

THERAPEUTIC HOTLINE

Clearance of genital warts in pregnant women by mild local hyperthermia: a pilot report

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ABSTRACT: Genital warts acquired during pregnancy tend to grow fast, and management is challenging. We treated two cases of primipara with extensive genital warts by local hyperthermia at 44°C for 30 minutes a day for 3 consecutive days plus 2 additional days 1 week later, then once a week till there showed signs of clinical regression. The warty lesions in the patients resolved in 5 and 7 weeks, respectively. There was no sign of recurrence during a 6-month follow-up. This suggests that local hyperthermia seems to be a promising method for treating genital warts in pregnant women.

KEYWORDS: genital warts, hyperthermia, pregnancy

Genital warts are a common infection of the anogenital epithelium caused by human papillomavirus (HPV) and are usually transmitted sexually. Anogenital HPV-related lesions occur more frequently or worsen during pregnancy (1). Genital warts in pregnant women pose a treatment challenge. Selection of treatment options is restricted because of concerns about the effects on the mother and fetus (2). Ablative carbon dioxide laser is commonly used for genital warts in pregnant

women. However, this method is undesirable because of its destructive nature, possible secondary infection, scarring or ulceration, and it is a painful experience for the patients with a long healing time, especially in patients with extensive lesions. The recurrence rate is about 5–50% (3).

Local hyperthermia (such as hot water and Neodymium-doped Yttrium Aluminum Garnet Laser) has been used in treating different clinical types of HPV infection, such as plantar warts and common warts. The cure rates vary greatly from 41 to 93.5%, possibly due to differences in hyperthermia conditions (from 40–150°C), the protocols (successive or intermittent hyperthermia), and/or responsiveness of specific conditions (4–6). We recently reported that intermittent mild local hyperthermia at 44°C for 30 minutes cleared 53.57% of plantar warts (7). In the study, we used a patented hyperthermia device with a light source from a tungsten-halogen lamp (Patent No. ZL

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200720185403.3, China Medical University, Shenyang, China) (7), most (>90%) wavelengths were from 760 to 2300 nm, with a peak wavelength at 1200 nm (data supplied by the lamp supplier). Heat emitted by the device was concentrated locally on designated skin areas without direct skin contact. Using a similar protocol, we treated two pregnant women with extensive genital warts. The patients were reviewed weekly. The trial was approved by the Ethics Committee of China Medical University (2009 no. 22).

Case 1

A 24-year-old otherwise healthy primipara at 8 weeks of gestation noticed a warty rash on her genitalia for 1 week. She was diagnosed with condyloma acuminata at her local hospital. She refused to receive laser surgery because of concerns that aggressive treatment might affect the fetus. The warts were asymptomatic, and there was no associated bleeding or vaginal discharge. Physical examination revealed red, cauliflower-like papules and coalescing plaques covering the entrance to the vagina (FIG. 1a). Gynecological exam found similar masses on her vaginal wall. HPV type 6 was identified from the scrapes of the lesion by flow hybridization and gene chip (Hybridio, Fujian, China). HIV antibody screening and serological tests for syphilis were negative. With her consent, we chose a confluent plaque as the target lesion (circled in FIG. 1a). The target lesion was subjected to local hyperthermia at 44°C, once a day for 3 consecutive days, each treatment lasted 30 minutes. A week later, the patient received two more consecutive treatments. Then the patient was followed-up once a week, at 4 weeks after the first treatment, there was an obvious decrease in the size of the lesions, both the targeted and adjacent lesions (FIG. 1b) with complete resolution of the

warts at the fifth week after treatment (FIG. 1c). The patient experienced a burning sensation and a transient stabbing pain in the treated area during the treatment procedure, the pain abating several minutes upon cessation of the treatment. The patient scored the severity of pain at 5–6 by a 0–10 ascending visual analog scale (0, no pain; 10, excruciating pain). The lesions on her vaginal wall were examined 1 month postpartum, and had resolved. No other significant side effects, such as blistering, dyspigmentation or scar formation were observed. There was no sign of recurrence during a follow-up period of 6 months. The patient delivered a healthy baby at full term by cesarean section.

Case 2

A 20-year-old otherwise healthy primipara at 24 weeks of gestation noticed had a warty rash on her genitalia and peri-anal region for two months. The warts gradually increased in size. HPV type 11 was identified. We choose a perianal wart (the largest one) as the target lesion (FIG. 2a). We applied the same protocol as for case 1. Five weeks after completion of the last treatment, the lesion had decreased in size (FIG. 2b) with complete resolution of her wart at the seventh week after treatment (FIG. 2c). The patient also felt a temporary burning sensation and a transient stabbing pain at the treated site, scored at 3–4 by visual analog scale. There was no sign of recurrence during a 6-month follow-up. The patient delivered a healthy baby at full term by cesarean section.

