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Case Report
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Electrosurgery and 5% Imiquimod Cream as a Combination Therapy for Perianal Condyloma Acuminata in a HIV Patient

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ABSTRACT

Background: Condyloma acuminata (CA) is a common sexually transmitted infection caused by the human Papillomavirus (HPV) infection. It is characterized by single or multiple lesions in the anogenital area accompanied by itching, discharge, or bleeding. CA in HIV (human immunodeficiency virus) - positive patients can experience a low response to various therapeutic modalities, which may lead to consideration of choosing combination therapy to increase the effectiveness of therapy. **Case Report:** We report a case in a twenty-one-year old male with multiple warts on the perianal area. Within four months, the warts had covered the perianal area, with hemorrhoids emerging as complications. The patient had trichloroacetic acid treatment three times but did not respond. The patient is male who have sex with male, and there has been a history of multisexual partners. The diagnosis was made by clinical and histopathological examinations. The patient is HIV-positive and has been receiving antiretrovirals regularly. He got a combination therapy of electrosurgery and 5% imiquimod cream for 9 weeks and showed excellent results. **Discussion:** Standard topical medication is an effective treatment for condyloma acuminata, but infiltrative and recurrent lesions often require ablative and surgical treatment. Electrosurgery in combination with imiquimod proved to be effective and shortening the treatment regimen in the treatment of perianal CA.

Keywords: Electrosurgery, Human Immunodeficiency Virus, Perianal Condyloma Acuminata, Imiquimod.

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BACKGROUND

Anogenital wart, known as condyloma acuminatum (CA), is an infection caused by the human papillomavirus (HPV). Types 6 and 11 are found to be the most common strains of HPV that manifest as anogenital warts. HPV is a deoxyribonucleic acid (DNA) virus that is mainly transmitted by sexual contact.[1,2]

With 9 - 13% of those infected in the global population, HPV infection has become the most prevalent sexually transmitted infection. Patients between the ages of 20 and 39 are the most frequently affected. The prevalence of CA increases with histories multiple sexual partners, gonorrheal and chlamydial infections, and infection with HIV.[1,3–6] Anogenital warts have a global incidence that ranges from about 160 to 289 cases per 100,000 individuals/year.[7] Immunosuppressive conditions, particularly in patients with HIV, are tenfold more likely to cause condyloma acuminata, and homosexual men who are HIV-seropositive, have a higher risk of CA-infected, with a prevalence rate of 53%.[8]

Physical ablative treatments, such as electrosurgery, can be used in the perianal and intra-anal areas, whereas pharmacological treatment is indicated when the lesion only affects the perianal area.[7] In addition, CA in HIV-infected patients may have a poor response to various therapeutic modalities, thus leading to treatment combinations to increase the effectiveness of therapy.[8]

Imiquimod is a drug that regulates immune mechanisms and induces an immune response to achieve an antiviral effect.[9] In clinical studies, 35-75% of patients treated with imiquimod cream for up to 16

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weeks reported clearing warts completely.[10] Electrosurgery is a type of cytodestructive therapy. According to Gilson et al., the rate of recurrence treatment using electrosurgery for CA is 22%.[10-11] Persistent or recurrent genital warts should be considered a failure of previous treatment and often require more than one treatment. This case used a combination of electrosurgery and 5% imiquimod cream as treatment. The purpose of this case report is to find out the effectiveness of both treatments in an HIV-seropositive male, 21 years old, a man who has sex with men (MSM), who was diagnosed with perianal condyloma acuminata.

CASE REPORT

A 21-year-old male complained of warts appearing on his perianal in the last 4 months. Initially, there was only one small wart, then warts enlarged, multiplied, and almost covered the anal. Trichloroacetic Acid (TCA) with an 80-90% concentration was applied, but warts reappeared. Warts are not painful but they are itchy and bleed easily. There were no warts on the penis and surrounding areas.

In his previous medical history, the patient admitted that he had never had similar complaints before. There were no other complaints, such as sores on the genitals, discharge from the genitals, or pain in the testicles. The patient had a history of HIV since 4 months ago, which was discovered during a screening at the public health center after the patient experienced enlarged and multiplied warts which almost covered the anal. Since then, the patient has regularly taken antiretroviral (ARV) drugs. There was a history of hemorrhoid surgery in the past 3 months; currently, the complaints are improving.

The patient is MSM and has a history of anogenital and oro-genital sexual intercourse with two other males. During sexual intercourse, the patient alternates between top and bottom positions and never uses a condom. The patient had his first anogenital sexual intercourse when he was 19 years old. The patient was an active smoker.

Physical examination revealed multiple papules and plaques with a verrucous surface. There was no tenderness, and some papules were bleeding easily. Anoscopy could not be performed because the lesion covered most of the anal. The acetowhite test on the lesion was found positive (figure 1).

