Case Report From the Field

Recalcitrant Giant Molluscum Contagiosum in a Patient With Advanced HIV Disease — Eradication of Disease With Paclitaxel

Silver Cree Sisneros, DO

Background

Molluscum contagiosum is a poxvirus skin infection that is self-limited and harmless, usually causing numerous single, umbilicated papules in immunocompetent people. However, a patient with immunodeficiency such as that associated with HIV disease may present with giant, widespread, and chronic lesions, for which no single intervention has been shown to be convincingly effective for curative treatment. Poxviruses utilize the microtubule cytoskeleton within the cytoplasm of eukaryotic cells for movement into the human host cell during the establishment of infection and for facilitating the continued spread of virus infection. Paclitaxel, a chemotherapeutic drug used for treatment of cancer, targets the host cell's microtubule cytoskeleton, resulting in apoptotic programmed cell death and potential disruption of the molluscum contagiosum virus (MCV) lifecycle. This, in turn, potentially leads to decreased viral replication and ultimately decreased burden of disease. We report here an unusual case of giant molluscum contagiosum lesions in a person with AIDS, refractory to conventional therapy but responsive to treatment with paclitaxel. No similar case appears to have been described previously.

Case Presentation

A 25-year-old, HIV-infected, heterosexual man from Mexico presented for an initial consult, reporting a 12-month history of extensive groin and facial lesions. The lesions had worsened despite the initiation of antiretroviral treatment 3 months earlier. At the time antiretroviral therapy was initiated, the patient's CD4+ cell count was 23/μL and plasma HIV RNA level was 32,640 copies/mL. His antiretroviral treatment consisted of atazanavir 300 mg daily, ritonavir 100 mg daily, and fixed-dose combination emtricitabine/tenofovir 200 mg/300 mg daily. Additional medications included fixed-dose combination trimethoprim/sulfamethoxazole 800 mg/160 mg daily and clarithromycin 500 mg twice daily, for prophylaxis of *Pneumocystis* pneumonia and disseminated *Mycobacterium avium* complex disease, respectively. On initial presentation to the clinic, 3 months after starting antiretroviral treatment, his CD4+ cell count was 59/μL and plasma HIV RNA level was 337 copies/mL.

Initial examination revealed large papules, nodules, and plaques, some of which were extensive, ulcerating lesions, predominantly affecting the groin area and bilateral thighs, with perinodular scarring, evidence of bleeding, and hyperpigmentation. The lesions ranged in diameter from 4 mm to 20 mm, were quite tender to palpation, and caused tremendous pain during ambulation (Figure 1). Numerous facial lesions were also present that ranged in diameter from 3 mm to 5 mm. Biopsy specimens from 2 thigh lesions revealed positive pathology for MCV infection, with characteristic histologic features of large, eosinophilic, intracytoplasmic inclusion bodies (Figure 2).

Therapeutic Challenge

In patients with advanced HIV disease, molluscum contagiosum can present as an opportunistic infection and cause widespread, giant lesions that are particularly resistant to therapy.[1,2] Antiretroviral therapy may result in reconstitution of the host's immunity and may assist with resolution or improvement of MCV lesions, but success may be difficult to achieve. Historical treatment approaches, such as excision, topical treatment, and cryotherapy, are often minimally effective for treatment of extensive and severe disease.

Initial treatment with continued antiretroviral therapy in addition to topi-

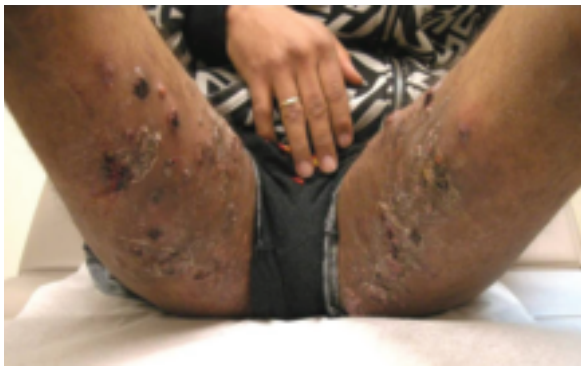

Figure **1**. Lesions in the groin and thigh areas on presentation of a 25-year-old, HIV-seropositive man with molluscum contagiosum virus infection. Extensive, ulcerating lesions were accompanied by perinodular scarring, signs of bleeding, and hyperpigmentation.

Dr Sisneros is a physician with a private practice in internal medicine in Marietta, Ohio.
Send correspondence to Silver Cree Sisneros, DO, at DrSisneros@live.com. Received August 26, 2010; accepted November 23, 2010.

