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The Combination Therapy of Condyloma Acuminata Patient with Diabetes Mellitus: Case Report

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ABSTRACT

Introduction: Condyloma acuminata with immunocompromised influences the choice of therapy and disease prognosis. This case report aims to provide an overview of the clinical outcome of condyloma acuminata in patients with diabetes mellitus.
Case report: Male, 53 years old, with a mass on the penis from the coronary sulcus to the glans penis, lesions resembling cauliflower. An acetowhite and histopathological investigation support the diagnosis of condyloma acuminata. Therapy with trichloroacetic acid (TCA) 90% and zinc sulfate monohydrate 55mg/day. The lesions disappeared, and there were no new lesions after 2 weeks of treatment. There was no recurrence after 3 months of follow-up.
Discussion: There is no consensus governing the line of therapy for KA. So, there is no one therapy that is definitely ideal for all patients in general. Several previous studies used TCA and oral zinc with various doses and durations of therapy.
Conclusion: Giving TCA 90% every week and zinc sulfate monohydrate 55mg/day gave satisfactory results in the treatment of condyloma acuminata with diabetes mellitus.

Keywords: Condyloma acuminata**,** diabetes mellitus, therapy

INTRODUCTION

Sexually Transmitted Infections (STIs), including diseases with a relatively high number of cases, remain a focus of attention for the World Health Organization (WHO). It is reported that there are more than 20 STIs worldwide, one of which is the infection by the human papillomavirus (HPV).[1] Anogenital HPV infection or condyloma acuminata (CA) is the most prevalent STI in the United States, accounting for approximately 43 million cases annually.[2] In Indonesia, particularly in Bali, CA is among the top three most frequent cases of STIs, with fluctuating case trends.[3]

Medical conditions accompanying CA patients, particularly those with immunocompromised, can worsen the disease prognosis. The body's inability to respond to infection due to decreased cellular immunity accelerates the progression of CA. This condition is a concern for CA patients with immunocompromised, including diabetes mellitus (DM).[4,5]

Several therapeutic modalities are available for CA. However, single therapy is often less effective in immunocompromised patients, necessitating combination therapy to enhance both short-term and long-term treatment effectiveness.[4,6]

Until now, there are not many studies addressing the association between condyloma acuminata and diabetes mellitus, especially considering that both diseases have a high incidence rate in Indonesia.

Therefore, this case report aims to provide a clinical outcome overview of CA in patients with diabetes mellitus, with the hope that it can be beneficial in therapeutic considerations for such patients.

CASE REPORT

Male, 53 years old, with a mass on the genitals for 2 months. Initially small, then increased in size and number. The mass is sometimes itchy but not painful, odorous, or prone to bleeding. No other complaints were reported. No previous history of similar complaints. Denies a history of sexually transmitted infections such as vesicles, genital sores, or discharge. The patient has diabetes mellitus (last blood glucose level 507 mg/dL) and denies other systemic diseases. Treatment for the complaint only applied traditional oil to the lesion. Other treatments include Insulin Glargine 1x22 IU and Glimepiride 1x4 mg prescribed by an Internal Medicine Specialist for type 2 diabetes therapy. No history of drug or food allergies. The patient is a private employee. He is married, has had sexual intercourse approximately 3 times per week last month, occasionally with women other than his wife, and rarely uses condoms. Similar complaints are unknown in sexual partners. The patient's general condition is good, and vital signs and general examination are within normal limits. Venereological status in the genital region (from the coronal sulcus of the penis to the glans penis) reveals multiple papules, well-defined borders, flesh-colored, variable sizes ranging from 0.2x0.3x0.2 cm to 0.5x1x0.5 cm, solid consistency, some lesions coalesce resembling cauliflower. The patient was differentially diagnosed with condyloma acuminata, condyloma lata, and squamous cell carcinoma. Acetowhite examination was positive, histopathological showing acanthocondylomatous features, parakeratosis, orthokeratosis, and prominent vacuolated cytoplasm (koilocytotic impression). Thus, the patient was diagnosed with condyloma acuminata. The patient was referred to voluntary counseling and testing (VCT) with non-reactive anti-HIV results. The patient was treated with 90% trichloroacetic acid (TCA) every week and zinc sulfate monohydrate 4x55 mg/day (every 6 hours orally, after meals). DM therapy continued according to the Internal Medicine Specialist's recommendation. The patient was educated about the course of the disease and treatment. The next day, the patient reported nausea after consuming the second dose of zinc. Therefore, the dose of zinc sulfate monohydrate was adjusted to 1x55 mg/day, and TCA was continued according to the treatment plan. The lesions disappeared after 2 weeks of treatment, and there was no recurrence after a 3-month follow-up.

