

Acitretin for the treatment of recalcitrant plantar warts

Deep Joshipura MD¹, Ari Goldminz MD¹, Jacqueline Greb BA, MS¹, Alice Gottlieb, MD PhD²

Affiliations: ¹Department of Dermatology, Tufts Medical Center, Boston, Massachusetts, ²Department of Dermatology, New York Medical College, Valhalla, New York

Corresponding Author: Deep Joshipura, MD, Department of Dermatology, Tufts Medical Center, 800 Washington Street, Boston, MA 02111, Email: djoshipura@tuftsmedicalcenter.org

Abstract

Plantar warts caused by human papilloma virus (HPV) may be challenging to treat when conventional modalities fail. We report a case of severely recalcitrant plantar warts, successfully treated with oral acitretin and topical 40% urea cream.

Keywords: verruca vulgaris, acitretin, urea cream, recalcitrant plantar warts

Introduction

Verrucae vulgaris are caused by human papilloma virus (HPV) strains 1, 2, 4, 7, 57 [1] and have a prevalence of approximately 10% [2]. Although verrucae are often self-limited, palmoplantar warts can be particularly recalcitrant to multiple treatment modalities and symptomatic when located periungually or on the palmar and plantar surfaces. We report a 33-year-old man with recalcitrant plantar warts with a significant response to a combination of oral acitretin and 40% urea cream.

Case Synopsis

We report a 33-year-old man with a 3-4-year history of recalcitrant, diffuse verruca vulgaris over the bilateral plantar feet and toes who required treatment with daily oral acitretin 25 mg and twice daily urea cream 40% for symptomatic and clinical control (**Figure 1**). After 1 month of this new treatment regimen, his multiple, thick, verrucous papules were significantly thinner (**Figure 2**). At the end of 4 months he experienced near complete clinical clearance. Additionally pain with ambulation that had been present for years had completely resolved.



Figure 1. Pre-treatment showing presence of warts over soles



Figure 2. Post-treatment picture showing markedly reduced size of the warts.

The patient had previously failed cryotherapy, cimetidine, and 'formaldehyde with scraping.' He was also unable to tolerate intralesional candidin injections owing to pain. He had no history of

constitutional symptoms, immunosuppression, risk for human immunodeficiency virus, or family history of warts or immunodeficiencies,

Owing to severe pain with walking, systemic treatment with daily oral acitretin was initiated in January 2016 in combination with urea cream 40% twice daily. Baseline routine laboratory evaluations including liver function tests and lipid profile were notable for mildly elevated triglycerides and cholesterol. The patient's hypertension, was being monitored and treated by the patient's primary care physician. The only side effect of acitretin and urea cream was dryness, controlled with liberal moisturizing. Liver function tests remained within normal limits and lipid profile was unchanged during the treatment period.

Case Discussion

Treatment of viral warts can be challenging in the face of recalcitrant lesions. Plantar warts can be associated with significant pain and may therefore interfere with activities of daily living.

Previous case reports in immunocompetent patients have demonstrated improvements in recalcitrant warts with acitretin. Choi et al. reported significant improvement after 2 months of 1 mg/kg/day acitretin in a 25-year old man with multiple warts on the bilateral hands [3]. Although after discontinuing acitretin the warts recurred, improvement was again seen after restarting treatment with acitretin [3]. Another report describes successful clearance of long-standing periungual warts in a 46-year-old woman after with a three-month course of acitretin, 25 mg daily, followed by every other day dosing. Clinical remission was maintained 6 months after discontinuation of treatment [4].

Recalcitrant warts on the scalp and beard areas, resistant to conventional treatments have been successfully treated with acitretin 0.5mg/kg/day for 3 months in combination with cryotherapy during the first month, with improvement observed as early as four weeks. Clearance was maintained 5 months after stopping acitretin [5]. In another report a 20-year old man with warts on face, palm, and left extremity present for a duration of 6-years experienced complete clearance of his lesions with acitretin 0.5

mg/kg/day continued for 3 months. The patient was followed-up for 6 months after treatment with no recurrence of lesions [6]. Another report documented significant regression in wart size at 1 month and complete flattening after 3 months in a 32-year-old man with multiple warts on his hands, fingers, and periungual area after treatment with acitretin 0.3 mg/kg/day. There was no recurrence 3 months after stopping treatment [1].

Oral acitretin has been also been successful in treating giant condyloma acuminatum, giant warts in an immunocompromised patient, and epidermodysplasia verruciformis, an autosomal recessive disorder marked by widespread HPV infection [12-15].

The side effect profiles of acitretin among these cases are mild and include xerosis and cheilitis, without clinically significant laboratory abnormalities or other side effects. Selection of appropriate patients for treatment with acitretin is also important. In particular, one should avoid this medication in women of childbearing potential and in those with other medical co-morbidities such as mood disorders and alcoholism.

The efficacy of retinoid in wart therapy is believed to be related to their influence on the regulation of cell growth and differentiation with resulting inhibition of viral replication and assembly within infected cells [3, 9]. An inverse relationship between retinoid concentration and level of HPV DNA supports the role of retinoids in inhibition of viral replication [7]. Retinoids are not only potent immunomodulators [8], but also have apoptotic activity, which likely contributes to wart clearance [10]. Whereas topical vitamin A (i.e. tretinoin) also can be effective for warts [11], oral therapy was preferred in our patient owing to significant wart thickness.

