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Giant Anogenital Condyloma Acuminata In HIV-Infected Patient: A Rare Case And Therapeutic Challenge

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Abstract
Introduction*: Giant Condyloma Acuminata (GCA) is a sexually transmitted infection in the perineum and genitalia caused by Human papillomavirus (HPV) strains 6 and 11. GCA is often associated with malignancy.*
Case*: A 29-year-old man presented with presented with cauliflower-like and rooster comb-like lumps with a solid consistency in the anus and penis that had appeared for the past 2 years. In 2020, the patient was confirmed HIV positive. The patient admitted to having frequent sexual intercourse with multiple partners of the same sex and the opposite sex. The patient is currently taking antiretrovirals. Dermatological examination of the testicular region, corpus penis, and anus showed hyperpigmented papules and nodules with a verrucous surface, guttata-numular size, multiple numbers, discrete arrangement, confluence configuration, regional distribution. The patient was diagnosed with giant condyloma acuminata. The patient was then consulted to the Urology Surgery department, and surgery was performed to remove all lumps on the penis and anus.*
Discussion*: In HIV patients, GCA shows rapid growth, is infiltrative, and has a high risk of becoming malignant. The diagnosis of GCA is usually made clinically without the need for supporting examinations. The treatment is surgical excision. This choice is based on the large size of the lesion and is considered the most effective option.*
Conclusion*: GCA in HIV patients is a rare but serious case and requires a multidisciplinary approach. The management poses a significant challenge due to the high recurrence rate, limited effectiveness of topical therapy, and the need for an aggressive surgical approach. Early detection, aggressive management, and control of HIV infection are key to successful therapy and recurrence prevention.*
Keywords: *human papillomavirus, sexually transmitted infections, HIV, antiretrovirals*

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I. Introduction

Giant Condyloma Acuminata (GCA) or known as Buschke-Lowenstein Tumor (BLT) is a sexually transmitted infection (STI) caused by Human papillomavirus (HPV) in the perineum and genital area. The virus is the agent of condyloma cases that cause abnormalities in the form of fibropapilloma on the mucosa, the main transmission of infection through sexual intercourse where there is contact with epithelial lesions and through genital fluids containing HPV. Condyloma acuminata is caused by HPV strains 6 and 11, however, it can also be caused by other HPV strains, such as strains 6, 18, 31, 33 which are generally identical to malignancy.[1]

The prevalence of GCA is estimated at 0.1% of the general population. The male-to-female ratio is reported to be 2.7:1, with an age range of 24-77 years, with an average age of 43 years.1 The incidence of condyloma acuminata tends to increase in several hospitals. At Dr. Soetomo Regional General Hospital, cases increased from 0.78% to 3.09% between 2011 and 2014. The highest incidence was in the 25-44 age group, at 69.8%. The highest number of patients according to partners was heterosexual, at 58.7%. At Prof. Dr. R. D. Kandau Regional General Hospital in Manado, 40 cases of GCA were found, representing 3.7% in 2013. The highest distribution was in the 25-44 age group, with women dominating the incidence rate at 62.5%.[3]

HIV patients are at greater risk of developing condyloma acuminata than patients without HIV, and lesions are more difficult to heal and prone to recurrence due to decreased cellular immunity. [5] The first symptom of condyloma acuminata is a solitary or multiple mass. Other accompanying symptoms include pain, purulent discharge, fetid odor, bleeding, itching, and difficulty defecating. The lesion initially presents as a keratoconus plaque that gradually develops into a cauliflower-like and exophytic mass that can infiltrate the underlying tissue, eventually forming fistulas and abscesses. Clinical examination will reveal a mass that is freely mobile against the fascia and tissue. In men, the penis (81-94%), anorectum (10-17%), and urethra (5%), are typically affected, while in women, the vulva (90%). [6]

The choice of therapy for giant condyloma acuminata depends on the size, location, type, and number of lesions. Treatment for giant condyloma acuminata is classified based on the type of application. These include

antitumor preparations (cytotoxic, physical ablative), antiviral and immunomodulatory, and combination therapy. 8 The purpose of this case report is to contribute to the body of knowledge of giant condyloma acuminata and to initiate comprehensive management to improve the patient's quality of life.

