

Recalcitrant Molluscum Contagiosum in an HIV-Afflicted Male Treated Successfully with Topical Imiquimod

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GOAL

To discuss molluscum contagiosum in the immunocompromised patient.

OBJECTIVES

1. To describe the clinical appearance of molluscum contagiosum.
2. To identify the relationship of this viral infection to human immunodeficiency virus.
3. To outline therapy for molluscum contagiosum.

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Molluscum contagiosum is a common cutaneous infection complicating the course of patients afflicted with acquired immunodeficiency syndrome. We describe a human immunodeficiency virus-positive patient with a disfiguring molluscum contagiosum infection of the face. Conventional cytoreductive therapies failed in this patient, but imiquimod 5% cream, an immunomodulator, clinically cleared his cutaneous disease.

A variety of cutaneous viral infections are well known to complicate the course of human immunodeficiency virus (HIV) infection. Two of the most common of these are human papilloma virus¹⁻⁵ and molluscum contagiosum.^{1,4,6-8}

Treatments for both, including topical applications (cryotherapy, trichloroacetic acid, cantharone, or podophyllin), intralesional injections (5-fluorouracil, bleomycin, or interferon), or surgical interventions (laser, electrocautery, or blade excision) are generally aimed at up-regulating the host immune response. With the exception of interferon, all of these therapies are cytoreductive, and although demonstrating efficiency in lesion elimination, they fail to address the primary problem: a viral infection.

Imiquimod, or 1-(2-methylpropyl)-1H-imidazo[4,5-c]quinolin-4-amine, is a heterocyclic non-nucleoside amine and a potent stimulator of interferon- α production. In addition, imiquimod has also been shown to induce tumor necrosis factor- α , interleukin-6, and interleukin-8.⁹⁻¹⁵

Activity against the herpes simplex virus,¹⁶⁻¹⁸ cytomegalovirus,¹⁹ and human papilloma virus^{9,10,20} has been shown in animal models by imiquimod through the induction of these cytokines and up-regulation of the cell-mediated immune system. In addition, imiquimod has also been shown in a murine model to have an antitumor effect.²¹

We present the case of a man afflicted with acquired immunodeficiency syndrome (AIDS) compli-

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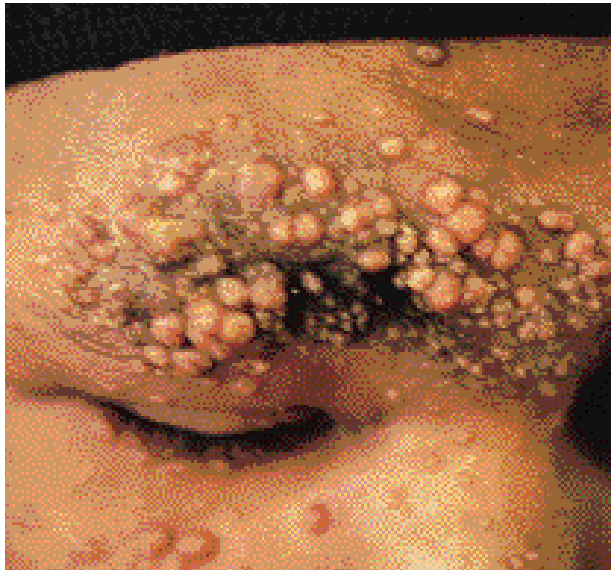


FIGURE 1. Coalescence of multiple lesions of molluscum contagiosum with overlying serous crust and associated periorbital swelling.



FIGURE 2. After 3 weeks of nightly application of imiquimod 5% cream, only a few small molluscum lesions remain with associated postinflammatory hyperpigmentation.

cated by molluscum contagiosum, refractory to treatment with topical cryotherapy and trichloroacetic acid crystalline solution, who responded completely to the topical application of 5% imiquimod cream.

Case Report

A 26-year-old black male presented in February 1998 with a 3-month history of lesions growing and spreading on the face. Physical examination demonstrated several hundred small (<0.5 cm) yellow-to-flesh-colored papules with central umbilication distributed over the right forehead, cheek, and beard area, extending to involve the left eyebrow. Extensive counseling of the patient revealed a history of unprotected intercourse with multiple sexual partners, but no history of intravenous drug abuse. Subsequent serologic analysis by both enzyme-linked immunosorbent assay and Western blot were positive for antibodies to HIV. In March 1998, the patient's total CD4 count was 20 cells/cm², with a white blood cell count of $3.2 \times 10^3/\mu\text{l}$, and HIV viral load of 20,000 copies/ml. Approximately 50 lesions were treated at the time of initial presentation with two cycles of topical cryotherapy. Three weeks later, little change was noted on physical examination, and again approximately 50 lesions were treated with two cycles of cryotherapy. In addition, Retin-A 0.05% cream was prescribed for nightly application to the involved areas, but the patient failed to fill the prescription.

