

# Oral Acyclovir in the Treatment of Verruca

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## ABSTRACT

**Objective:** To describe a case in which persistent plantar warts resolved after a ten-day treatment course of oral acyclovir prescribed for herpes zoster.

**Case Summary:** A 49 year-old Caucasian female with non-significant past medical history presented to the podiatry clinic for treatment of verrucae. Debridement was performed and monochloroacetic acid was applied to affected areas seven times over seven months. The patient was diagnosed and treated for herpes zoster with acyclovir for ten days. Following acyclovir completion, only one verruca remained with complete resolution at the next follow-up podiatry visit.

**Discussion and Conclusion:** Few previous trials have supported the use of acyclovir cream in treatment-resistant plantar warts. However, no case reports to date describe the efficacy of oral acyclovir in the treatment of verruca. While a causal relationship has not been solidified between verrucous lesion resolution and treatment with acyclovir, it can be inferred and warrants additional attention.

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## INTRODUCTION

Verruca (plantar warts) are a common problem caused by the human papilloma virus (HPV) that can be irritating and painful. Current treatment of verruca is limited to traditional therapies that are quantified by two distinct mechanistic activities—either destructive or immunomodulating.<sup>1</sup> Destructive therapies can be further segregated into those that are topical pharmacologic in nature (eg, salicylic acid, monochloroacetic acid) or physical (eg, surgery, cryotherapy). Susceptibility of HPV to antivirals is not possible as HPV is not conducive to being cultured in vitro.

An initial Cochrane Database review of nongenital wart treatments was performed in 2006 in an effort to assess the quality of existing evidence.<sup>2</sup> The authors concluded that there was a lack of evidence to substantiate treatment with topical agents. Specifically, most evidence supported the use of topical treatments that contained salicylic acid. This review was updated in 2011 with similar recommendations after reviewing 26 new additional studies.<sup>3</sup> An alternate systematic review of 15 trials was performed in 2012, analyzing the efficacy of systemic treatment of cutaneous warts, including levamisole, homeopathy, zinc sulphate, and cimetidine. While levamisole and homeopathy were found ineffective, zinc sulphate and cimetidine evidence was also limited due to methodological flaw and inconclusive efficacy, respectively.<sup>4</sup>

Acyclovir is a synthetic purine nucleoside analogue with activity against herpes simplex virus type 1 (HSV-1), 2 (HSV-2), and varicella-zoster virus (VZV). Acyclovir uses viral thymidine kinase to convert to acyclovir monophosphate, a nucleotide analogue that is eventually converted to its active form of acyclovir triphosphate. Through this mechanism of utilizing viral thymidine

kinase to convert to its active form, acyclovir specifically targets viral DNA, preventing replication of the herpes virus in the host. A dose of 800mg every 4 hours for 7 to 10 days is commonly used for acute treatment of herpes zoster (shingles).<sup>5</sup> Early reports have indicated no difference in the treatment of verruca with topical acyclovir versus traditional therapy.<sup>6</sup>

There remains a paucity of data to support the use of oral acyclovir which achieves systematic concentrations in the body, for the treatment of verruca.<sup>7</sup> We report a case where verruca incidentally resolved in a patient receiving acyclovir for the treatment of shingles.

## CASE

A 49 year-old Caucasian female with non-significant past medical history presented to the podiatry clinic in March 2014 for treatment of verruca. Upon examination, two 3mm and three 2mm verrucae were identified on the second medial and metatarsal head of the left foot. The patient complained of discomfort and a pain level of 5/10. Debridement was performed and monochloroacetic acid was applied to affected areas. Further debridement and monochloroacetic acid application were performed at each of the six subsequent visits over the next seven months, with the last treatment in October 2014. The pain subsided to a score of 3/10, however the size of the verrucae remained unchanged.

Approximately one month later, the patient presented to her primary care provider with a visible rash on the base of her neck and right shoulder with visible blisters that started four days prior. A diagnosis of herpes zoster was given and the

TABLE 1.

## Previous Cases of Oral Valacyclovir in the Treatment of Verruca

Case No.	Age (yr)	Sex	Previous Treatment	Therapy	Clinical Findings
1	30	M	1. Cryotherapy	Valacyclovir 1g daily - 37 days	History of plantar warts for 3 years, complete disappearance occurred
2	14	M	1. Topical salicylic acid/lactic acid x3 mo 2. Cryotherapy 3. Topical imiquimod 5% cream BID x4 mo	Valacyclovir 1g daily - 60 days	History of plantar warts for 4 years, complete disappearance occurred

Tandeter H, Tandeter ER. Treatment of plantar warts with oral valacyclovir. *Am J Med.* 2005;118(6):689-90.

patient was treated with acyclovir 800mg five times daily for ten days. Five days after completion of the medication, the patient presented to podiatry for discussion of surgical removal of persistent verruca. However, only one 1mm verruca remained, with complete resolution at next follow-up visit, rendering the procedure unnecessary.

## DISCUSSION

There have been two previous case reports demonstrating the efficacy of oral valacyclovir in treating verruca, unresponsive to standard therapies. Table 1 provides a brief overview of the clinical findings of these reports. The patients in which treatment with valacyclovir has reportedly been effective share common characteristics of a long history of verrucous lesions and ineffectiveness of conventional therapies.<sup>8</sup> To date, there are no double-blind placebo-controlled trials assessing the efficacy of oral acyclovir or valacyclovir in verruca.

The use of topical acyclovir in the treatment of verruca has been controversial. Gipson, et al. demonstrated lack of statistical significance of acyclovir cream in the treatment of viral verruca when compared with liquid nitrogen and placebo.<sup>6</sup> Conversely, a brief Letter to the editor of *Cutis* described successful treatment with acyclovir cream in twenty-four patients with a variety of warts unresponsive to prior treatments.<sup>9</sup> Acyclovir cream was reported successful in an additional three case reports of patients with verruca that had persisted for years following ineffective traditional therapies.<sup>7,10</sup>

In the case described above, the patient possessed similar characteristics to previous case reports analyzing the use of valacyclovir in treatment-resistant verruca in that traditional therapies including debridement and topical creams had proven ineffective in resolving their plantar warts. However, unlike previous reports, resolution of the majority of the warts was evident only 5 days after conclusion of oral acyclovir therapy.

The mechanism behind the possible efficacy of acyclovir in the treatment of plantar warts was briefly discussed by Bauer.<sup>10</sup> It has been suggested that if in vitro studies of human wart tissue evidenced the capacity to convert acyclovir to its active form through viral thymidine kinase, acyclovir treatment in plantar warts could be justified.

In this case, acyclovir was prescribed for the acute treatment of herpes zoster. Upon follow-up for scheduled debridement, it was noted that the verruca, persistent following previous seven rounds of debridement and monochloroacetic acid application, was completely resolved. While an exact causal relationship cannot be elicited in regards to acyclovir and verruca healing, based on previous case reports and findings from this case, further controlled clinical trials are warranted. To our knowledge, this is the first case to present a patient with failed trials of standard therapy that responded to a short course of acyclovir.

## CONCLUSION

The case described above is suggestive of the utility of oral acyclovir therapy in the treatment of verruca resistant to standard therapy. While few cases have previously suggested this correlation, primarily using topical creams, this is the first to exhibit verruca improvement with a short course of oral acyclovir therapy. Additional trials are necessary to affirm a direct causal relationship between acyclovir and verruca resolution.

## DISCLOSURE

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