Intravenous Cidofovir for Recalcitrant Verruca Vulgaris in the Setting of HIV

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF A CASE

A 34-year-old human immunodeficiency virus (HIV)–seropositive man with a history of Kaposi sarcoma and ocular cytomegalovirus presented with an 8- to 10-month history of multiple, progressively enlarging verrucous papules on the proximal nail fold and the distal interphalangeal joint of the right third finger (Figure 1). His CD4 cell count was 21/µL during retroviral therapy. A clinical diagnosis of verruca vulgaris was made, and the patient was treated unsuccessfully with a variety of therapeutic modalities, including liquid nitrogen cryosurgery and hyperthermia, as well as topical imiquimod, tretinoin solution, 0.1% tazarotene gel, and 25%, 50%, and 75% podophyllin, singly and in combination. Subsequently, the patient developed molluscum contagiosum, condylomata acuminata, and periungual warts on 6 other fingers. These conditions were also treated with multiple destructive and topical modalities, without improvement.

The verrucous papules on the right third finger coalesced to form a 2-cm, fungating plaque, with resultant nail deformity. The findings of a biopsy that was performed to rule out squamous cell carcinoma showed verruca vulgaris. Because multiple treatments had failed, the verruca was treated with 3% cidofovir ointment, under occlusion, for 8 to 10 hours per day. The molluscum contagiosum and condylomata were treated with topical cidofovir ointment without occlusion. Despite this therapeutic approach, the verrucous plaque on the right third finger enlarged to 2.5 cm. This entire wart was surgically removed, and treatment with topical cidofovir, under occlusion, was re-instituted immediately after reepithelialization. A pathologic examination again showed verruca vulgaris. Within 1 month of debulking, the verruca recurred and enlarged to 3.5 cm. The molluscum contagiosum and condylomata also failed to respond to topical cidofovir therapy.

THERAPEUTIC CHALLENGE

Impaired cell-mediated immunity can interfere with the resolution of viral infections. In the setting of AIDS and low CD4 cell counts, verruca vulgaris and molluscum contagiosum may be particularly resistant to therapy. Reconstitution of host immunity with antiretroviral therapy is most efficacious, though often difficult to achieve. Other treatment approaches, such as excision and local destruction with cryotherapy and hyperthermia, are often minimally effective. Topical 5% imiquimod has been successfully used in some cases of resistant viral infections. Topical cidofovir therapy has recently shown some benefit, but is extremely expensive. Although very well tolerated, it reportedly produced adverse systemic effects in 1 case. Our patient’s verrucae enlarged despite all of the treatments we attempted.

SOLUTION

The decision was made to treat the patient with outpatient intravenous cidofovir therapy at a dosage of 375 mg every 2 weeks, with standard pretreatment with probenecid and intravenous hydration. After 2 cycles of therapy, crusting and weeping of all the molluscum contagiosum papules were observed. After 5 cycles, all the periungual verrucae, except for the one on the right third finger, and the condylomata acuminata exhibited inflammation and focal areas of hemorrhagic crust. The verruca on the right third finger, which showed minimal inflammation, was again surgically debulked. One month after debulking and after a total of 7 cycles of cidofovir therapy, the verrucae, molluscum contagiosum, and condylomata resolved (Figure 2). After the conditions cleared, the patient un-
derwent 3 more cycles of cidofovir to treat any potentially remaining dormant virus. He tolerated the treatment well. Laboratory evaluation revealed moderate proteinuria, with no change in the serum urea nitrogen or creatinine levels. The proteinuria self-resolved and did not recur after a minor change in dosage.

**COMMENT**

Cidofovir is effective against DNA viruses such as orf virus, vaccinia virus, monkeypox, cowpox, human papillomavirus, molluscum contagiosum, human herpesvirus 8, acyclovir-resistant herpes simplex virus, and cytomegalovirus. Cidofovir is approved by the Food and Drug Administration for treating cytomegalovirus retinitis in patients with HIV. Intravenous treatment is limited by adverse effects, including nephrotoxicity, neutropenia, metabolic acidosis, and possible teratogenicity.

In a double-blind placebo-controlled phase 2 trial, 9 of 19 HIV-positive patients with condylomata treated with topical cidofovir gel had complete clearing of their lesions; none of the 11 placebo-treated patients demonstrated clearing. Progression was not observed in any of the cidofovir-treated patients, whereas 5 of 11 placebo-treated patients showed progression. Statistical significance was achieved for the end points of clearance and lack of progression in the cidofovir-treated cohort (compared with the placebo-treated group) \( P = .006 \). Of note, the CD4 cell counts in the 2 groups were not reported. Other open trials have shown a combination of surgery and cidofovir therapy to be effective.

We describe an HIV-seropositive patient with extensive acral verruca vulgaris that was resistant to numerous therapeutic modalities, including treatment with cidofovir ointment, who responded to 7 cycles of intravenous cidofovir therapy. Remarkably, clearance was observed in the setting of persistent severe immunosuppression. Attempts at reconstituting the patient’s impaired cell-mediated immunity proved to be unsuccessful despite the involvement of several different highly active antiretroviral therapy regimens over the course of 5 years.

To our knowledge, the successful use of intravenous cidofovir in multiretroviral-resistant HIV-associated verruca vulgaris has not been previously reported. Successful treatment of recalcitrant molluscum contagiosum with intravenous cidofovir in an HIV-seropositive patient has been described in 1 report. The patient refused treatment for his HIV infection. The molluscum contagiosum resolved completely with intravenous cidofovir therapy despite continued immunologic failure.

Treatment-resistant human papillomavirus infections present a daunting challenge to clinicians who treat patients with HIV and AIDS. Immune reconstitution, the preferred approach, is imperfect despite currently available combinations of highly active antiretroviral therapies, and may become even more difficult as retroviral resistance emerges in the years ahead. Identification of agents that will be efficacious in the treatment of resistant human papillomavirus infections is therefore urgently needed. As the present report demonstrates, intravenous cidofovir therapy holds promise in this setting. Further data, in the form of case series and, ideally, clinical trials, are needed to better characterize treatment response to this therapeutic modality.

**REFERENCES**