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The Condyloma Acuminatum's Recurrence Can Be Reduced by Lesional Auto-Transplantation

Epipode Ntawuyamara[1,2], Bashir Zeeshan[1], Yuan Liang[3], Yanhua Liang[1*]

[1]Department of Dermatology, Cosmetology and Venereology, Shenzhen Hospital of Southern Medical University, Shenzhen, China
[2]Department of Dermatology and Venereology, Kamenge Teaching Hospital of University of Burundi, Bujumbura, Burundi
[3]Shenzhen (Nanshan) Concord College of Sino-Canada, Shenzhen, China
Email: *liangdoctor@163.com

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Abstract

Background: Condyloma acuminatum (CA), also known as a genital wart (GW), is a sexually transmitted disease caused by human papillomavirus (HPV). HPV lesions, recurrence tendency, and risk of malignant formation are primarily dependent on the person's immunity level. GW recurrence is a major challenge in CA treatment. The aim of this study was to explore how lesional auto-transplantation (LT) can be used to treat CA and decrease its recurrence. **Methods:** We treated CA through the preparation and implantation of tissue from nine CA patients in our dermatology clinic. Transplantation of small pieces of HPV lesions to the subcutaneous fat of the inguinal region was carried out with the help of a simple surgical method under local anesthesia. Patients were followed up for six to eight months. We searched PubMed and the Web of Science for treatment options for CA to compare our treatment method recurrence rate with existing treatment options. **Results:** During three months of follow-up, seven patients experienced no recurrence of condyloma lesions, while two patients experienced recurrence of small lesions of condyloma acuminatum. The recurrence rate of CA once treated by auto-transplantation was relatively low compared to other CA treatment options. **Conclusions:** Transplantation of HPV lesions to the inguinal area reduces the recurrence rate in sexually active individuals. The 2/9 recurrence after implantation could be due to poor hygiene, sexual relationships or immune factors.

Keywords

Auto-Transplantation, Condyloma Acuminatum, Human Papillomavirus, Recurrence

1. Background

Condyloma acuminatum (CA), often known as genital warts (GWs), is a sexually transmitted infection (STI) caused by human papillomavirus (HPV) types 6 and 11. HPV is the most common STI and is frequently transmitted from one individual to the next after the first sexual activity [1] [2]. HPV is transmitted through direct skin-to-skin contact with an infected person, most commonly during intercourse. The term "HPV" does not describe a single specific virus. It is a group of double-stranded DNA viruses with several characterized subtypes [3]. The CA presents the clinical features of epidermal lesions in, over and around the genitalia. It usually appears near moist surfaces but may include dry surfaces as well. Subclinical lesions have oncogenic and infectious potential. The prevalence of genital HPV infections is estimated to be between 10% and 20%, with only 1% showing clinical manifestations. The rate of HPV infection has been on the rise, and approximately 80% of those affected fall within the age range of 17 to 33 years, with the highest occurrence observed among individuals aged >20 to 24 years. Moreover, men are prone to GWs, which could be due to a less hygienic environment or multiple sexual partners. However, the infection may be more prevalent in women.

Therapeutically, there is no basic cure for HPV infection, but the elimination of HPV lesions is needed because this approach would be very beneficial for patients and reduce the risk of developing malignancies. However, further evidence that the recurrence or transmission of viral infection can be reduced by removing visible lesions is still lacking. To treat confirmative HPV lesions, various treatment modalities, such as salicylic acid, trichloroacetic acid, microwave treatment, retinoids, podophyllin, levamisole, imiquimod and zinc sulfate, were used. None of them achieved a full cure without the possibility of recurrence. Additional treatment options include radio cautery, cryotherapy, surgical excision, and the use of a carbon dioxide laser. Nevertheless, it is important to note that these approaches carry a significant risk of scarring [4] [5].

In the case of pharmacological methods, medicines are applied topically on cutaneous surfaces, although these agents may cause a skin reaction or local allergic side effects. On the other hand, surgical ablation is a much quicker and more efficient method for removing superficial wart lesions. A number of surgical procedures are available for the treatment of CA [6].

Prevention of CA recurrence is highly essential for the new generation for many reasons. The patient may experience pain and additional treatment expenditures again due to recurrent viral lesions. Repeated viral attacks also cause self-discomfort, social dissatisfaction, relationship problems and mental distress. These factors may cause patients to not visit medical centers, which increases susceptibility to disease severity, complications, and vulnerability in the form of cancer. Vaccination for HPV is still unavailable in many countries. Poor medical facilities and inadequate health funding also cause an increase in viral disease incidence in many third-party countries worldwide. Considering all the reasons cited above, in this study, we explored a therapeutic technique to decrease recurrent viral attacks

in HPV-infected people by transplanting the viral pathogen into other body areas.

