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Case Report

Case Report: Combination of Electrocautery and Echinacea Therapy in Condylomata Acuminata

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ABSTRACT

Introduction: Condylomata acuminata or genital warts are classified as sexually transmitted infections caused by the Human Papilloma Virus. The main purpose of Condylomata acuminata treatment is to remove warts and prevent recurrence. Monotherapy is often unsatisfactory. Combination therapy can be done for a better response and minimizing recurrences, one of which is by using an immunomodulator, namely Echinacea.

Case Presentation: A 47-years-old woman, widowed, heterosexual, with complaints of genital warts since 2 months ago. Dermatovenerological examination on the major and minor labia showed papules with skin and mucosa color, verucose, multiple, no tenderness and no bleeding. Inspeculo examination found no lesions on the vaginal wall. The acetowhite test showed a positive white color. Patient was diagnosed with condylomata acuminata. The patient received electrocauter therapy once and Echinacea 500 mg for 3 months. Follow-up for 6 months did not reveal any new or recurrent lesions.

Conclusion: Therapy for condylomata acuminata is still challenging. Monotherapy is often unsatisfactory due to high degree of recurrence. The use of combination therapy is aimed at minimizing recurrences, one of which is the use of imunomudulator. In this case report, there were no relapses in the 6th month of follow up with combination treatment. These case report can increase knowledge about therapeutic options for CA to avoid recurrences.

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INTRODUCTION

Condylomata acuminata (CA), also known as genital warts or anogenital warts refers to a sexually transmitted infections (STIs) caused by the Human Papilloma Virus (HPV). HPV is primarily transmitted through contact with infected skin, mucosa, or genital fluids containing HPV (1,2) A study of the incidence and prevalence of CA worldwide shows that the incidence of CA per year ranges from 160-289 per 100,000 people per year. In Indonesia, the prevalence of CA in the community ranges from 5-19% [3,4].

The primary treatment goal is to eliminate wart lesions and prevent recurrence. Several standard regimental therapy or modalities therapy can be used, including podophylline tincture 10-25%, trichloroacetic acid (TCA) 80-95% solution, imiquimod 5%, surgical excision, frozen surgery, and electrosurgery. The ideal therapy for CA should be adequate (high clearance rate and low recurrence), with common local and systemic adverse effects. Monotherapy is often unsatisfactory, thus combination therapy is more beneficial [5]. Combination therapy, namely immunomodulatory agents including Echinacea, associated with better response rate and lower recurrences. Previous studies stated that Echinacea could be used as an immunomodulator in cases of genital warts and no recurrences were found [6]. Health professionals might consider Echinacea in high risk patient, recurrent lesions, multiple lesions, recalcitrant lesions, and difficult to treat areas [7].

We reported a case of condylomata acuminata in a 47-year-old woman treated with combination therapy, electrocautery and Echinacea as immunomodulator. Hopefully, this case report can increase knowledge

about the therapeutic options for CA in order that there is no recurrence.

CASE PRESENTATION

A 47-year-old woman presented to dermatology and venereology clinic of DR. Saiful Anwar Hospital, Malang, with multiple genital warts persisting in two last month. The warts were initially single and small in size before multiplying to a larger wart. There was no complaint of pain (VAS 2/10), the warts were not easily brittle nor bleed.

She never experienced similar symptoms previously and there were no other STI complaints. History of fever, prolonged cough, prolonged diarrhea, and significant weight loss were denied. History of using illegal drugs, needles, tattoos, or blood transfusions were also denied.

She is a household assistant, had been married once and had two children. During the marriage she never changed partner, had genito-genitally sex with her husband and did not use condoms. After her husband died, she admitted had changed sexual partners three times, in genito-genitally way, and never use condom. The patient had sex one month ago. Another STI complaints were denied.

Investigation

She looked mildly ill. Blood pressure were measured 120/80 mmHg, pulse of 88x/minute, respiratory rate of 16x/minute, and axillary temperature of 36.3°C. No enlargement of the neck, axillary or inguinal lymph nodes were found.

Dermatovenereological examination skin-colored papules and mucosa, multiple, verrucous surface, no tenderness, and not easy to bleed, in the major and minor labia (**Fig. 1**). Inspeculo examination showed there were no lesions on the vaginal wall.