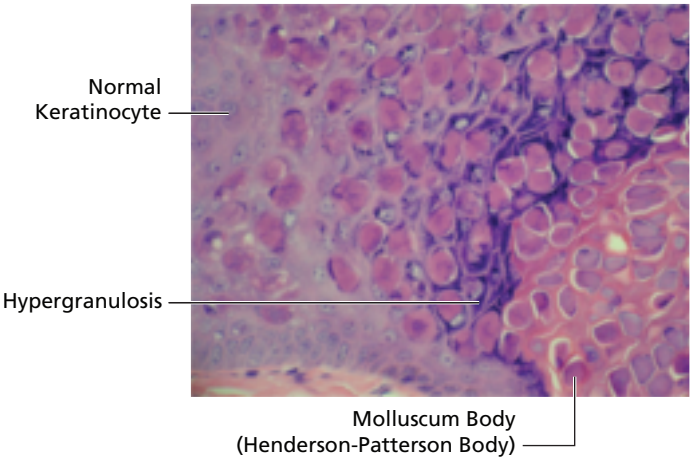

Figure **2**. A section of a biopsy specimen from a thigh lesion revealing histologic features characteristic of infection with molluscum contagiosum virus: large, eosinophilic, intracytoplasmic inclusion bodies (Henderson-Patterson bodies).

cal liquid nitrogen cryotherapy was not associated with any improvement in this patient's lesions. Consideration was given to using topical therapy with imiquimod or cidofovir, but because of the extent of the lesions, further topical treatment was expected to offer no benefit. The decision was made to use intravenous paclitaxel because of the drug's potential ability to alter the life-cycle of the MCV via disruption of the host's cellular microtubule cytoskeleton kinetics.

The patient was administered "off-label" treatment (ie, not approved by the US Food and Drug Administration [FDA]) with intravenous paclitaxel 100 mg/m^2 (108 mg), which is a lower dose than that recommended for the treatment of ovarian, breast, or non–small cell lung cancer. This dose (100 mg/m^2) has been used successfully for the treatment of AIDS-related Kaposi sarcoma. There are no known drug-drug interactions between the patient's antiretroviral drugs and paclitaxel. Paclitaxel was administered intravenously on an outpatient basis every 21 days for 4 cycles of therapy, along with standard pretreatment with famotidine, dexamethasone, and diphenhydramine. Within 15 days of receiving the first injection, the patient experienced rapid and complete resolution of all skin lesions, despite persistent immune suppression (Figure 3).

The patient continued with the 4 scheduled cycles of chemotherapy without any complications and remained free of MCV disease at his last visit, 7 months after the initial consultation (Figure 4). Complete resolution of molluscum contagiosum persisted despite the patient's nonadherence with his antiretroviral therapy and an increase in his plasma HIV RNA level to 10,600 copies/mL. The CD4+ cell count at the last follow-up visit was 145/µL.

Discussion

MCV was first described in the medical literature in 1817[3] and in 1905, molluscum contagiosum was found to be caused by a large DNA poxvirus (reviewed in reference[3]). A major breakthrough came in 1996, when the genome of this tumorigenic virus was sequenced.[4] With the eradication of smallpox, MCV is now the only member of the poxvirus family that currently causes substantial disease in humans.[5]

The study of MCV has been hampered by the inability to grow this virus in the laboratory and the lack of an animal model to study the infection. Vaccinia virus has therefore become the laboratory prototype and most-studied DNA poxvirus, and our knowledge of poxvirus biology is derived largely from studies of this virus.[6] These studies show that poxviruses utilize the microtubule cytoskeleton within the cytoplasm of eukaryotic cells for movement into the human host cell during establishment of infection and for facilitating the continued spread of virus infection.[7-9] Microtubules are protein-based structural components of the host cell cytoskeleton and are involved in maintaining cell shape, intracellular transport, and cell signaling, along with cell movement, reproduction, and division.

Infection with MCV has a worldwide incidence of as much as 8%.[10] Up to 18% of patients with HIV infection have symptomatic molluscum contagiosum, an incidence that increases to 33% for patients with CD4+ cell counts less than 100/µL.[11] In the United States from 1990 to 1999, the estimated number of physician visits for MCV infection was 280,000 per year.[12] Acquisition of the virus follows contact with infected persons or contaminated objects and sources such as towels, sponges, swimming pools, public baths, tattoo instruments, gymnasium equipment, instruments used in beauty salons, and public benches.[3,11,13] The estimated incubation period ranges from 14 days to 6 months.[14] Three distinct disease patterns are observed in 3 different patient populations: children who are generally healthy; adults who are generally healthy; and immunocompromised children and adults.[11]

MCV infection is most common in children who become infected either directly through skin-to-skin contact or indirectly through skin contact with contaminated objects. In adults, MCV infection is considered primarily a sexually transmitted disease. In immunocompetent children and adults, MCV infection is a harmless, self-limited disease that produces a papular erup-

