

# Successful Treatment of Multiple Plantar and Periungual Warts by Local Hyperthermia Treatment: A Case Report

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**Abstract:** Local hyperthermia treatment, a common immunoadjuvant therapy, has been used in treating various human papillomavirus (HPV) infections. For multiple warts, it can clear off all warts of the body through targeted irradiation on one wart. We reported a case of a 22-year-old patient with multiple plantar warts combined with periungual warts, in which previous treatments were ineffective. Therefore, we utilized local hyperthermia treatment at 44°C using the largest fused-wart plaque on the right plantar as the treatment target for 30-minute irradiation each time. The hyperthermia induction therapy was performed on day 1, 2, 3, 12 and 13, followed by weekly maintenance therapy for 6 times. After 2 months of treatment, both irradiated and non-irradiated lesions disappeared, and no recurrence occurred during the follow-up period. This case indicates that local hyperthermia treatment may be a safe and effective approach for patients with multiple, recalcitrant, and site-specific viral warts due to the ineffectiveness of conventional treatment.

**Keywords:** local hyperthermia treatment, multiple, plantar warts, periungual warts

## Introduction

Warts refer to benign proliferative lesions of the skin caused by human papillomavirus (HPV) through infection of basal epithelial cells; The pathogenesis may be related to immunization, and they are frequently found in easily traumatized areas such as the periungual area, palms and soles of the feet.<sup>1</sup> Treatment of warts mainly includes hyperthermia drug therapy, physical therapy, immunotherapy and photodynamic therapy.<sup>2</sup> However, for multiple warts, most treatments are not ideal. Local topical drug therapy and physical therapy have the disadvantages of long healing time, pain, scarring, damage, and easy relapse. Although photodynamic therapy has been reported to be effective in treating plantar and periungual warts, it still has some limitations in treating relatively thick lesions because the photosensitizer does not penetrate the keratinized lesions well and the treatment expense is high.<sup>3</sup> The treatment choice for multiple warts is determined by a variety of factors, including patient age, the number, size, and site of lesions, treatment cost, availability, and side effect. Local hyperthermia treatment using infrared radiation is considered as a form of physical therapy. Infrared radiation generates heat in the body's tissues, which can be used to destroy or remove abnormal cells, such as warts. As physical therapy, local hyperthermia treatment is a non-invasive, external treatment that does not involve the use of drugs or surgery Huo et al<sup>4</sup> conducted a multi-center, open, 2-arm, non-randomized concurrent controlled trial that included 1027 patients, and the results showed both local hyperthermia and cryotherapy had similar efficacy for clearance of plantar warts; while local hyperthermia had a lower recurrence rate and lower pain sensation during treatment. Here, we report a case of a patient with multiple plantar warts combined with periungual warts successfully treated by local hyperthermia treatment at 44°C on the same lesion on days 1, 2, 3, 12, 13, followed by weekly maintenance treatment for 30 minutes each time, and all lesions disappeared after 2 months of treatment.

## Case Report

A 22-year-old male patient had multiple warts on the right plantar and periungual area of both hands for 2 years. Although the patient experienced no significant pain or itching, it had a serious impact on his psychological and social life. He had no history of trauma, surgery, immunosuppressive use or systemic symptoms. The patient was treated with 8 times of cryotherapy, external traditional Chinese medicine (TCM) immersion, vitamin A cream, imiquimod, and self-purchased online medicine rubbing, but did not improve, and the number and size of warts were still increasing. Dermatologic examination: more than 10 warts were on the right plantar, part of them fused into plaque-like warts, and similar rashes were around the nails of the left thumb, middle finger and right middle finger, ring finger, which were rough and hard. Treatment: The patented infrared processing equipment (Factory No. WRY-V01-20039, Liaoning Yanyang Medical Equipment Co. Ltd) was applied at 44°C (Figure 1), and the largest fused-wart plaque on the right plantar was selected as the target site for irradiation for 30 minutes each time. The patient was treated with hyperthermia immune induction therapy on day 1, 2, 3, 12 and 13, followed by weekly maintenance therapy for 6 times. This treatment was not combined with other treatments. During the treatment, the patient experienced no significant discomfort except for slight pain at the irradiated site. After a 2-month treatment, all warts around the nail on the patient's right plantar had fallen off without special post-treatment care (Figure 2), and there was no sign of relapse at the 2-month follow-up. The informed consent form of this patient has been obtained.

