T-cell counts, may potentiate the patient’s immune response to MCV. However, although this patient did have a marked decrease in her viral load with multidrug therapy, she had had no clearing of her MCV during a 5-month period.

The MCV genomes encode a conserved domain of epidermal growth factor–like (EGF) proteins. It is these EGF proteins that vary between MCV subtypes. Patients with HIV-1 have a disproportionate percentage of MCV due to subtypes other than type 1, which is by far the most prevalent subtype. The variability in EGF proteins in different subtypes, in combination with host-specific factors related to HIV-1 infection and perhaps other concurrent infections, may be a factor in explaining the large verrucous lesions that are seen in some HIV-1–positive patients. A cytokine–helper T-cell 2 (Th2) pattern of immune deregulation is seen with progression of HIV-1–positive disease. This pattern of immune deregulation may play a role in decreased resistance to infections in patients with HIV-1, but especially in the decreased ability of these patients to fight intracellular infections.

In the United States, imiquimod, 5% cream (Alldara), is available for treatment of external genital and perianal warts. Imiquimod has no direct antiviral effects; however, it can induce a number of proinflammatory cytokines that may potentiate immune responses. Human epidermal keratinocytes can produce increased levels of interleukin 6 (IL-6), IL-8, interferon alpha (IFN-α), and tumor necrosis factor α (TNF-α) after stimulation with imiquimod. Although fibroblasts appear to show a less pronounced response to imiquimod, with less elevation of IL-8 and TNF-α, Langerhans cells and macrophages are major contributors to the increased cytokines seen locally with topical imiquimod through their production of IFN-α and TNF-α.

The IFN-α may potentiate cellular responses against viruses through a number of different mechanisms. Not only does IFN-α have a direct anti-inflammatory effect, IFN-α also increases the frequency of IFN-γ producing CD4+ T cells and can induce a Th1 cytokine profile in some T-cell clones, promoting IgG2a synthesis and inhibiting IgE. The IFN-α also induces the expression of major histocompatibility complex (MHC) class I cell surface antigens that are necessary for cytotoxic CD8+ T-cell responses. It antagonizes the suppressive effects of IL-4 on IFN-γ production and inhibits antigen-induced proliferation and cytokine production by Th2 clones. Through the induction of IFN-γ, IFN-α also potentiates natural killer cell cytotoxicity, macrophage activation, and MHC class II expression. The TNF-α may potentiate the clearing of MCV lesions locally through its direct cyto-
totoxic effects and by the production of free radicals. The IL-8 and IL-6 are both proinflammatory, and together with the other cytokines they can potentially moderate the down-regulation of immune and inflammatory responses induced by MCV products.

Because MCV does not appear to be capable of developing latency, clearing of lesions is more consistently a reflection of long-term cure than with other viruses, such as herpes simplex virus and human papilloma virus, and even in this severely immunosuppressed patient treatment with imiquimod appears to have resulted in cure.

Because imiquimod potentiates the immunologic and inflammatory responses against MCV, it has the potential to be used not only as a single agent, but also in combination with topical antivirals, such as topical cidofovir, which are active against MCV.

Accepted for publication April 30, 1999.

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REFERENCES


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