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CASE REPORT

Local Hyperthermia Combined With Imiquimod Cleared Recalcitrant and Extensive Warts in a Patient With Systemic Lupus Erythematosus

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Abstract: Viral warts, a common dermatological condition caused by human papillomavirus infection (HPV) infection, present a particular challenge for systemic lupus erythematosus (SLE) patients due to their compromised immunity, which increases the susceptibility to HPV infection and complicates treatment efforts. Imiquimod, an immunomodulatory agent, has demonstrated efficacy in managing warts. Furthermore, local hyperthermia, a non-invasive therapeutic modality, has demonstrated significant potential in the management of warts. We report the case of a SLE patient developed recalcitrant and extensive viral warts on limbs. We applied hyperthermia at 45 °C on a target lesion for 1 hour / day with imiquimod cream 3 times/week. All the lesions cleared in 8 months and there was no sign of recurrence.

Keywords: human papillomavirus, hyperthermia, systemic lupus erythematosus, immunity

Introduction

Viral wart, mostly induced by HPV infection and are typically characterized by hyperkeratotic papules or plaques, most commonly on the hands and feet. Cutaneous warts are mainly caused by HPV type 1/2/27/57, among over 200 hPV types.[1] HPV can spread through direct or indirect contact with the individual exhibiting an injury. The presence of the epithelial barrier dysfunction, which is caused by minor trauma, allows the penetration of the virus. After inoculation, the incubation period ranges from three weeks to eight months. Multiple cutaneous warts are common in patients due to virus spreading or self-inoculation. According to reports, 22.2% of the patients with plantar warts having more than one lesion.[2] Most cases of cutaneous warts have a self-limiting clinical course of approximately 2–3 years, however, patients often seek treatment due to discomfort, load-bearing pain or other reasons. Traditional treatments for warts encompass cryotherapy, laser therapy, topical imiquimod, salicylic acid preparations, and oral isotretinoin.[3]

SLE is an autoimmune disease characterized by multiple systemic inflammations, increased levels of circulating autoantibodies, and various clinical manifestations. Patients with SLE are more susceptible to HPV infection due to they fail to induce effective cellular immune responses and take immunosuppressants for a long time, presenting numerous and more recalcitrant injuries.[4] Moreover, female patients have a high risk of developing abnormal cervical smears and squamous intraepithelial lesions of the cervix. Therefore, the treatment choice of patients with extensive warts and low immunity should be more cautious, because treatment may lead to secondary infection, prolong the healing time, and even aggravate complex diseases.

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Hyperthermia, with a temperature of 39–48°C, has been successfully used in the treatment of some neoplasms. Also, local hyperthermia has been used in treating mucocutaneous warts. The remarkable advantages of this method are non-invasive, painless, and the resolution of targeted lesion is often accompanied by clearance of untargeted lesions. Our previous open trial in patients with plantar warts observed that applying local hyperthermia at 44°C on a single lesion resolved the lesions of 59.1% (150 out of 254 cases) of the patients with multiple untreated plantar warts.[5] Here, we report a case of severe multiple warts with SLE successfully treated with local hyperthermia on one target lesion combined with imiquimod cream.

Case Presentation

A 38-year-old male, with an established diagnosis of SLE for more than ten years, had been controlled by oral tacrolimus since 2014. He complained of warty lesions on hands and feet (Figure 1A and B) for 5 years, with rapid increase in

Figure 1 Warty lesions before treatment (**A** and **B**), complete clearance of lesions 8 months after local hyperthermia (**C** and **D**).

numbers and sizes. He was diagnosed cutaneous warts and received treatment with cryotherapy, oral traditional Chinese medicine, retinoids intermittently at the local clinic, but to no avail, which led to his depression. In July 2021, the patient presented to our hospital. Physical examination showed that there were dense patches of reddish brown warts of different sizes on both hands and feet.

Starting from July 2021, we used a patented hyperthermia device (Patent No. ZL 200720185403.3, China Medical University, China)[6] with a light source from a tungsten-halogen lamp, most wavelengths (490%) were from 760 to 2300 nm, with a peak wavelength at 1200 nm (data supplied by the lamp supplier), combined with topical 5% imiquimod cream, on one target lesion of the patient's right foot. For this patient we chose a confluent plaque on his right sole as the target lesion. The patient received local hyperthermia at 45 °C for 1 hour / day on days 1, 2, 3, 17, 18, and then once a week for a total of thirty times. Imiquimod cream was applied three times a week. Two months after the treatment, the lesions appeared to subside. Six months after the treatment, the skin lesions on both feet were mostly cleared. After eight months, the skin lesions on the whole body basically subsided (Figure 1C and D) and there was no sign of recurrence. There had been no remarkable change of the patient's general condition during the treatment. Even better, the removal of viral warts helped him escape from depression.

Discussion

This case report highlights the successful treatment of recalcitrant and extensive viral warts in a patient with SLE using a combination of local hyperthermia and imiquimod cream. The integration of these two modalities resulted in the clearance of all lesions within eight months, with no recurrence observed, which is significant given the patient's immunocompromised state.

HPV is known to cause viral warts, and individuals with SLE are particularly vulnerable due to their impaired cellular immune responses and long-term use of immunosuppressants. This patient's warts were extensive and unresponsive to conventional treatments such as cryotherapy and oral medications, which underscores the challenges in managing HPV infections in immunocompromised hosts.

The application of hyperthermia at 45°C for 1 hour/day to a target lesion, in conjunction with imiquimod cream, represents an innovative approach to treating warts. Imiquimod, as an immunomodulator, enhances the production of IFN-α, TNF-α, and various interleukins, which are crucial for modulating immune responses and antiviral activity.[7] Local hyperthermia for wart treatment is increasingly recognized not only for its non-invasive and painless nature but also for its unique ability to achieve systemic clearance of lesions through single-lesion treatment. A randomized controlled trial demonstrated that hyperthermia achieved a 54.5% clearance rate compared to 27.2% with cryotherapy after four months, with respective recurrence rates of 4.3% and 20% within one year.[8] Local hyperthermia can activate immune cells, promote T cell proliferation, and stimulate the production of IFN-γ, further strengthening the immune system's response to HPV.[9] Furthermore, it is hypothesized that increased temperature may facilitate the skin's absorption of imiquimod, thereby potentiating the body's immune response. The non-invasive nature of this treatment, coupled with its painless application, makes it an attractive option for patients who may be intolerant to more aggressive therapies.

The success of this treatment protocol is further emphasized by the patient's improvement in depressive symptoms following the clearance of the warts. This highlights the psychosocial impact of skin conditions and the importance of comprehensive care that addresses both physical and mental health.

Our findings are consistent with previous studies that have demonstrated the efficacy of local hyperthermia in treating mucocutaneous warts, with the added benefit of clearing untargeted lesions as well.[10–12] The synergistic effect of hyperthermia and imiquimod in this case suggests a potential paradigm shift in the treatment of HPV-induced warts, particularly in patients with SLE or other immunocompromising conditions.

Conclusion

In conclusion, the combination of local hyperthermia and imiquimod cream offers a promising treatment option for patients with extensive and refractory warts, especially in the context of immunosuppression. Further studies are

warranted to confirm these findings and to explore the mechanisms underlying the therapeutic effects of this combined approach.

Ethics Statement

The publications of images were included with the patient's consent.

Consent Statement

Informed consent was provided by the patient for publication of the case.

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Disclosure

Dr Xing-Hua Gao reports a patent ZL 2007 2 0185403.3 licensed to China Medical University. The authors report no other conflicts of interest in this work.

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