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 accuminata, 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 reinstituted immediately after reepithelialization. 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.1 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.2 Our patient’s verrucae enlarged despite all of the treatments we attempted.

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 accuminata 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-
were not reported. Other open trials have shown a combina-
tion therapy of acyclovir and foscarnet to be effective in the 
treatment of recalcitrant molluscum contagiosum with in-
travenous 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 con-
tinued immunologic failure.8

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 avail-
able combinations of highly active antiretroviral thera-
pies, 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 resis-
tant human papillomavirus infections is therefore ur-
gently needed. As the present report demonstrates, in-
travenous cidofovir therapy holds promise in this setting. 
Further data, in the form of case series and, ideally, clini-
cal trials, are needed to better characterize treatment re-
response to this therapeutic modality.

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Cidofovir is effective against DNA viruses such as orf vi-
rus, vaccinia virus, monkeypox, cowpox,3 human pap-
illomavirus, molluscum contagiosum,4 human herpes-
virus 8,5 acyclovir-resistant herpes simplex virus,9 and 
cytomegalovirus. Cidofovir is approved by the Food and 
Drug Administration for treating cytomegalovirus reti-
nitis in patients with HIV. Intravenous treatment is lim-
ited by adverse effects, including nephrotoxicity, neu-
ropenia, metabolic acidosis, and possible teratogenicity.2

In a double-blind placebo-controlled phase 2 trial,6 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 
progression. 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 combi-
nation of surgery and cidofovir therapy to be effective.7

We describe an HIV-seropositive patient with ex-
tensive acral verruca vulgaris that was resistant to nu-
merous therapeutic modalities, including treatment with 
cidofovir ointment, who responded to 7 cycles of intra-
venous cidofovir therapy. Remarkably, clearance was ob-
served in the setting of persistent severe immunosup-
pression. Attempts at reconstituting the patient’s impaired 
cell-mediated immunity proved to be unsuccessful des-
pite the institution of several different highly active anti-
tiretroviral therapy regimens over the course of 5 years.

To our knowledge, the successful use of intravenous 
cidofovir in multiretreatment-resistant HIV-associated ver-
ruca vulgaris has not been previously reported. Successful 
treatment of recalcitrant molluscum contagiosum with in-
travenous cidofovir is a 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.