Imiquimod for Plantar and Periungual Warts

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Plantar and periungual warts are notoriously difficult to eradicate. Two cases of nongenital warts in teenage girls are presented. Imiquimod was used in combination with cryotherapy for the periungual warts and with occlusion for the plantar warts. Both cases showed complete resolution and that imiquimod may be more effective on thicker keratinized (nongenital) skin when occluded or used in combination with cryotherapy.

Because there is no uniformly effective treatment for warts, therapy is often difficult and unrewarding. Imiquimod 5% cream has proven to be safe and effective for genital warts.[1] We report 2 cases of adolescents who responded to either imiquimod alone or imiquimod combined with liquid nitrogen.

Case Reports

Patient 1—A 14-year-old girl with 10 periungual warts that were unresponsive to cryotherapy requested an alternative nonsurgical method of wart removal. Imiquimod 5% cream was applied at bedtime 3 times weekly without occlusion for 2 months without benefit. We questioned whether imiquimod penetrated the acral skin deeply enough to be effective. Therefore, we applied liquid nitrogen to each wart once in the office and increased the frequency of imiquimod application to every night at bedtime (with duct-tape occlusion). After 12 weeks, all warts had resolved. Treatment was well tolerated.

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Patient 2—A healthy 17-year-old young woman had 2 large plantar warts, 1 on each foot. The wart on the left foot (Figure 1) measured 2.0×4.8 cm. Given the size and the location of these lesions, nondestructive methods of treatment were discussed. Imiquimod 5% cream was applied to the warts nightly for 6 weeks (with duct-tape occlusion). Follow-up examination showed complete resolution of both warts (Figure 2). The patient had no complaints during the 6 weeks of treatment.

Comment

Most conventional wart therapies work by destroying infected keratinocytes rather than directly inhibiting human papillomavirus (HPV) replication.[1] There are 3 methods of keratinocyte destruction: freezing with liquid nitrogen, burning with electrodessication, and CO_2 laser ablation.[2] These modalities are often painful and may result in scarring. Even when scarring is not as much of a concern, pain alone may be just as problematic, especially in children and adolescents.

Research over the past decade has focused on inhibiting HPV replication and infection with interferon alfa (IFN-α), a well-characterized immune modulator released by leukocytes in response to viral infection. Although studies of IFN-α treatment of genital warts have shown clearance rates as high as 62%, administration in these studies required multiple injections because IFN-α is not well absorbed.[3,4] Recurrence was significant. Imiquimod 5% cream is an immune response modifier that has been shown to induce production of IFN-α and other immune system mediators, including interleukins 1, 6, and 8; interleukin 1 receptor antagonist; and tumor necrosis factor α.[5,6]

Although the precise mechanism of action of imiquimod is not known, activation of immune mediators is believed to be responsible for virus eradication as opposed to nonspecific tissue destruction. This shift in mechanism and in

Figure 1. Large verrucose plaque on the left plantar surface of patient 2 before imiquimod therapy.

Figure 2. Resolution of large wart on patient 2 after 6 weeks of nightly application of imiquimod 5% cream with duct-tape occlusion.

results represents a major advancement in wart therapy, and activation of immune mediators holds promise as a less destructive treatment modality for HPV infections.

The efficacy of imiquimod in the treatment of genital warts is encouraging.[7] In a randomized, double-blind, placebo-controlled study, eradication of all treated baseline warts occurred in 50% of patients who received imiquimod 5% cream 3 times weekly for as long as 16 weeks.[1] It is reasonable to assume that the same cellular immune modifications induced by imiquimod for genital warts will occur for plantar and periungual warts.

The case of patient 1 shows that freezing warts with liquid nitrogen just before applying imiquimod may weaken the stratum corneum enough to allow imiquimod to penetrate deeper in the more keratinized areas of the skin. Pretreatment with topical

salicylic acid may do the same. An obvious and valid criticism of this case is that the patient had already had multiple treatments with liquid nitrogen and was therefore more likely to respond to any subsequent treatment modality. However, it may be that 2 or 3 combination-therapy treatments may be more efficacious than 4 or 5 liquid-nitrogen–only treatments. Blind randomized trials are required to resolve this issue.

The large plantar warts of patient 2 resolved completely over a relatively short time. No destructive or painful procedures were necessary, and there were no adverse effects.

We have used imiquimod to treat more than 15 patients with multiple types of warts. In our experience, not all periungual or plantar warts resolve completely with either imiquimod alone or imiquimod combined with liquid nitrogen. Perhaps incomplete resolution is the result of limited penetration of these therapies through these highly keratinized areas. In the genital-wart study cited earlier,[1] women responded much better than men did (72% vs 33%), which may be because of the decreased thickness of the stratum corneum of the vulva compared with that of the penis. Our 2 cases show that imiquimod combined with cryotherapy and occlusion may work better for plantar and periungual warts.

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