2. Methods

2.1. Study Settings

The research was carried out at the Dermatology, Cosmetology, and Venereology Department of Shenzhen Hospital, which is affiliated with Southern Medical University. Nine patients who were diagnosed with CA and willing to participate in this study were enrolled and treated by auto-transplantation after providing informed consent.

Diagnosis and treatment procedure

Clinical features and acetic acid tests were used for diagnosis. All other STDs, including syphilis, HIV/AIDS, chlamydia and gonorrhea, were ruled out for better experimental results. Patients were briefed about their medical status, disease progress, disease complications, and plans to deal with the lesions before auto-transplantation.

The procedure consists of three steps:

The first part included patient preparation for surgery. Infected lesions were sterilized with gauze and povidone-iodine tincture. The specimens that were required to be transplanted were chosen according to their size, location, and clinical appearance. Local anesthesia was applied with the help of 2% xylocaine hydrochloride without adrenaline around and under genital warts. Surgical or CO_2 ablative treatment is typically performed for CA, but the only difference in our study was the removal of the wart lesions and the transplantation of the lesions to another body area. Defined incisions were made around the HPV lesions with a surgical blade, and the whole cauliflower-like cluster was removed for transplantation. Additional clusters of HPV lesions were removed with the help of the same surgical blade, after which the lesions were ready for transplantation through the designated area. For short and not very classical GWs, a CO_2 laser was used. Bleeding due to the incision was stopped either by the pressure method or with the help of the laser ligation method.

The second part of the procedure involved preparing and transplanting the incised cluster of CA tissue. Small Metzenbaum scissors were used to cut the incised lesions into many small pieces that could be easily implanted into the target area. A 2 cm incision was made over the inguinal region. A space was drawn between the subcutaneous fat under the incised skin with the help of forceps. Half of the incised wart lesions were implanted into the subcutaneous fat precisely and adequately. Two to three surgical sutures (number 0.4 - 0.75 cm long and 18 mm needle diameter) were made after the lesions were inserted into the subcutaneous fat. The same procedure was repeated on the second side of the inguinal area to attain the maximum result.

Third, in the last part of this new treatment, all remaining HPV lesions were removed with the help of CO_2 laser therapy. All the bones were cleared of any genital lesions.

2.2. Postoperative Follow-Up

All patients who agreed to participate in the study completed the follow-up period. Patients were advised to return to the hospital the next day to receive a new wound dressing and for further examination. All patients were followed up for six to eight months. The primary aim of this follow-up was to rule out inflammation, pain, swelling, itching, recurrence or any other irritating conditions.

2.3. Data Collection and Presentation

The proper medical history and full demographic data were collected for each enrolled patient. The data were collected on the basis of age, sex, lesion site, duration and number of lesions, recurrent attacks, and postoperative follow-up duration in an Excel file. We searched the PubMed and Web of Science recurrence rates of CA treated by different modalities for comparison with our new method. The results are presented in the table and figures.

3. Results

Nine patients, including six males and three females, received lesional transplantation therapy. Among these nine patients, the ages ranged between 20 and 29 years in females and between 23 and 46 years in males. In male participants, HPV lesions were found on the penile foreskin, penile shaft, penile body, penis glans, frenulum, corona and around the pubic area, while in female patients, HPV lesions were present on the labia majora, labia minora, vestibule, perineal body and around the vaginal opening. The size of the CA lesions ranged from 0.1 cm to 0.5 cm in diameter. Most of the lesions presented a nodular or cauliflower-like appearance. However, some lesions are round or oval-shaped. All patients tested negative for HIV infection, gonorrhea, Chlamydia and trichomoniasis.

Seven patients (77.8%) did not experience any recurrent attacks after the initial surgical or auto-transplantation therapy, while two patients experienced recurrent attacks during the six-month follow-up duration. All female patients achieved complete remission of the CA lesions. Among the six male patients, four were negative for recurrent attacks, while two were positive (Table 1). Among those two patients who had recurrent complaints, one patient had recurrent lesions only once, while the other patient came to the hospital four times with recurrent GW.