## Discussion

The effective treatment of intractable and multiple plantar warts and periungual warts is still a challenge for clinicians. Due to the specificity of the growth site, traditional destructive treatment methods tend to damage the nail and have a high recurrence rate in treating patients with perineural warts.<sup>5</sup> In this case, given that the patient had tried many treatments without any improvement, we tried local hyperthermia treatment.

Hyperthermia treatment is to expose part of the human body or local tissues to a temperature higher than body temperature. This type of heating is often referred to as “radiative heating” and does not necessarily rely on electricity as the heat source, although electricity may be used to power the equipment that generates the infrared radiation.

As a common immune-assisted therapy, hyperthermia treatment has been used in treating a variety of HPV-infected skin diseases and achieves good results. Compared with conventional treatments, hyperthermia treatment is characterized by non-invasiveness, a low recurrence rate and no requirement on specific contraindications. In addition, patient



**Figure 1** The patented infrared processing equipment.



**Figure 2** Treatment of multiple plantar and periungual warts in the patient with local hyperthermia. (**A** and **B**) Warts around the nails, and on the right plantar before treatments (By the first visit, warts and nails had become discolored due to topical TCM) (**C** and **D**) After 11 treatments, almost all warts disappeared.

acceptance and compliance treated by hyperthermia treatment are higher than those of conventional treatments. In treating multiple HPV-associated warts, when one targeted wart was radiated, warts in the rest of the untreated area would also shed.<sup>6</sup> A study compared the efficacy and safety of local hyperthermia at  $43 \pm 1^\circ\text{C}$  versus liquid nitrogen cryotherapy for plane warts during 6 months, and the results suggested that although local hyperthermia and cryotherapy achieved similar clearance rates, local hyperthermia had the lower recurrence and adverse events rates, and was preferred by more patients due to its treatment-friendly nature.<sup>7</sup> Similar results were also reported by Izadi et al,<sup>8</sup> they demonstrated that the clearance rate was 79.2% in the thermotherapy group, which is higher than 58.3% in the cryotherapy group; besides, the rate of scarring in the thermotherapy group was also lower.

The mechanism of this treatment may be to clear multiple warts by activating a systemic-specific immune response against HPV. The heat applied during hyperthermia can cause changes in the local environment, including increased blood flow and increased cellular metabolism. These changes can stimulate the immune system, leading to an increase in the production and activity of immune cells. It is well-accepted that hyperthermia can enhance the activity of natural killer cells, which are an important part of the body's immune system. In addition to enhancing the activity of natural killer cells, hyperthermia can also increase the production of cytokines, which are proteins that help regulate the immune response. Moreover, hyperthermia has also been shown to increase the permeability of cell membranes, which can make it easier for immune cells to access and attack infected or abnormal cells.<sup>9</sup> Moderate hyperthermia treatment can promote the migration and maturation of Langerhans cells (LCs) and enhance the antigen presentation ability of LCs, and induce HPVE2 gene mutation, cellular regulation and autophagy.<sup>10</sup> Currently, studies on the application of hyperthermia treatment to HPV-infected diseases mainly concentrate on the treatment of flat warts, condyloma acuminata and plantar warts, and there are also case descriptions of successful treatment of periungual warts with local hyperthermia treatment.<sup>11,12</sup> However, our patient had a combination of both multiple plantar and periungual warts, involving multiple

areas of the hands and feet. Besides, the patient showed no response to conventional treatment due to the large therapeutic range and many treatment sites. To our knowledge, it is the first clinical case report of the successful application of local hyperthermia treatment to treat multiple plantar warts combined with periungual warts, which provides a good basis for effective clinical treatment of multisite intractable warts. However, a few resistant warts may resolve spontaneously which are hard to exclude, thus further studies are required.

## Conclusion

This case report shows that local hyperthermia treatment is an alternative treatment for multiple, recalcitrant, and site-specific warts. Because treatment of multiple warts is challenging and often yields unsatisfactory results, further systematic studies of more patients and long-term evaluation of recurrence after treatment are needed to identify the effectiveness of local hyperthermia treatment in long-term follow-up.

## Consent Statements

Written informed consent was provided by the patient to have the case details and any accompanying images published. Institutional approval was not required for this case study.

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## Disclosure

The authors have no conflicts of interest to declare for this work.

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