Figure 1. Day-1

Figure 2. Day-7

Figure 3. Day-14

DISCUSSION

Condyloma acuminata (CA) is caused by the human papillomavirus (HPV) that infects the anogenital area. Approximately 90% of cases are infected by low-risk HPV (types 6 and 11), while some are caused by high-risk types 16 and 18 and leading to malignancy. Diagnosis of CA is established through anamnesis, physical and complementary examinations. [6,7]

CA occurs in both males and females of all ages. A study in China found that 59.6% of cases were in males, 32% were over 50 years old, and 48.7% were married.[8] In this case, the patient is a 53-year-old married male.

Transmission of condyloma acuminata occurs through sexual contact, direct contact with HPV-contaminated objects, and from an infected mother to a child during childbirth. Risk factors include a history of multiple sexual partners, homosexuality, inconsistent condom use, chronic genital infections, pregnancy, immunosuppression, and smoking. [7,8] In this case, risk factors include multiple sexual partners, inconsistent condom use, and immunosuppressive condition (diabetes mellitus).

The incubation period of CA varies from 2 weeks to 9 months. Physical complaints usually appear 2-3 months after exposure. Besides physical changes, CA is often asymptomatic. Some cases may have complaints of itching, pain, and bleeding due to friction. [2,6,7] In this case, physical changes such as mass on the genitals, increasing in size and number, accompanied by intermittent itching, have been observed since 2 months ago.

Three morphologies of CA include 1) Acuminata form, consisting of solitary-multiple papules, flesh-colored/mucous, lesions that can coalesce resembling cauliflower, 2) Keratotic form, consisting of solitary-multiple papules or plaques, verrucous surface resembling common warts, 3) Papular form, consisting of papules resembling domes, flesh-colored/mucous, with a smooth and sleek surface. Predilection in males includes the frenulum, coronal sulcus, glans penis, prepuce, penile shaft, and scrotum. In homosexual individuals, it affects the anal opening, perianal, and oropharyngeal areas.[6,7] In this case, a non-homosexual male has a predilection for the penis from the coronal sulcus to the glans penis, with the morphology of acuminata.

Several complementary examinations for CA include the Acetowhite test with the application of 3-5% acetic acid to the lesion. A positive result is indicated by the whitening of the lesion due to protein coagulation. Histopathological, shows koilocytosis, acanthosis, parakeratosis, and elongated rete ridges. Polymerase chain reaction (PCR) testing can detect HPV subtypes. However, it is not routinely recommended for the routine diagnosis of anogenital HPV infection. [7] HIV screening can be done if the test results are positive for certain STIs because of the high risk.[1] In this case, the acetowhite test showed positive results, histopathologically it presented acanthocondylomatous features, parakeratosis, orthokeratosis, prominent vacuolated cytoplasm cell (koilocytotic), and non-reactive Anti-HIV. The medical history, physical, and complementary examinations support the diagnosis of condyloma acuminata.

Patients with CA accompanied by immunocompromised conditions due to diabetes mellitus (DM) tend to have larger warts, relapses, and a higher risk of developing precancerous and cancerous lesions than immunocompetent patients.[5,9] Studies in Denmark found a higher incidence of anogenital cancer in males with DM than in those without DM.[5] In China, a significant relationship was found between blood glucose levels and the risk of multiple HPV infections in women.[9] Hyperglycemia increases vulnerability to virus infection, cell-mediated immune deficiency, and inhibits HPV clearance. Hyperinsulinemia directly binds to cancer cell insulin receptors or indirectly increases Insulin-like

Growth Factor-1 (IGF-1) levels, showing a mitogenic effect.[5,9]

Therapeutic options for CA include antitumor agents (cytotoxic and physical ablative), antivirals, and immunomodulators. The CDC also divides therapy based on the applicator, whether it is the patient or a healthcare worker. Until now, there is no consensus for the best therapy. The chosen therapy recommendations are those with high efficacy, low recurrence, and low local and systemic adverse effects.[7,10]