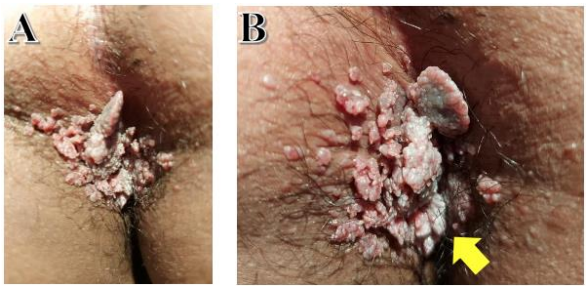

Figure 1. Physical Examination. A. Multiple papules and plaques with verrucous surfaces. B. Positive acetowhite test (yellow arrow).

Syphilis tests were non-reactive, while the result of the HIV rapid test was positive. Histopathology examination of the patient showed tissues containing tumor growth arranged in papillary structures that consisted of hyperplasia of parakeratotic squamous cells, acanthosis, and koilocytes with fibrovascular stalk. The conclusion was condyloma acuminata (Figure 2).

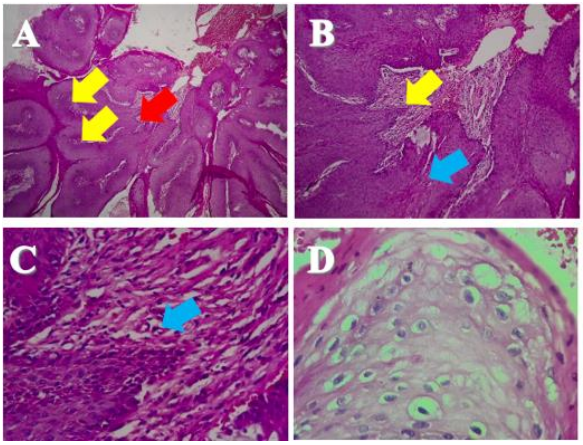

Figure 2. Histopathology examination. A and B. Tumor growth consisting of hyperplasia of parakeratotic squamous cells, acanthosis, and papillomatosis (yellow arrows) with fibrovascular stalk (red arrows). (x40 and x100; H&E). C and D. Koilocytes. (x400 and x1000; H&E).

The diagnosis of CA was established. The was treated with electrosurgery at 2-week intervals, followed by applying 5% imiquimod topical once daily every three days. After being treated with electrosurgery three times combined with imiquimod cream, physical and anoscopy examinations showed no new warts (Figure 3).

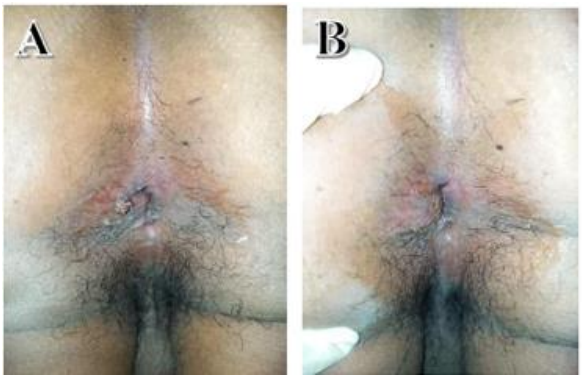

Figure 3. Post-therapy A. at week 6. Two new multiple verrucous papules emerged. Another session of electrosurgery was done. B. At the 8th week of observation, no new warts was found.

DISCUSSION

Genital warts or condyloma acuminata, are characterized by skin tissue or mucosal hyperplasia. Human papillomavirus (HPV), dominantly types 6 and 11, is known to be the causal of this sexually transmitted infection (STIs).[12]

Condyloma acuminata (CA), affects roughly 1% of the sexually active population. In the last five years, Indonesian Study Group of Sexually Transmitted Infections has reported an increasing trend of anogenital CA. This could be attributed to the peak period of sexual activity, with a high incidence of CA among people aged 19 to 26.[13]

Immunosuppressive conditions, receptive anal intercourse (RAI), multiple sexual partners, smoking, men who have sex with men (MSM), and transgender women are the risk factors for anal HPV.[1,14.] HIV patients have a 10-fold greater risk of CA compared to immunocompetent individuals. HIV-seropositive MSM have a higher risk of getting CA, with a prevalence rate of 53%.[8] A cohort study showed an association between the incidence of anal HPV and the number of partners. It was found that HIV-positive MSM with more sexual partners and new oro-anal partners who engaged in more frequent sexual intercourse with RAI were significantly more likely to have an incidence of anal HPV.[1]

Anal condyloma acuminata (CA), especially in MSM, often showed malignancy due to the content of squamous cell carcinoma and high-grade squamous intraepithelial lesions (HSIL). This is supported by histopathology findings in anogenital CA showing the coexistence of high levels of HSIL (more than 35% in MSM) in surgically excised warts. It can be concluded that HIV-infected men with anal CA are a population at high risk for developing anal squamous cancer. Therefore, special attention should be paid to clinical practice in this population.[7]