II. Case

A 29-year-old man presented to the dermatology and venereology clinic at RSUDZA complaining of a lump resembling cauliflower and a rooster's comb with a firm consistency in the anus and penis that had appeared for the past two years. Initially, the lump, the size of a corn kernel, appeared on the anus and was only noticed when the patient felt something stuck in his anus during a bowel movement. Over a period of approximately three months, the lump, which was initially small, grew larger and spread to the penis. The lump was itchy, painful, had an unpleasant odor, and sometimes bled. The pain was characterized by a burning and stabbing sensation. The lump was friable and peeled off on its own. The patient reported pain during bowel movements, but no complaints during urination.

In 2019, the patient had previously developed a lump in his anus. The lump was then excised and completely removed. However, less than a year later, the lump reappeared on his genitals and now appears to be more numerous than before. In 2020, the patient was confirmed HIV positive. The patient admitted to having regular sexual intercourse and having multiple partners of the same sex and the opposite sex. The patient stated that his last sexual intercourse was in 2020 and that he is currently taking antiretrovirals (ARVs) in the form of a fixed-dose combination (FDC) containing Tenofovir 300 mg, Lamivudine 300 mg, and Dolutegravir 50 mg. A dermatological examination revealed hyperpigmented papules and nodules with a verrucous surface, guttate-numular size, multiple numbers, discrete arrangement, confluent configuration, and bilateral distribution in the testicular region, corpus penis, and anus. The patient was diagnosed with giant condyloma acuminata. The patient was consulted to the Urology Surgery department, and then surgery was performed to remove all the lumps.

Figure 1. Venereological status picture, in the testicular region, corpus penis, and anus, hyperpigmented papules and nodules with verrucous surface, guttata-numular size, multiple number, discrete arrangement, confluent configuration, regional distribution.

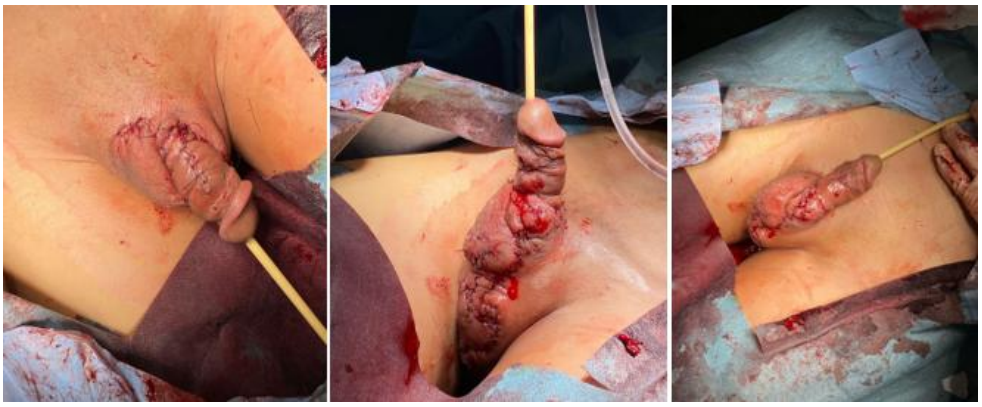

Figure 2. Post-operative image and total removal of GCA lesion by Urological Surgery Department.

III. Discussion

A 29-year-old male patient presented with a cauliflower- and cockscomb-shaped lump on his anus and penis for the past two years. The lump was itchy, painful, had a foul odor, and even bled. Based on the patient's history, the complaint began with a small, corn-sized lump on his anus, which he noticed when he felt an obstruction during bowel movements. Over a period of approximately three months, the lump, which initially was only one, multiplied and enlarged until it covered his penis. The lump was itchy, painful, had a foul odor, and bled easily.

This patient's presentation is consistent with Giant Condyloma Acuminata (GCA) or Buschke-Löwenstein tumor, a rare variant of anogenital warts with an incidence of approximately 0.1%. GCA is anogenital wart caused by Human papillomavirus (HPV), particularly HPV types 6 and 11.[1] HPV is a highly contagious double-stranded DNA virus that is easily transmitted through skin or mucosal contact, primarily infecting squamous epithelial cells. HPV can remain in a latent state for several months before triggering symptoms.Click or tap here to enter text. The incubation period ranges from 3 weeks to 8 months. Most people infected with HPV typically develop genital warts within 2-3 months of infection.