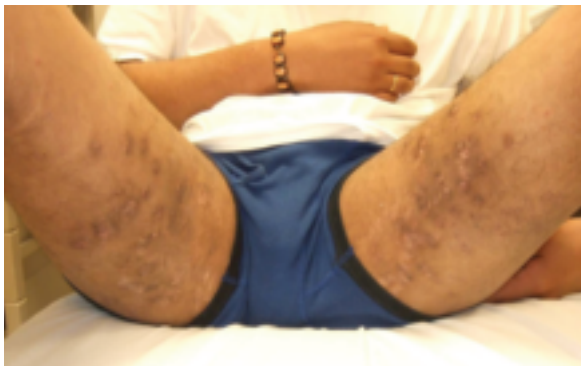

Figure **3**. Photograph of the patient 15 days after the first administration of intravenous paclitaxel, showing resolution of all skin lesions.

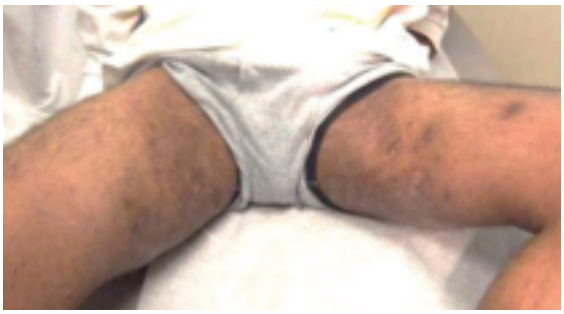

Figure 4. Photograph of the patient 4 months after the first administration of paclitaxel, showing sustained resolution of disease despite the patient's nonadherence to his antiretroviral regimen.

tion of numerous benign, umbilicated tumors.[14] The individual tumors are small, skin colored, firm, smooth, and painless, and they have a central white caseous plug. Individual lesions heal spontaneously and are seldom present longer than 2 months.[11] In patients who are severely immumocompromised or have advanced HIV disease and low CD4+ cell counts, the tumors may become a widespread, chronic opportunistic infection[2,15] characterized by giant, nodular,[1] necrotic,[16] symptomatic, and disfiguring lesions, with secondary infection.[17] In these patients, the impaired cell-mediated immunity can interfere with the resolution of disease and the tumors may be very resistant to therapy.[18] In immunocompromised patients, the differential diagnosis of MCV disease is important to consider; it can include atypical mycobacterial infection, cryptococcosis, pyogenic granuloma, basal cell carcinoma, histoplasmosis, penicillinosis, pneumocystosis, and keratoacanthoma.[19]

Little data exist with regard to the best treatment of MCV infection. No single intervention has been shown to be convincingly effective, and no reliable evidence-based recommendations exist.[14]

In healthy adults and children, treatment is not necessary for recovery, and awaiting spontaneous resolution is a potential management strategy. Treatment, when used, is intended to hasten this process. Three broad categories of treatment options have been used historically for MCV disease: physical destruction of the tumor, topical treatment, and systemic treatment. Cryotherapy, curettage, and evisceration are examples of destructive therapy. Treatment may be painful and result in scarring.[14] Topical treatments include cantharidin, potassium hydroxide, podophyllotoxin, tretinoin, liquefied phenol, imiquimod, and cidofovir. Systemic treatments that have been tried include cidofovir and cimetidine.[14,20]

Traditional antiviral drugs are directed against the proteins and functional pathways of the virus itself. Because poxviruses rely on cellular pathways to propagate, another possible antiviral treatment approach is to direct treatment that interferes with the viral functions that are dependent on the functional machinery of the cell.[21] The microtubule cytoskeleton pathway plays a role in the lifecycle of poxviruses[7] and may thus represent a new target for poxvirus therapy.[21]

Paclitaxel targets the host cell's microtubule cytoskeleton. The drug was discovered in 1964 and is derived from the bark of the Pacific yew tree (*Taxus brevifolia*). Paclitaxel is approved by the US FDA as a chemotherapeutic drug for the treatment of ovarian cancer, breast cancer, non–small cell lung cancer, prostate cancer, and AIDS-related Kaposi sarcoma.[22] It belongs to the class of drugs called taxanes, which are anticancer drugs that have validated the concept of microtubules as effective cancer chemotherapeutic targets.[23] Cells treated with paclitaxel produce too many microtubules and as a result are unable to coordinate cell division; they die after continued attempts to replicate their DNA without the ability to divide.[24]

The rapid clearance of disease in this case supports the possibility that treatment with intravenous paclitaxel might disrupt the MCV lifecycle, thereby resulting in decreased viral replication and ultimately, decreased burden of disease. Further clinical studies are recommended to fully characterize the nature of this response.

Financial Disclosure: Dr Sisneros has served as a scientific advisor and paid lecturer for Gilead Sciences, Inc.

References

1. Vozmediano JM, Manrique A, Petraglia S, Romero MA, Nieto I. Giant molluscum contagiosum in AIDS. *Int J Dermatol*. 1996;35:45-47.