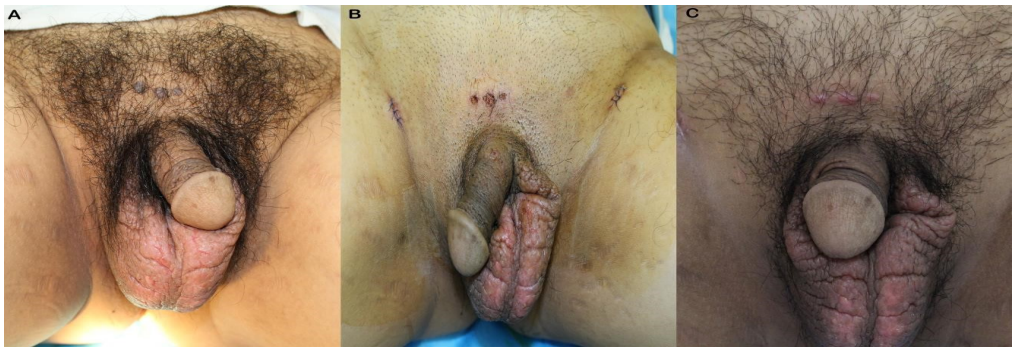
Table 1. Patients presentation.

Gender	Male	Female
Number of participants	6	3
Age level (years)	24 - 50	22 - 28
Size of lesions(cm^2)	0.1 - 0.5	0.1 - 0.3
Duration of CA presentation (months)	1 - 6	1 - 4
Recurrent attacks (persons)	2	0

The treatment outcomes are illustrated in Figure 1 for female patients and for males (Figure 2).

(a) (b) (c)

Figure 1. Clinical changes of a female at different time points. (a) Before procedure; (b) Immediately after the procedure; (c) 60 days after the procedure.



(a) (b) (c)

Figure 2. Clinical changes of a male at different time points. (a) Before procedure; (b) Immediate after the procedure; (c) 15 days after the procedure.

Recurrence rates in patients receiving several treatment options, such as imiquimod (50% - 73%), podophyllin (46% - 60%), a carbon dioxide laser (2.5% - 77%), trichloroacetic acid (18% - 36%), 5-flurouracil (50%), and interferon (9% - 69%), were greater than the 22.2% reported in our study (Table 2).

Table 2. The recurrence rate of condyloma acuminata treatment options.

Treatment	Success rate (%)	Recurrence rate (%)
Imiquimod	89	50-73
Trichloroacetic acid	66 - 100	18 - 36
Podophyllotoxin	70 - 100	45 - 94
Sinecatechins	40 - 81	7 - 12
Cryotherapy	46 - 96	18 - 39
Surgery	89 - 93	18 - 65
CO_2 laser	23 - 95	2.5 - 77
Podophyllin	42 - 46.9	46 - 60

Continued

Photodynamic therapy	76 - 100	10 - 14
Electrosurgery	35 - 94	20 - 25
Immunotherapy	66 - 98	2
5-fluorouracil	10 - 50	2 - 50
Interferon	17 - 67	9 - 69
Isotretinoin	39 - 60	9.5
Electrocautery	93	24
Cidofovir	90.91	9.09

4. Discussion

The recurrence rate of CA is very high, reaching 100% in some studies [7] [8]. This fact constitutes a big challenge in CA treatment. CA causes numerous physiological and psychological problems due to its high likelihood of recurrence [9] [10]. In most cases, patients visit medical centers to seek better and faster cures for GW, but recurrent viral infections usually cause considerable frustration. Such persistent behavior of CA makes it a crucial disease to address in the modern era [11]. Different types of treatment, such as imiquimod, immunotherapy, CO_2 laser therapy, PDT, and cidofovir isotretinoin, are used to treat CA, but frequent therapies are required to address recurrent attacks.

Our study ultimately revealed the enormous impact of this virus on the lives of many HPV-infected individuals and improved treatment methods by preventing repetitive disease. The principle behind auto-transplantation is to trigger cell-mediated immunity, which is unaffected by HPV infection, by introducing a larger amount of the same antigen at a site where a robust immune response can take place. A single wart is completely removed, and the minced particles are subsequently inserted into a dermal pocket. Planting of incised pathogens in the same infected person will lead to a scenario of resistance against that particular viral infection and cessation of further growth. The similar technique was described by Gordon Falkner in 1969 with higher cure rate. The technique is based on the rationale that the creation of small "prickles" inside the wart which destroy HPV-infected cells stimulates an immune response [12]. Needling technique for treatment of plantar warts is unfortunately widely unknown and underused within dermatology [13].

In this study, we planned to establish immunity from previous viral lesions to further decrease disease manifestations. After pathogens are propagated to the subcutaneous fat, the infection cannot be established in the subcutaneous area due to the structural and pathogenic capacity of the virus in the subcutaneous region [14]-[16]. On the other hand, body immunity works more efficiently when the pathogen is in a mute state, producing antibodies against it. Later, these antibodies are transferred to the blood and slowly circulate to all body areas even over the

genital tract so that secondary attack will be terminated much easier and faster. This methodology also facilitates body immunity against other identical viral attacks, as has just been demonstrated in other studies [17].

