The management of vulvovaginal warts using intraloesional Bacillus Calmette–Guérin immunotherapy

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Abstract

Genital warts/condyloma acuminata is the most common mucosal human papillomavirus (HPV) infection encountered by the dermatologists. They can be asymptomatic or symptomatic. They can present as discrete lesions or confluent masses. Depending on the HPV strains, lesions can either be benign or may turn malignant. The treatment modalities for genital warts range from topical, systemic, intraloesional immunotherapy, and surgical interventions (intraloesional immunotherapy has shown promising results in the treatment of viral and genital warts). However, there are very few reports that have used Bacillus Calmette–Guérin (BCG) as immunotherapy in genital warts. Here, we report, in author’s opinion, the first case of female vulvovaginal warts successfully treated with intraloesional BCG immunotherapy, leading to complete resolution of injected warts as well as near-distant warts.

Key words: Bacillus Calmette–Guérin, genital warts, immunotherapy, intraloesional immunotherapy, vulvovaginal warts

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INTRODUCTION

Condyloma acuminata is the manifestation of human papillomavirus (HPV) infection that either present as discrete papules, plaques or confluent, cauliflower-like masses that are pink, tan brown, or skin colored usually affecting the partially keratinized epithelium such as frenulum, corona, glans penis, prepuce, shaft, scrotum in males and labia, clitoris, perineal area, perineum, vagina, cervix in females. Perineal, perianal, anal canal, rectal, urethral meatus, urethra, bladder, and oropharynx are affected in either sex.\textsuperscript{[3]} In an immunocompetent individual, the warts may either self-regress or require treatment, especially if symptomatic and to minimize the chances of sexual transmission. There are various modalities available for the treatment. We present a case of female patient with extensive genital warts whom we administered intraleisonal immunotherapy in the form of Bacillus Calmette–Guérin (BCG) vaccine.

CASE REPORT

A 30-years married, homemaker presented in the outpatient department with complaints of progressive growth over the genital area for the past 3 months. The growth over the genital area initially started as a small pea size and gradually progressed to the present size. It was associated with intense itching and pain. She had a history of on and off burning micturition and dyspareunia for the past 5 years for which she had taken multiple courses of antibiotic with little response. She had two male children of 5 years and 3 years with no history of abortion. Her husband was a driver by occupation, and on examination, he did not have similar lesions on the genital area. On her examination, there were multiple hyperpigmented papules and plaques of variable size, with verrucous surface, over mons pubis, labia majora, labia minora, surrounding the urethral meatus, and the vaginal introitus [Figure 1]. There was no vaginal discharge. On per speculum examination, a growth was visible in the cervical area with a rough surface.

Her routine blood investigations were within normal limits. Her viral markers (HIV I and II, hepatitis B antigen, and anti-hepatitis C virus antibodies) were negative. The serological test for syphilis was nonreactive.

She was initially prescribed topical imiquimod 5% and systemic therapy (oral zinc) for 1 month, but she did not respond, and lesions were increasing. Hence, the treatment was stopped, and she was treated with intraleisonal immunotherapy in the form of BCG injections at the affected site in a dose of 0.1 ml/cm\textsuperscript{2} at the base of the warts (the maximum being 0.5 ml or injecting 5 warts) in one sitting. The injections were moderately painful but tolerable. The patient was followed up after 1 week where she complained of the appearance of inflammatory swelling in the vulval area, along with fever, that appeared 1–2 days after applying the injections and gradually regressed in the next 5 days. Four weeks later, when the patient came for the second sitting, per speculum examination was also done that showed intravaginal wart extending up to the external os of the uterine cervix [Figure 2]. The intraleisonal injections were given to other uncovered areas in the first sitting and also intravaginally but not to previously treated area as most of those lesions were regressed. The patient was followed up for 4 weeks later, and there was a complete regression of all the warts after it [Figure 3]. Per speculum examination was also done at the follow-up to see the status of intravaginal wart and even that had regressed.

DISCUSSION

Genital warts are mucocutaneous manifestations of HPV. Genital warts are predominantly caused by the HPV strains of 6, 11, 16, 18, 31 and 33. They are usually benign and asymptomatic. However, in certain cases, there may be itching, burning, bleeding, vaginal or urethral discharge, dyspareunia, and obstruction (in cases of larger mass).\textsuperscript{[3]} The therapeutic options include topical therapy (imiquimod, podophyllin, and sinecacheticin), systemic therapy (zinc, cimetidine, levamisole, echinacea, and propolis), intraleisonal agents (Mycobacterium w (Mw) vaccine, BCG vaccine, purified protein derivative (PPD), Measles, mumps and rubella (MMR) vaccine, candida antigen, trichophyton antigen, tuberculin, Vitamin D3, and interferon alpha 2b), surgical interventions (cryosurgery, laser, and electrosurgery), and autoinoculation.\textsuperscript{[3]} Of these, the topical and surgical interventions act locally and target the warts. However, systemic therapy, intraleisonal agents, and autoinoculation act as immunomodulators. Intraleisonal immunotherapy basically causes delayed-type hypersensitivity against the wart tissue and other antigens. They activate the cytotoxic Th1 cells and natural killer cells that eradicate the HPV infection.\textsuperscript{[3]}
Our patient was initially prescribed topical imiquimod 5% and systemic therapy (oral zinc) for a month, but she did not respond. She was apprehensive about the surgical interventions and did not consent for the same. Since her lesions were constantly increasing in size and number, and she also had symptoms, we resorted to immunotherapy with BCG vaccine (cheap and easily available). After giving two injections, not only her warts regressed but also she was symptom free. Per speculum examination showed that her intravaginal wart had also regressed.

The principle behind using BCG vaccine is the delayed hypersensitivity response against the HPV antigen that produces a clinical response against the warts. It increases the serum levels of interleukin (IL)-12 and decreases the level of IL-4. Furthermore, it stimulates the T and B lymphocytes and NK cells that help in clearing the viral wart.

There are studies that have demonstrated the effect of BCG in clearing the warts. Two different studies showed the effects of topical BCG in clearing the genital warts (60% and 80% of patients in treatment groups). Another therapeutic intervention showed the effect of single-dose BCG intralesional therapy in clearing the genital wart. Other studies compared the effect of intralesional BCG versus intralesional 5-fluorouracil (5FU) in viral warts where BCG was found to be effective, and the injections were more tolerable. Another study showed the effectiveness of intralesional BCG vaccine in not only clearing the injected wart but also clearing the distant wart. A recent double-blind, randomized study compared the effectiveness and safety of intradermal BCG vaccine with intradermal PPD in the viral warts, and there was a significantly greater reduction in the mean number of warts in the former group than the latter. Nofal et al. used intralesional BCG for recalcitrant viral warts which showed a promising result and led to the resolution of not only the treated wart but also the distant ones. Another case series on seven patients demonstrated regression of warts in 85.7% and complete clearance in 28.6% of patients.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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