Conclusion

Plantar warts may be challenging to treat with traditional therapies; persistent, symptomatic warts may require alternative approaches to treatment. Acitretin is a promising therapeutic option for symptomatic viral warts recalcitrant to other conventional treatment modalities among certain patient populations.

References

1. Proietti I, Skroza N, Bernardini N, Nicolucci F, Tolino E, La Viola G, et al. Acitretin in management of diffuse common warts: A case report. *Dermatol Ther*. 2011;24(6):581–3. [PMID: 22515673]
2. Laurent R, Kienzler JL. Epidemiology of HPV infections. *Clin Dermatol*. Jan;3(4):64–70. [PMID: 3880029]
3. Choi Y-L, Lee K-J, Kim W-S, Lee D-Y, Lee J-H, Lee E-S, et al. Treatment of extensive and recalcitrant viral warts with acitretin. *Int J Dermatol*. 2006 Apr;45(4):480–2. [PMID: 16650187]
4. El-Khayat RH, Hague JS. Use of acitretin in the treatment of resistant viral warts. *J Dermatolog Treat*. 2011;22(4):194–6. [PMID: 20443666]
5. Kaliyadan F, Dharmaratnam AD. Rapid response to acitretin, combined with cryotherapy, for extensive and recalcitrant verruca vulgaris on the scalp. *Indian J Dermatol Venereol Leprol*. Jan;77(3):338–40. [PMID: 21508580]
6. Krupa Shankar DS, Shilpakar R. Acitretin in the management of recalcitrant warts. *Indian J Dermatol Venereol Leprol*. Jan;74(4):393–5. [PMID: 18797072]
7. Reppucci AD, DiLorenzo TP, Abramson AL, Steinberg BM. In vitro modulation of human laryngeal papilloma cell differentiation by retinoic acid. *Otolaryngol Head Neck Surg*. 1991 Oct;105(4):528–32. [PMID: 1662346]
8. Sidell N, Connor MJ, Chang B, Lowe NJ, Borok M. Effects of 13-cis retinoic acid therapy on human antibody responses to defined protein antigens. *J Invest Dermatol*. 1990 Nov;95(5):597–602. [PMID: 2146325]
9. Orfanos CE, Braun-Falco O, Farber EM, Grupper C, Polano MK, Schuppli R, editors. *Retinoids*. Berlin, Heidelberg: Springer Berlin Heidelberg; 1981.
10. Oridate N, Lotan D, Mitchell MF, Hong WK, Lotan R. Inhibition of proliferation and induction of apoptosis in cervical carcinoma cells by retinoids: implications for chemoprevention. *J Cell Biochem Suppl*. 1995 Jan;23:80–6. [PMID: 8747381]
11. Garry CE, Garry JA, Garry RF. Treatment of warts. *N Engl J Med*. 2004 Oct 14;351(16):1692–3; author reply 1692–3. [PMID: 15483294]
12. Tian YP, Yao L, Malla P, Song Y, Li SS. Successful treatment of giant condyloma acuminatum with combination retinoid and interferon- γ therapy. *Int J STD AIDS*. 2012 Jun;23(6):445–7. [PMID: 22807543]
13. Erkek E, Basar H, Bozdogan O, Emeksiz MC. Giant condyloma acuminata of Buschke-Löwenstein: successful treatment with a combination of surgical excision, oral acitretin and topical imiquimod. *Clin Exp Dermatol*. 2009 Apr;34(3):366–8. [PMID: 19175780]
14. Simone C De, Capizzi R, Carbone A, Fossati B, Valenzano F, Amerio P. Use of acitretin in a case of giant common warts in an HIV-infected patient. *Eur J Dermatol*. Jan;18(3):346–7. [PMID: 18474473]
15. Anadolu R, Oskay T, Erdem C, Boyvat A, Terzi E, Gürgey E. Treatment of epidermodysplasia verruciformis with a combination of acitretin and interferon alfa-2a. *J Am Acad Dermatol*. 2001 Aug;45(2):296–9. [PMID: 11464195]

Supplement

Table 1: Previously reported successful treatment of warts with acitretin.

2011	Proietti et al	-Acitretin in common warts over the dorsal hands and periungually. -Acitretin used for 12 weeks with complete resolution by 8 weeks.
2011	Kalidayan et al	-Complete resolution of scalp warts with acitretin 0.5mg/kg/once daily and cryotherapy. -Response achieved after 4 weeks. -Acitretin continued for 2 additional months.
2011	El-Khayat et al	-Acitretin resulting in complete clearance of periungual warts which did not respond after 10 years of other treatments.
2008	Krupa shankar et al	-Warts on face, palms and lower limbs responding to acitretin 0.5mg/kg/day, -No recurrence 6 months after treatment.
2006	Choi at al	-Acitretin 1 mg/kg/day with regression of recalcitrant warts on hands in 1 month, continued treatment for 2 additional months,