The immunoserology examination of the Venereal Disease Research Laboratory (VDRL), Treponema pallidum Haemagglutination Assay (TPHA), and the rapid anti-HIV were found to be non-reactive.

Based on the historya and physical examination, the patient was diagnosed with condylomata acuminata. Patient received 1 x therapy session of electrocautery and 1 x 500 mg of Echinacea daily for three months. Patient receive post-operative wound care therapy with 0.1% gentamicin cream twice daily. There are no side effects during electrocautery therapy. HIV results, non-reactive TPHA VDRL.

Outcomes and Follow Up

She was suggested to have monthly check-ups to assess recurrence and was also educated about STI prevention, namely not changing sexual partners, using a condom during sexual intercourse, and checking the patient's sexual partner.

There were no new lesion found in third month follow-up. Dermatovenereological examination of the major and minor labia did not show the presence of lesions. Inspeculo examination did not find any lesions on the vaginal wall. There were no sign and symptoms of side effects during three months of Echinacea administration in the form of hypersensitivity reactions, anaphylaxis, urticaria, or digestive disorders.

Evaluation at sixth months, no new lesions were found. Dermatovenereological examination of the major and minor labia did not show the presence of lesions. Inspeculo examination did not find any lesions on the vaginal wall.

Fig. 1. Major and Minor Labia Regions of the Patient

DISCUSSION

Condylomata acuminata (CA), also known as genital warts, consists of epidermal and dermal papules/nodules caused by the human papillomavirus (HPV). HPV types 6, 11, 42, 43, and 44 are low risk and are associated with genital warts (types 6 and 11 cause HPV in 90% of cases), while HPV types 16, 18, 31, 33, 35, 39, 45, 51 and 52 are included in the high risk [1,2].

Risk factors include bisexual partners, frequent change of partners, sexual intercourse at an early age, sexual relations with unknown partners, and immunosuppressed states. Screening tests that need to be done are VDRL, TPHA, and HIV. Patient and partner education has an essential role in preventing recurrence [5,8]. The patient was sexually active with men in a genito-genitally way, admitted to have changed partners three times and never use condoms. HIV results, non-reactive TPHA VDRL. Patients are advised to have regular check-ups every month to evaluate recurrence and be given education about condom use during sexual intercourse and not changing partners.

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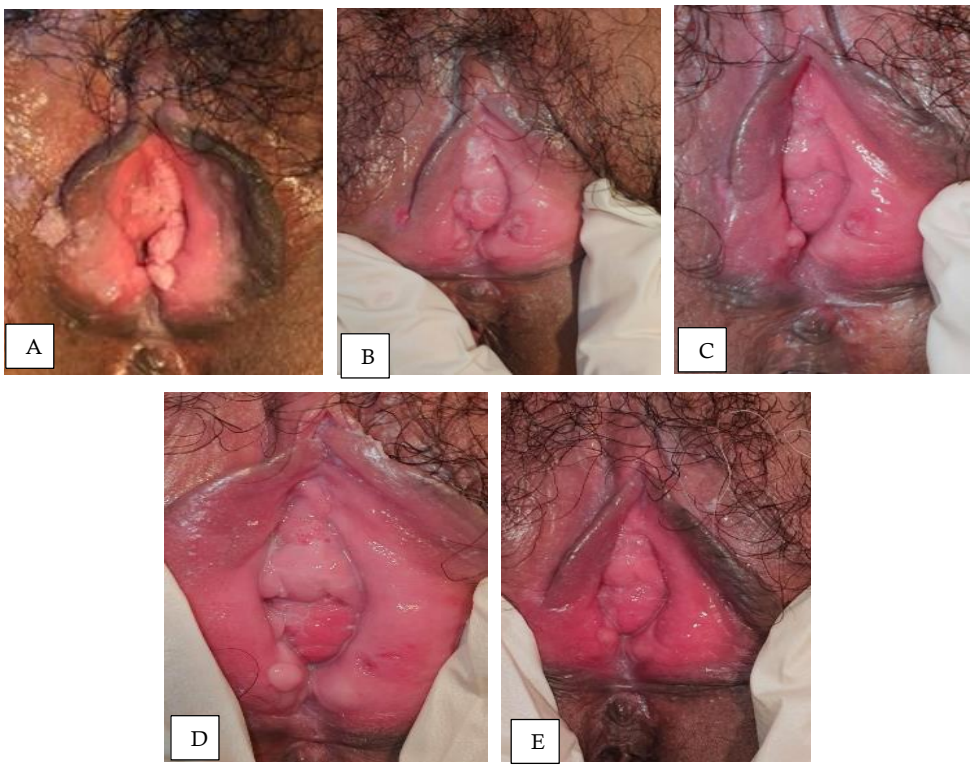

