Intralesional cidofovir for treatment of recalcitrant warts in both immunocompetent and immunocompromised patients: A retrospective analysis of 58 patients

To the Editor: Cutaneous warts, caused by human papilloma virus, often regress spontaneously or respond to common treatments, but they may be refractory or recur.[1] Refractory warts, innumerable warts, or warts too large for traditional treatments occur most often in immunocompromised patients.[1]

Cidofovir is an antiviral drug with broad-spectrum activity, originally approved for AIDS-related cytomegalovirus retinitis.[2] However, intralesional (IL) or topical cidofovir can also be effective in the treatment of recalcitrant warts.[3,4] Although case reports support IL cidofovir for refractory warts, there are limited data among broader populations.

To understand the effectiveness of IL cidofovir for refractory warts, including in immunocompromised patients, we conducted a retrospective review of patients treated with IL cidofovir at the University of Pennsylvania (UPenn) between 2014 and 2019. The standard protocol used at UPenn is cidofovir (75 mg/mL) diluted with normal saline to create a 15-mg/mL solution. Patients with severe probenecid or sulfonamide hypersensitivity should not use cidofovir. Patients can be scheduled in batches, and the pharmacy can use a single cidofovir vial to draw up multiple doses at once for immediate use. For community dermatologists, sterile compounding pharmacies may assist. Each vial is 375 mg/mL × 5 mL; up to 25 1-mL syringes can be compounded from each vial. After local anesthesia is obtained, cidofovir is injected directly into the wart (no deeper than the papillary/superficial dermis) with either superficial crosshatching or serial puncture techniques.[5] As an example, 0.2 to 0.5 mL is needed per session for periungual warts (maximum, 1 mL); patients are seen back no sooner than 4 weeks for reinjection.

For patients treated during the study period, we collected data on age, sex, comorbidities, location/number of warts, previous treatments, number of injections, amount of cidofovir used, and adverse effects. Primary outcomes were improvement or resolution of warts. We conducted 1) a per-protocol analysis that included patients who completed treatment and were not lost to follow-up and 2) an intent-to-treat analysis that included all patients who began treatment, including those lost to follow-up. This study was approved by the institutional review board at UPenn.

Table I. Characteristics and treatment outcomes of study patients

Characteristics	Completed treatment (n = 43)	Intent-to-treat population (n = 58)
Female, n (%)	17 (39.5)	25 (43.1)
Age, y, n (%)		
10-29	10 (23.3)	14 (24.1)
30-49	13 (30.2)	19 (32.8)
50-69	15 (34.9)	19 (32.8)
>70	5 (11.6)	6 (10.3)
Location of warts, n (%)		
Hands	32 (74.4)	41 (70.7)
Feet	16 (37.2)	20 (34.5)
Face	3 (7.0)	5 (8.6)
Genitals	4 (9.3)	6 (10.3)
Body	2 (4.7)	2 (3.5)
Number of warts, n (%)		
1	11 (25.6)	12 (20.7)
2-5	15 (34.9)	20 (34.5)
6-10	7 (16.3)	11 (19.3)
11-15	3 (7.0)	5 (8.6)
>15	7 (16.3)	9 (15.5)
Wart duration, y, n (%)		
<1	6 (14.0)	7 (12.1)
1-2	6 (14.0)	8 (13.8)
2-3	6 (14.0)	6 (10.3)
3-5	6 (14.0)	10 (17.2)
>5	19 (44.2)	27 (46.6)
OTC treatments,* n (%)	24 (55.8)	29 (50.0)
Prior cryotherapy, n (%)	40 (93.0)	54 (93.1)
≥3 wart treatments before cidofovir,† n (%)	27 (62.8)	40 (69.0)
History of HIV, n (%)	5 (11.6)	7 (12.1)
History of diabetes, n (%)	3 (7.0)	9 (15.5)
History of cancer, n (%)	6 (14.0)	9 (15.5)
History of transplant, n (%)	4 (9.3)	8 (13.8)
Number of treatments, mean (SD)	3.4 (2.2)	3.4 (2.5)
Improved, n (%)	43 (100)	57 (98.3)
Resolved, n (%)	42 (97.6)	44 (75.9)

OTC, Over the counter.