History and clinical examination are usually enough to diagnose most cases of CA. Additional supporting examinations are the acetowhite test, histopathology, cytology, colonoscopy, immunohistochemical, detection for HPV antigen, and HPV deoxyribonucleic acid.[11] Recently, the most sensitive technique for detecting HPV has been polymerase chain reaction (PCR).[13,15,16] Histopathology examination in CA shows hyperkeratosis and acanthosis accompanied by papillomatosis. Vacuolated koilocytes are usually seen in the upper malpighian layer. Keratohyalin granules are sometimes visible. An abundance of Langerhans cells indicates that they are functionally impaired. In this case, a histopathology examination was done to rule out the possibility of a risk of malignancy.[17] It displayed sections of tissue containing tumor growths arranged in papillary structures, consisting of parakeratotic squamous cell hyperplasia, acanthosis, and koilocytes with fibrovascular stalk.

The goal of CA treatment is to clear visible warts. Various therapeutic options are available for the treatment of CA, such as cytotoxic agents, physical ablation (electrical destruction and cryotherapy), and immunomodulators (Imiquimod, Interferon, pure protein derivatives, and vaccines for HPV). Despite the wide range of available therapeutic modalities for the treatment of CA, there is still no definitive therapy as a gold standard. Acid therapies such as BCA and 50% - 80% TCA cause skin breakdown by coagulation cellular protein. A cotton applicator is used to apply directly to the surface of warts. Acid therapies are suitable for small wart collections but are less effective for large warts. The clearance rate with this therapy is up to 80% within a few weeks, but the large size prolongs the treatment period.[18]

Electrosurgery is a type of cytodestructive therapy. The mechanism of action of electrosurgery is protein coagulation of the treated tissue. Electrosurgery requires a good ability to minimize scarring due to its risk of causing damage to deep thermal tissue, severe bleeding, scarring, and slow or delayed wound healing. Removal of warts by electrosurgery can be achieved up to 94%, with a recurrence rate of up to 18%.[19] Electrosurgery is fairly effective but painful and often requires local or even intravenous anesthesia, as in surgical excision.[20] Cauterization of internal lesions can be done under anesthesia to visualize the anal canal; thus, so electrosurgery is relatively better compared to cryotherapy.[20]

Imiquimod cream in a showed good efficacy for external anogenital CA, while it may increase the risk of severe inflammation if used for mucosal warts. However, a study by Irisawa et al. concluded that 5% imiquimod cream is safe to use on anal mucosa as long as it is used with the patient's consent and under supervision.[21]

Imiquimod acts as immunotherapy for external anogenital warts. It is applied three times a week and can be discontinued if warts are completely gone or 16 weeks for maximum use. The most common side effect of imiquimod is a local inflammatory reaction, but it is generally well tolerated.[22]

Clinical studies found that 35-75% of individuals treated with imiquimod cream for up to 16 weeks had completely cleared warts. A common side effect is local inflammation. If more severe reactions occur, clinicians can reduce the frequency or discontinue the medication immediately. Local side effects are more common when imiquimod is used daily, as it does not increase wart clearance when compared to a dose of three times a week.[12]

Prior to this case report, we could not find any studies on a combination of electrosurgery and imiquimod cream in perianal CA. Meanwhile, in persistent or recurrent genital warts, it is necessary to consider the failure of previous therapy, and more than one type of therapy is often needed. People with HIV generally have a weak response to all treatment modalities. Secondary infection may occur if ulceration is present and requires regular post-therapy monitoring.[10]

There were cases of severe CA that were treated with ablation or surgical methods followed by imiquimod to prevent a recurrence. In other cases, anogenital CA that had been pretreated with imiquimod cream was then treated by surgical excision to remove residual warts. Treatment with local therapy for external CA can be effective, but infiltrative and recurrent lesions often require a combination of ablative and surgical treatment.[23] Based on the theory described above, as therapy for perianal CA, a combination of electrosurgery and imiquimod is expected to effectively strengthen immune function by regulating cytokines and T lymphocytes, improve clinical efficacy, and lower the recurrence rate of anogenital CA with minimal side effects.

A case of recurrent CA has been reported in a 21-year-old male. The diagnosis of recurrent perianal condylomata acuminata is based on history, physical examination, and histopathology examination. The patient was treated with a combination of electrosurgery, followed by the application of 5% imiquimod creams. During the eighth week of observation, the warts were completely clear; there were no new warts discovered and there were no complaints of irritation in the application area of imiquimod. The combination therapy showed relatively rapid clearance of large perianal warts with no signs of new warts. Electrosurgery was discontinued but imiquimod cream was continued for up to 16 weeks to prevent a recurrence.

In our study, the treatment of CA with 80-90% TCA showed a limited response rate and high rates of recurrence. Our findings suggest that electrocautery therapy is a promising modality for safe and efficient treatment of CA when used in combination with imiquimod in HIV-positive MSM. Since this combination can easily be done in an outpatient setting, they could serve as first-choice treatment of CA in HIV-positive MSM.

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