Fig. 2. Major and Minor Labia at (A) before Treatment; (B) 1 Weeks after Treatment; (C) 1 Month after Treatment; (D) 3 Months after Treatment; and (E) 6 Months after Treatment

Transmission of HPV occurs through contact with visible or subclinical epithelial lesions and/or genital fluids containing HPV. Transmission of HPV infection is mainly through sexual intercourse [8]. In this case, transmission is by genital-genital contact. The incubation period for CA ranges from 2 weeks to 9 months and is clinically visible from 2-3 months after contact. During active infection, HPV will replicate independently of host cell division and trigger the host to proliferate to form many lesions ranging from flat to papillary warts [8]. In this case, the patient admitted that she had last sexual intercourse one month before coming to the DV clinic.

The clinical presentation of CA is as a papule or pedunculated lesions, with granular papules on the surface giving rise to a verrucous appearance. Lesions initially appear as small papules ranging in diameter from 2-5 mm but can grow to form large, confluent clusters up to several centimeters long. There are three clinical CA forms: acuminata, keratotic, and papules. In this case, the patient complained of the presence of warts two months ago on the genitals [1,8,9]. Initially, the wart is one piece and small, and then warts becomes larger and numerous. Warts form skin-colored papules and mucosa, multiple, verrucous surface, no tenderness, and do not bleed easily.

Condylomata acuminata can extend to the rectum, urethra, vagina, and cervix. Most cases of CA are asymptomatic, but some patients may experience pruritus, mild burning, bleeding, or irritation. CA lesions can be traumatized due to friction due to sexual intercourse or clothing, resulting in secondary infection [1,9]. In this case, the lesion was on the majora and minor labia, not extending to the cervix or rectum.

Most HPV infections are temporary and not detected within two years. However, about 30% of CAs will regress within the first four months of infection. The latency period may last from several months to years [1]. In a prospective study it was found that the majority of infected women specific HPV types within 6 to 12 years did not indicate infection by the same specific HPV type as before. This cohort study supports that the median duration of detection of the same type-specific HPV is 1 year [10,11]. So we conclude that follow up can be done up to 1-2 years, and patients are educated to do a pap smear at least once every 3 years. Patients are still advised to have monthly follow-up visits to evaluate recurrence until 1-2 years.

The diagnosis of CA can generally be made based on the clinical picture, physical examination with good lighting, and a magnifying glass. Supporting examinations include acetic acid test (acetowhite), colposcopy,histopathological examination, dermoscopy examination, and polymerase chain reaction (PCR) examination [8]. The patient underwent an acetowhite test, and the results was positive. Histopathological

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examination was not performed because genital warts did not have to bleed, were skin-colored, and were well-defined.

Several therapeutic modalities can be used, including tincture of podophyllin 10-25%, trichloroacetic acid (TCA) 80-95% solution, imiquimod 5%, surgical excision, cryotherapy, and electrosurgery. Electrosurgical therapy uses high-frequency of electrical energy to damage infected tissues with electrocautery. Local anesthesia is required before the procedure is performed. Side effects that often follow electrosurgery therapy for CA are pain, bleeding, scarring, and bacterial infection [12]. The patient receives electrocautery therapy in one therapy session. Postoperative wound care gentamicin ointment 0.1% cream twice daily.