Trichloroacetic acid (TCA) at 80-90% concentration is a cytotoxic preparation, with a treatment success rate of over 80% and a recurrence risk of approximately 35%. Post-application, the lesions become white clots due to protein denaturation, coagulation, and superficial tissue necrosis that is hyperkeratotic. Administration is done weekly until the lesions disappear.[3,7] No studies discussing the interaction of TCA with antidiabetic drugs were found. However, it is known that TCA is not systemically absorbed and is commonly used in the treatment of diabetic foot ulcers.[11] Several studies on patients infected with HPV anogenital lesions, especially those with multiple lesions or immunocompromised, have reported unsatisfactory results with monotherapy only. [4,6]

Immunomodulators or biological response modifiers (BRMs) are substances that can stimulate the immune system, including zinc.[4,12] Research by Luong TN et al. found that serum zinc levels in subjects with condyloma acuminata (CA) were lower than in control subjects.[13] Proteins E6 and E7 of HPV play a crucial role in the pathogenesis of HPV infection, especially in inhibiting tumor suppressor genes (p53 and pRB) in the host, allowing the virus to replicate and transcribe to maintain the viral genome. The apoptotic effect of zinc inhibits HPV E6 and E7 proteins, as well as the formation of reactive oxygen species (ROS). Inhibition of ROS prevents the activation of NF-κB, transcription factors for growth (VEGF, cyclin D1, EGFR), and anti-apoptotic molecules (Bcl2, BclXL, cIAP-2) that play a role in cancer cell proliferation.[10,13] Zinc deficiency is also found in patients with diabetes mellitus (DM). Studies in Saudi Arabia found that zinc levels in patients with DM were lower than in non-DM, and a significant relationship was found between poor glycemic control and low zinc levels. Zinc plays a role in glucose metabolism through insulin signaling crystallization, storage, and secretion mechanisms, as well as inhibiting the formation of ROS to prevent mitochondrial DNA damage and dysfunction of β-pancreatic cells. [14]

Zinc supplementation is reported to be more effective than the immunomodulator cimetidine in treating recalcitrant warts.[4] Administration of zinc sulfate 10mg/kg/day (equivalent to elemental zinc 2.5mg/kg/day) up to a maximum of 600mg/day for 1-3 months in subjects with persistent HPV infection showed clinical improvement and low recurrence in several studies.[4,6,10] A study in Iran found that the consumption of zinc sulfate 220mg every 12 hours for 3 months increased HPV clearance and lesion resolution in subjects infected with cervical HPV.[10] A case study on a patient with anogenital warts and HIV given zinc sulfate 100 mg/day as an adjuvant resulted in a reduction in the size and number of lesions by the third week.[6] Oxford University Hospital recommends the consumption of elemental zinc 15-30mg/day for 3 months in the treatment of warts in children and adults.[15] The consumption of elemental zinc in adults is a maximum of 40mg/day from food and supplements. Side effects include nausea, vomiting, severe headache, and abdominal pain. High doses of elemental zinc 142mg/day are reported to interfere with the absorption and balance of magnesium. Zinc sulfate monohydrate is a zinc sulfate preparation with 36% elemental zinc content, reported to be safe and affordable. A dose of 55mg zinc sulfate monohydrate is equivalent to 20mg elemental zinc.[12]

In this case, the patient was treated with the cytotoxic agent TCA 90% weekly and the systemic immunomodulator zinc sulfate monohydrate 55 mg/day. The patient also continued antidiabetic medication according to the specialist's recommendation and followed the recommended lifestyle. After 2 weeks of combination therapy, the lesions disappeared. No complaints of local or systemic irritation were reported during and after combination therapy. Zinc consumption continued for 1 month.

The prognosis for CA patients with immunocompromise is at risk of relapse, around 67-70%. Relapses often occur 3 months after treatment.[6,8] In this case, there was no recurrence after a 3-month follow-up.

CONCLUSION

The administration of 90% trichloroacetic acid (TCA) weekly and zinc sulfate monohydrate 55mg/day gives satisfactory results in the treatment of condyloma acuminata accompanied by diabetes mellitus.

Declaration by Authors

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