2. Gona P, Van Dyke RB, Williams PL, et al. Incidence of opportunistic and other infections in HIV-infected children in the HAART era. *JAMA*. 2006;296:292-300.

3. Kauffman CL and Beatty CN. Molluscum contagiosum. eMedicine Dermatology Web site. July 23, 2010. http://emedicine.medscape.com/article/1132908-overview. Updated July 23, 2010. Accessed November 29, 2010.

4. Senkevich TG, Bugert JJ, Sisler JR, Koonin EV, Darai G, Moss B. Genome sequence of a human tumorigenic poxvirus: prediction of specific host response-evasion genes. *Science*. 1996;273:813-816.

5. Krathwohl MD, Hromas R, Brown DR, Broxmeyer HE, Fife KH. Functional characterization of the C-–C chemokine-like molecules encoded by molluscum contagiosum virus types 1 and 2. *Proc Natl Acad Sci U S A*. 1997;94:9875-9880.

6. Harrison SC, Alberts B, Ehrenfeld E, et al. Discovery of antivirals against smallpox. *Proc Natl Acad Sci U S A*. 2004;101:11178-11192.

7. Ploubidou A, Moreau V, Ashman K, Reckmann I, González C, Way M. Vaccinia virus infection disrupts microtubule organization and centrosome function. *EMBO J*. 2000;19:3932-3944.

8. Hollinshead M, Rodger G, Van Eijl H, et al. Vaccinia virus utilizes microtubules for movement to the cell surface. *J Cell Biol*. 2001;154:389-402.

9. Laliberte JP, Moss B. Lipid membranes in poxvirus replication. *Viruses*. 2010;2:972-986.

10. Billstein SA, Mattaliano VJ, Jr. The "nuisance" sexually transmitted diseases: molluscum contagiosum, scabies, and crab lice. *Med Clin North Am*. 1990;74:1487-1505.

11. Crowe MA. Molluscum contagiosum. eMedicine Pediatrics Web site. April 26, 2010. http://emedicine.medscape.com/article/910570-overview. Updated April 26, 2010. Accessed November 29, 2010.

12. Molino AC, Fleischer AB, Jr., Feldman SR. Patient demographics and utilization of health care services for molluscum contagiosum. *Pediatr Dermatol*. 2004;21:628-632.

13. Postlethwaite R. Molluscum contagiosum. *Arch Environ Health*. 1970;21:432-452.

14. van der Wouden JC, van der Sande R, van Suijlekom-Smit LWA, Berger M, Butler C, Koning S. Interventions for cutaneous molluscum contagiosum. *Cochrane Database Syst Rev*. 2009;CD004767.

15. Schwartz JJ, Myskowski PL. Molluscum contagiosum in patients with human immunodeficiency virus infection. A review of twenty-seven patients. *J Am Acad Dermatol*. 1992;27:583-588.

16. Baxter KF, Highet AS. Topical cidofovir and cryotherapy--combination treatment for recalcitrant molluscum contagiosum in a patient with HIV infection. *J Eur Acad Dermatol Venereol*. 2004;18:230-231.

17. Lin HY, Linn G, Liu CB, Chen CJ, Yu KJ. An immunocompromised woman with severe molluscum contagiosum that responded well to topical imiquimod: a case report and literature review. *J Low Genit Tract Dis*. 2010;14:134-135.

18. Hivnor C, Shepard JW, Shapiro MS, Vittorio CC. Intravenous cidofovir for recalcitrant verruca vulgaris in the setting of HIV. *Arch Dermatol*. 2004;140:13-14.

19. Hogan MT. Cutaneous infections associated with HIV/AIDS. *Dermatol Clin*. 2006;24:473-95, vi.

20. Meadows KP, Tyring SK, Pavia AT, Rallis TM. Resolution of recalcitrant molluscum contagiosum virus lesions in human immunodeficiency virus-infected patients treated with cidofovir. *Arch Dermatol*. 1997;133:987-990.

21. Yang H, Kim SK, Kim M, et al. Antiviral chemotherapy facilitates control of poxvirus infections through inhibition of cellular signal transduction. *J Clin Invest*. 2005;115:379-387.

22. McEvoy GK, Miller J, Litvak K, eds. *AHFS Drug Information 2004*. Bethesda, MD: American Society of Health-System Pharmacists; 2004:1100-1111.

23. Zhou J, Giannakakou P. Targeting microtubules for cancer chemotherapy. *Curr Med Chem Anticancer Agents*. 2005;5:65-71.

24. The discovery of camptothecin and Taxol®. American Chemical Society. Published 2007. http://acswebcontent.acs.org/landmarks/landmarks/taxol/tax.html. Accessed November 29, 2010.

Top HIV Med. 2010;18(5):169-172