The ideal therapy for CA should be adequate (high clearance rates and low recurrence rates) and have common local and systemic adverse effects. Monotherapy is often unsatisfactory, so combination therapy is sometimes more beneficial. Combination therapy can be done for a better response rate and to minimize recurrence, one of which is immunomodulators [6]. *Immunomodulators* are drugs that can restore and repair an immune system whose function is impaired or suppress an over-functioning immune system. The function of immunomodulators is to improve the immune system by stimulating (immunostimulant) or suppressing/ normalizing abnormal immune reactions (immunosuppressants). Immunostimulants consist of two groups, namely biological and synthetic immunostimulants. Some biological immunostimulants are cytokines, monoclonal antibodies, fungi, and medicinal plants (herbs), while synthetic immunostimulants are levamisole, isoprenaline, and muramyl peptidase. Improving the immune system can be done in many ways, one of which is through drug supplements that function as immunomodulators. Many types of immunomodulators are currently available for dietary supplements, especially those using natural herbal ingredients such as Echinacea, Meniran, Noni, Sambiloto, and others [6,13].

Echinacea is the name of a genus of plants native to North America. This plant belongs to the aster group (Asteraceae) and is commonly known as the purple coneflowers. Research shows that Echinacea increases antibody production and the number and activity of white blood cells to boost the immune system. In vitro data, Echinacea stimulates the proliferation of bone marrow, phagocytosis and motility of macrophages, and increase in PMN cells. Echinacea will stimulate macrophages to produce TNF-α, IL 1, IL 6, and IL 10, increase leukocyte motility and activation of non-specific T lymphocytes. Echinacea can stimulate lymphocyte activity, increase phagocytosis and induce interferon production. In vitro studies have shown that Echinacea acts directly on NK cells, polymorphonuclear leukocytes, and macrophages. NK cells are the source of IFN-γ. IFN-γ is one of the mediators for latency prevention and macrophage activation [6,13,14].

A study from Devinder et al. compared the treatment of genital warts with surgery alone with combined surgery with Echinacea 600 mg daily for three months. As a result, combination surgical therapy with Echinacea did not show any recurrence for six months. In addition, in the study of Nicoletta et al., patients who received combined cryotherapy with Echinacea at a dose of 200 mg per day for four months had no recurrence compared to patients receiving cryotherapy alone [6,7,14]. An open trial randomized 261 patients with anal warts to surgery alone or surgery plus a formula combining unspecified proportions and amounts of Echinacea purpurea aerial parts for 1 month postoperatively. The recurrence was 7% (vs 27% control group). it means minimal reccurence if the treatment combined with echinacea.[18,19] Study from Mehedintu et al 2017, using echinacea as an immunomodulator for the treatment of patients with cervical HPV positive for 6 months [15]. Study from Riemma et al 2022, echinacea extracts supplementation in women with L-SIL (low-grade squamous intraepithelial lesions)/CIN-1 (cervical intraepithelial neoplasia) significantly boosts HPV lesion clearance, reducing the overall amount of diagnosis, histological, colposcopic and vaginal parameters after 6 and 12 months [16].

In Awad study (2020), Echinacea was well tolerated. Some of the patients in the study had symptoms of side effects such as indigestion and diarrhea. Research to find toxic and lethal doses is still not getting results. Several cases, hypersensitivity reactions, anaphylaxis, asthma, and urticaria have been reported [17]. To date, there is no standardized dose. According to Rondaneli et al., in respiratory tract infections, Echinacea was given at a dose of 2400 mg/day for prophylaxis for four months and 4000 mg/day in the acute phase of the disease, which has proven safe and beneficial in preventing and treating respiratory tract infections [18].

In this case, the patient received combination therapy with electrocautery 1x therapy session and Echinacea 1 x 500 mg daily for three months. During the six months of evaluation, there were no new lesions or side effects in the form of hypersensitivity reactions, anaphylaxis, urticaria, or digestive disorders.

CONCLUSION

CA therapy is still challenging; monotherapy options are often unsatisfactory because of the high recurrence rate. The use of combination therapy aims to minimize recurrence, one of which is the addition of an immunomodulators, namely Echinacea. Electrocautery

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combination therapy and Echinacea 500 mg for three months of treatment did not show any new lesions, recurrence, or side effects (gastrointestinal, hipersensitivity reaction). At the 6th month evaluation, there was no recurrence of the lesion. Randomized control trial (RCTs) are needed to find out further studies on the effectiveness of echinacea with various combinations of CA therapies to provide better evidence based medicine.

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CONFLICT OF INTEREST

The authors state that they have no conflicts of interest.

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