The patient was lost to follow-up for a period of 3.5 months and presented again in July 1998 with significantly more molluscum lesions, despite main-

tenance therapy of nelfinavir, lamivudine, and stavudine, with adjuvant azithromycin and dapsone therapy. Examination of the face and neck demonstrated several thousand molluscum lesions varying in size from less than 1 mm in diameter to over 1.5 cm (Figure 1). Serologic analysis revealed a white blood cell count of $1.9 \times 10^3/\mu\text{l}$, a total CD4 count of $41 \times 10^3/\mu\text{l}$, and an undetectable viral load. The patient was prescribed Keflex, 500 mg orally twice daily, and trichloroacetic acid (TCA) crystalline solution was applied topically to approximately 30 lesions until frost was visualized, and subsequently neutralized with cool water. Four days later, the patient presented with progressive swelling of the right periorbital area to the point of obscuring his vision. Again approximately 30 lesions were treated with TCA solution. In addition, tetracycline 500 mg orally twice daily was prescribed for presumed secondary infection and the patient was referred to the ophthalmology clinic for evaluation. One week later, the patient returned with progression of his molluscum and moderate improvement of the right periorbital swelling. The patient was maintained on the tetracycline, and again approximately 50 lesions were treated with topical TCA solution. In addition, the patient was instructed to apply Domeboro soaks three times daily to the area above the right eye in which a thick plaque of adherent scale and crust had formed. One week after this treatment, adjuvant therapy with topical imiquimod 5% cream (Aldara) was prescribed to be applied nightly to lesions on the head and neck. Three weeks later, after initiating imiquimod therapy, only



FIGURE 3. No lesions of molluscum contagiosum were apparent after 12 weeks of topical 5% imiquimod application. At the time of this photograph, the patient was applying imiquimod only once weekly.

a few small (<0.5 mm diameter) papules remained with residual hyperpigmentation at previously involved sites (Figure 2). The patient was instructed to continue imiquimod cream nightly for the next 2 weeks before tapering to an every-other-night application. He continued this treatment regimen for 1 month before tapering to a once-weekly application. Following more than 1 month of once-weekly applications, there were no lesions of molluscum contagiosum remaining. Only faint residual hyperpigmentation was detectable (Figure 3).

Discussion

Infection with molluscum contagiosum is caused by a large DNA virus of the pox family and presents classically as flesh-to-yellow-colored, dome-topped, papules with a central umbilication. Although approximately 90% of adults have been shown to have circulating antibodies to the virus causing molluscum,²²⁻²⁴ only 1% of HIV-negative patients have been found to have molluscum lesions at any given time.⁴ However, the incidence of molluscum lesions in patients afflicted with AIDS has been reported at 9 to 18%.^{1,4}

In addition to their classic appearance as small umbilicated papules, lesions of molluscum contagiosum in HIV patients may take on an appearance more similar to that of verruca, or may grow into large nodules, termed "giant molluscum contagiosum." Our patient demonstrated many umbilicated lesions ranging in size from a few millimeters to larger papules and nodules.

Infection with molluscum can be difficult to treat successfully with conventional cytoablative techniques in patients with an uncompromised immune system,²⁵ and can be extremely frustrating in the setting of HIV and AIDS. Only one case of successful treatment of chronic giant molluscum contagiosum with topical imiquimod has been reported.²⁶ In addition, Syed *et al*²⁷ have looked at the role of imiquimod as a 1% cream in the treatment of molluscum contagiosum; however, none of the patients included in this study were immunocompromised. Presently, topical imiquimod 5% cream is approved for every-other-night application in the treatment of condyloma acuminata. As a result, we speculate that imiquimod might prove useful in the treatment of molluscum contagiosum in both immunocompetent and immunocompromised patients.

Our patient represents an interesting case of severe and disfiguring cutaneous infection with molluscum contagiosum resistant to conventional topical ablative therapy with liquid nitrogen and TCA crystalline solution. During the time in which the patient's viral load declined to undetectable levels and his CD4 count doubled, he actually experienced a marked increase in the number of molluscum lesions. While clearing of molluscum lesions in HIV patients has been reported after beginning multidrug antiviral therapy, including protease inhibitors,²⁸ our patient's molluscum lesions began to resolve after the initiation of imiquimod therapy. We believe that topical imiquimod cream was instrumental in resolving the patient's molluscum infection and thus may prove to be an important therapeutic agent in the treatment of molluscum infections.

This case underscores the need to explore further the role of topical imiquimod in the treatment of viral infections in normal and immunocompromised patients.

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