Discussion

There are certain conditions that immunocompromised states may predispose an individual to the acquisition or worsening of HPV infection. AIDS

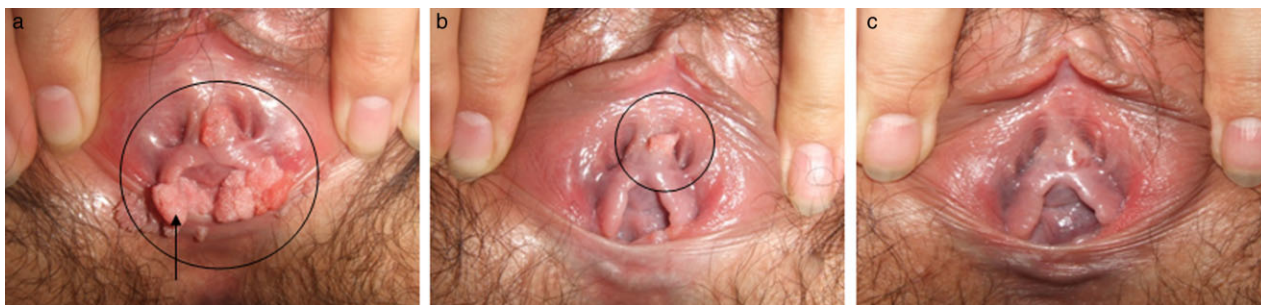


FIG. 1. Genital warts (cycled) treated with local hyperthermia at 44°C. Targeted lesion: arrowhead. (a) before treatment; (b) 4 weeks after treatment; and (c) 5 weeks after treatment.



FIG. 2. Genital warts (cycled) treated with local hyperthermia at 44°C. Targeted lesion: arrowhead. (a) before treatment; (b) 5 weeks after treatment; and (c) 7 weeks after treatment.

patients have a higher incidence of HPV infection, which are resistant to clearance by immune response modifier treatment (2,8). Genital HPV-related lesions occur more frequently or worsen during pregnancy. The HPV prevalence rate among pregnant women ranges from 5.5 to 65.0% (1). Pregnant women are not immunosuppressed in the classic sense, but the immunologic changes of pregnancy may induce a state of increased susceptibility to viruses, because of a shift from cell-mediated immunity to humoral immunity, which renders the mother tolerant to fetal antigens by suppressing cell-mediated immunity while retaining normal humoral immunity (9). Selection of treatment options for genital warts in pregnant women is challenging for both practitioners and the patients. Conventional treatments, including ablative, keratolytic, or cytotoxic agents, may cause pain, blistering, burning sensation, local irritation, itching, bleeding, secondary infection, scar, or ulceration, as well as high recurrence rate (10). Patients, as in the present cases, are reluctant to receive the ablative measures, for fear that ablative treatments may disturb their pregnancy or affect the fetus. The remarkable advantage of local hyperthermia is its high tolerability to patients. And the patients can tolerate the hyperthermia without local anesthesia. The disadvantages are temporary burning sensation and a transient stabbing pain at the treated site. Patients' tolerance of the local heating temperature depends on the site of the warts, for example, patients with common warts on their hand tolerate local hyperthermia temperatures at 43.5°C on average, for 30 minutes, those

with plantar warts on the soles of the feet tolerate temperatures of 45.3°C on average, for 30 minutes (11). Our patients tolerated local hyperthermia at 44°C for 30 minutes well. Side effects were minimal, except moderate heating and a burning sensation. It should be noted that tissue temperature of deep skin may be higher than the surface temperature because of transmission and accumulation of heat energy (12).

The exact mechanism of wart clearance in our approach is still unclear. Local hyperthermia could promote migrational maturation of Langerhans cells (13), stimulate cytotoxic and apoptotic effects (14), and induce production of endogenous interferon in genital warts (15). In the two cases, we noted that patients with multiple warts experienced almost simultaneous clearance of targeted warts as well as the remaining untargeted warts (in case 1, remote warts on the vaginal wall were unable to be followed regularly because of the patient's fear of virus transmission by examination). This phenomenon was also observed in our previous trial (11). We suggested that hyperthermia plays an indirect yet facilitating role in the specific immune response against HPV infection.

In summary, local hyperthermia was safe and effective treatment for anogenital warts in two pregnant patients. A randomized controlled trial is warranted to validate the efficacy of the method.

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