Giant condiloma acuminata lesions tend to be exophytic or endophytic in nature, are large, have a benign histological appearance, have the potential to grow and damage surrounding tissue, can invade and transform into malignant (around 56% of cases) although the risk of metastasis is low, and the risk of recurrence is high even after surgical removal (in 66% of cases.[3] The clinical symptoms of GCA are skin-colored stalked vegetations, verrucous surface, cauliflower-shaped, multiple, measuring ≥ 5 cm, and can spread in the perianal region to cover the anal region with several small verrucous papules around it.

In its early stages, GCA may be asymptomatic. As it progresses, it can be painful, itchy, and produce fluid or blood, producing an unpleasant odor. If left untreated, GCA can spread to the pelvis and cause serious symptoms and complications such as fistulas and abscesses. Some GCAs can even transform into more aggressive forms, such as squamous cell carcinoma, such as verrucous carcinoma. Therefore, GCA is often considered a transitional stage between condyloma acuminata and squamous cell carcinoma. Although GCA has histologically benign characteristics, it tends to be very large and can damage surrounding tissue. [4,5]

The patient in this case had a history of social habits, including frequent sexual intercourse with partners of the opposite sex and the same sex (bisexual). The primary transmission of GCA occurs through sexual intercourse, either through direct contact with epithelial lesions or via genital fluids containing the HPV virus. During intercourse, microscopic abrasions facilitate transmission of the virus from an infected partner to another. This repeated trauma then increases infectivity and viral replication. In the case of men who have sex with men (MSM), the risk of contracting STIs is much higher. [6] Anatomically and physiologically, the anus lacks natural lubrication and its mucosa is much thinner than the vagina, which makes the anus more susceptible to trauma from friction, vulnerable to infection. Furthermore, negative stigma against MSM partners also makes them reluctant to undergo routine health checks and treatment related to their sexual orientation.

The patient has also been confirmed HIV positive since 2020 and regularly undergoes check-ups at the voluntary counseling and testing (VCT) clinic and is taking an ARV regimen. The immune system plays a crucial role in detecting and responding to HPV infections and destroying infected cells. In immunocompetent individuals, approximately 90% of HPV infections in the anogenital area resolve on their own. Meanwhile, in individuals with HIV, especially those with low CD4 counts, HPV can develop more aggressively, leading to larger and more widespread lesions. In HIV-infected patients, even when receiving ARV therapy to suppress the virus, they can still experience abnormal growths in the anal area or intraepithelial lesions that can progress to cancer. [7]

The patient's complaint initially appeared in the anus in 2019. When the lump was first noticed, the patient was still sexually active and had multiple partners. The prevalence of GCA in men is 81-94% in the penis, 10-17% in the anorectum, and 5% in the urethra. In women, 90% of cases occur in the vulva. Anal GCA is common in HIV-coinfected patients, especially men who have sex with men (MSM). Anal HPV infection and anal intraepithelial neoplasia (AIN) are more common in HIV-positive MSM than in HIV-negative MSM. [7]

The patient had undergone excision of the lump on his anus and penis in 2022, but less than a year after the surgery, the lump reappeared in the same location. GCA is three times more common in men, especially those under 50 years of age. The prevalence of GCA increases with multiple sexual partners, a history of other STIs such as chlamydia or gonorrhea, smoking habits, and immunocompromised conditions (HIV, diabetes, cancer, post-transplant). Human Immunodeficiency Virus (HIV) infection has a complex interaction with HPV in the development of GCA.[5] HIV makes HPV more active and increases the production of the E7 protein, which is part of HPV to help the virus multiply in infected tissue. As a result, the amount of HPV DNA will increase in infected tissue. Meanwhile, local immune control by Langerhans cells, macrophages, and CD4 cells is disrupted because their numbers are reduced by HPV, making HPV infection more difficult to control. This puts HIV patients with GCA at a higher risk of recurrence.[1]