*These include OTC liquid nitrogen preparations, salicylic acid, and duct tape.

†Prior wart treatments reported include cryotherapy, electrodesiccation/curettage, shave removal, *Candida* injection, salicylic acid, imiquimod, paring, excision, 5-fluorouracil, topical retinoids, bleomycin, steroids, cantharidin, dinitrochlorobenzene, podophyllin, sinecatechins, laser, duct tape, and interferon.

In the intent-to-treat population (n = 58), 93.1% of patients were previously treated with cryotherapy. The most common locations affected were hands (70.7%), feet (34.5%), and genitals (10.3%). Forty-seven percent of warts were present for longer than 5 years. After a mean of 3.4 treatments (standard deviation, 2.5), 98.3% and 75.9% of warts were improved or resolved,

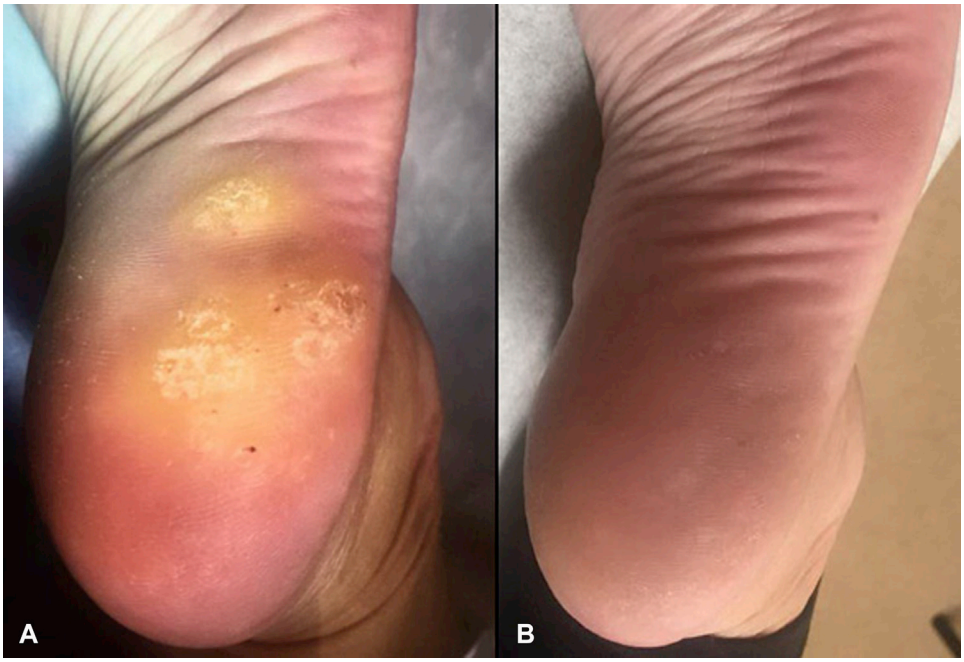

Fig 1. Plantar warts. Multiple large plantar warts in a patient with a kidney transplant (**A**) before and (**B**) after 1 injection of 3 mL total IL cidofovir (15 mg/mL).

respectively (Table I). Representative treatment response is shown in Fig 1. In the per-protocol population (n = 43), after a mean of 3.4 treatments (standard deviation, 2.2), 100% and 97.6% of warts improved or resolved, respectively (Table I). The most common local reactions (n = 58) included blistering (19.0%), pain (10.3%), swelling (5.1%), and erosion (1.7%).

In this retrospective case series of patients with recalcitrant warts, cidofovir was a highly successful option, with most patients' warts resolving after 3 to 4 treatment sessions. Although this study is limited by lack of control group and a small number of patients, these results suggest that IL cidofovir can be a successful treatment for patients, including those who are immunocompromised and those for whom other treatments failed. Randomized trials are needed to further understand the effectiveness of IL cidofovir.

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