Our results indicated that seven patients (77.8%) were negative for recurrent HPV infection after the initial surgical implantation of pathogens in inguinal sites, while the remaining (22.2%) patients were positive for recurrent HPV infection. During our study, we reviewed existing treatment modalities for CA and their recurrence rates. Our technique's recurrence rate was relatively low in comparison to other treatment options such as Imiquimod (50% - 73%), podophyllin (46% - 60%), podophyllotoxin (approximately 38%), Carbon dioxide laser (2.5% - 77%), trichloroacetic acid (18 - 36%), 5-Flurouracil (50%), Interferon (9% - 69%) [7]-[9] [18]-[23]. The findings of this study exhibited improved outcomes in contrast to the findings of Shivakumar *et al.*, in which a significant 73.3% of warts were completely cleared, with the majority of them (91%) experiencing clearance within a span of two months [17]. Nischal *et al.* used this therapy in the treatment of multiple recurrent palmoplantar warts, for which the clearance rate was 74.1%. Our results are also higher than those of similar techniques used for non-genital warts, for which 60.6% of the procedures were successful. Various studies have shown that subcutaneous embedding of autologous warts improves immune function and antiviral ability. It can effectively prevent the early recurrence of GW and has good clinical efficacy in the treatment and prevention of GW; thus, it is worth promoting clinical efficacy [5] [24] [25].

All patients were advised to maintain the operative sites clean and dry to attain effective results. Throughout their treatment interval, no patients received any physical ablative medication or any other photodynamic therapy (PDT) over the lesional sites. It is a low-priced experimental treatment used to treat and control CA, whereas other therapies cost more money and time. Other procedures, such as PDT and repeated CO_2 laser surgeries, are more painful than our experimental procedure. Our methodology of transplanting the pathogen to subcutaneous fat will limit all extra expenses and decrease patient discomfort.

Recurrent attacks in those two individuals can be explained by either failure to maintain the postoperative sanitary atmosphere or persistent viral exposure. Moist skin is known to be more favorable for virus growth and the production of warts [26]. This is the reason why it is important to maintain postoperative hygiene, and a dry environment decreases the vulnerability of viruses to attack. Another reason why a patient experienced a single recurrent attack in one week can be presumed to be that the new wart may indeed have arisen from previous lesion sites or scars that were not visualized during the first surgery or during CO_2 laser therapy. These viruses may reside in the skin epithelium in the latent stage and cause disease when they reach a suitable environment. After secondary CO_2 laser treatment, no recurrent lesions were recorded.

This method is similar to vaccination after that, weak or identical disease pathogens are given to individuals to create antibodies against the required disease

[27] [28]. Anti-HPV vaccination in case of high recurrence of GW could represent an immune booster to resolve the lesion. Vaccines targeting the E1 and E2 early proteins combined with immunomodulators would be a good combination [29]. However, many countries' health systems still do not involve HPV vaccination in the local medical system, implantation of such technique would be favorable and decrease the incidence of HPV in local populations. Once this technique is used in the local health care system, we expect that the recurrence rate of typical HPV infection will be reduced and that the burden of expenditure on patients can also be minimized compared to that of other therapeutic methods.

Once this technique is used in the local health care system, we expect that the recurrence rate of typical HPV infection will be reduced and that the burden of expenditure on patients can also be minimized compared to that of other therapeutic methods. As many countries' health systems still do not involve HPV vaccination in the local medical system, implantation of such techniques would be favorable and decrease the incidence of HPV in local populations.

After explaining our treatment technique, some patients did not consent to this surgical technique, and the number of participants was not high. To obtain the maximum results from this new technique, a larger sample size and longer follow-up may support the discoveries of the present work.

5. Conclusion

This study revealed that auto-transplantation of HPV lesions to other body areas is associated with a low recurrence rate in people diagnosed with GW. This implantation will introduce new immunity against the very specific pathogen that has been implanted. This newly formed immune system helps to decrease recurrent attacks in the CA within the same person. This treatment method will also be highly beneficial because of its low cost and decreased pain compared to other ablative treatments.

Availability of Data and Materials

The data are available upon request.

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Authors' Contributions

Conceptualization, methodology: Zeeshan Bashir; formal analysis and data curation: Yuan Liang; writing, original draft preparation, review, editing and submission: Ntawuyamara Epipode; supervision: Yanhua Liang. All the authors have read and approved the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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