The diagnosis of GCA is usually made clinically without the need for further examination. However, for smaller GCA lesions, an acetowhite test with 5% acetic acid can be performed. When the acid is applied to the

lesion for 3-5 minutes, the lesion will turn white. However, in larger lesions, differentiating GCA from verrucous carcinoma becomes more difficult. Therefore, histopathological examination is necessary to confirm the diagnosis of GCA. In this case, histopathological examination of tissue samples from the penis and scrotum confirmed the diagnosis. It revealed features classic for GCA, including acanthosis, papillomatosis, hyperkeratosis, and the pathognomonic koilocytosis. The squamous epithelial cells exhibited normal nuclear morphology, and the stroma showed loose fibromyxoid connective tissue with lymphocytic infiltration. Crucially, no signs of malignancy were identified, which helped to solidify the diagnosis of GCA and exclude a malignant transformation. Histopathological examination reveals GCA to exhibit features similar to condyloma acuminata, including the presence of papillomatosis, parakeratosis, koilocytosis, and acanthosis with an overlying hyperkeratosis layer. Koilocytosis is a cell that undergoes changes due to HPV infection, typically appearing as cells with large nuclei and a perinuclear halo. Condyloma acuminata can be distinguished from verruca vulgaris by the type of hyperplasia that occurs. Verruca vulgaris exhibits hyperplasia with a pointed and elongated surface, while condyloma acuminata exhibits more papilla-like growths. [2,5,8]

Low-risk HPV, such as types 6 and 11, have a low ability to cause cell transformation into cancer. However, high-risk HPV, such as types 16 and 18, through the E6 and E7 proteins, can cause damage to the tumor suppressor protein p53 (TP53) and the retinoblastoma protein (pRb), which play a role in controlling cell growth. As a result, infected cells experience abnormal growth and can transform into cancer cells. In contrast, low-risk HPV does not cause cell proliferation in the basal and parabasal layers of the epithelium, so the risk of malignant transformation is low. [3]

The primary goals of GCA therapy are to eliminate skin lesions, reduce the risk of transmission, manage symptoms, and prevent the disease from progressing to more invasive lesions. If left untreated, GCA can recur in less than a year, with lesions increasing in number or spreading. However, while therapy can eliminate lesions, it cannot completely eradicate the HPV virus or reduce its infectivity. There are various types of therapy for GCA, with the choice of therapy method based on the number, size, shape, and location of lesions, as well as whether previous treatments have failed. For non-surgical therapy, several options available include intralesional immunotherapy, as well as the use of topical agents such as imiquimod 5%, podophyllotoxin 25-30%, and trichloroacetic acid (TCA) 80-90%. Physical ablative modalities such as cryotherapy, CO2 laser, and electrocautery are also frequently used, especially for smaller or non-invasive lesions. In more complex cases, systemic therapies such as interferon-α, bleomycin, methotrexate, and 5-fluorouracil (5-FU) may also be options.

In this patient, excision was the preferred treatment, based on the large size of the lesion and considered the most effective. Wide radical excision, which involves removing the infected tissue with adequate margins, followed by reconstructive surgery to repair the surgical area, is considered the primary option for large cases that are difficult to treat with other therapies. This surgical treatment has a high success rate of 63-91% and a low recurrence rate compared to other treatment methods. However, post-operative side effects can occur, especially if the removed GCA is very large. These include bleeding, scarring, and anal stricture if the GCA is located in the anus and rectum. If the tumor is very large, chemotherapy or radiotherapy may be used to shrink the tumor and make the removal procedure safer. After surgery, patients require regular follow-up because GCA carries a high risk of recurrence. Mortality associated with GCA is usually caused by infectious complications, so maintaining cleanliness and ensuring proper wound healing after surgery is crucial to reduce this risk. [3,5,8]

IV. Conclusion

Giant Anogenital Condyloma Acuminata in HIV-infected patients is a rare but serious case, demonstrating a relationship between immunosuppression and the development of aggressive condylomatous lesions. Immunodeficiency due to HIV facilitates the massive growth of lesions due to Human Papillomavirus (HPV) infection, especially in high-risk patients. Management of this case is challenging due to the high risk of recurrence, the potential for malignancy, and the limited response to conventional therapy. A comprehensive therapeutic approach includes multidisciplinary collaboration, including surgery, adequate antiretroviral therapy, and monitoring for recurrence in patients. Therefore, early detection, aggressive treatment, and control of HIV infection are the keys to success in managing this case.

Conflict Of Interest

There is no conflict of interest in this case report.

Consent Form

Consent given by the patient in writing

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