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Case Report

Recurrent Giant Condylomata Acuminata Caused by Human Papilloma Virus in HIV with Homosexual Male

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ABSTRACT

Perianal giant condylomata acuminata (GCA) is a rare clinical condition associated with low-risk Human papillomavirus (HPV) type 6 and 11 infections. Human Immunodeficiency Virus (HIV) infection is one of the risk factors for GCA, that can increase the condylomata acuminata incidence and spread caused by HPV. A 28-year-old man came with a cauliflower-like mass complaint in his perianal and anal since 2 months ago. The patient did not complain of pain or itching on the mass but often bled when defecating. The patient is a male who has sex with men (MSM) and often changes partners. He has been diagnosed with HIV since 11 months ago and regularly taking anti-retroviral drugs, Efavirenz 600 mg daily. He was also diagnosed having lung tuberculosis at the same time, got 6 months treatment and was declared cured. The venereological examination of the perianal and anal region revealed erythematous and grayish stem-shaped vegetation and papules, verrucous surface, multiple, well defined, with 3 x 1.5 x 2 cm in size. A positive act of white examination was obtained. Blood tests revealed CD⁺4 230 cells / μ L. Polymerase chain reaction (PCR) examination for HPV obtained HPV types 6 and 11 infections. Histopathologic examination revealed acanthosis, papillomatosis, and hyperkeratotic epidermis and koilocytotic cells. The patient was treated with electrodesiccation three times but obtained mass in anal getting bigger with a size of 6 x 3 x 3 cm. Therefore, he agreed to be referred to the surgical department with an extensive surgical excision plan. Screening of GCA using PCR is not a routine examination but PCR has high sensitivity and specificity for determining the type of HPV, is useful for determining GCA prognosis and therapy, and is recommended for malignant and possible GCA recurrence detection.

Keywords: Giant condylomata acuminata, HPV, recurrent, HIV, MSM

ABSTRAK

Perianal Giant condylomata acuminata merupakan kondisi klinis yang jarang dan dihubungkan dengan infeksi rekuren Human Papillomavirus (HPV) low-risk tipe 6 dan 11. Infeksi Human Immunodeficiency Virus (HIV) merupakan salah satu faktor risiko GCA, yang dapat meningkatkan risiko kejadian kondilomata akuminata dan penyebaran yang disebabkan oleh HPV. Laki-laki 28 tahun datang dengan keluhan benjolan seperti bunga kol di anus dan sekitar anus sejak 2 bulan yang lalu. Pasien tidak mengeluhkan nyeri maupun gatal pada benjolan tersebut, namun sering berdarah saat buang air besar. Pasien berhubungan seksual dengan sesama jenis dan sering berganti pasangan. Pasien telah didiagnosis HIV sejak 11 bulan yang lalu dan rutin minum anti-retroviral, Efavirenz 600 mg setiap hari. Pasien juga didiagnosis menderita tuberculosis paru pada saat yang bersamaan, mendapatkan 6 bulan terapi dan dinyatakan sembuh. Pemeriksaan venereologis pada regio perianal dan anal didapatkan vegetasi bertangkai serta papul-nodul eritematous dan keabu-abuan, permukaan verukosa, multipel, batas tegas, ukuran 3 x 1,5 x 2 cm. Pemeriksaan acetowhite positif. Pemeriksaan darah CD⁺4 230 sel/ μ L. Pemeriksaan Polymerase chain reaction (PCR) untuk HPV, didapatkan hasil HPV tipe 6 dan 11. Pemeriksaan histopatologis didapatkan epidermis akantosis, papilomatosis, hiperkeratosis dan sel-sel koilositosis. Pasien diterapi dengan elektrodessikasi sebanyak 3x namun didapatkan benjolan semakin membesar dengan ukuran 6 x 3 x 3 cm sehingga pasien setuju dirujuk ke bagian bedah dengan rencana wide surgical excision. Skrining GCA dengan menggunakan PCR bukanlah pemeriksaan yang

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3 x 3 cm sehingga pasien setuju dirujuk ke bagian bedah dengan rencana wide surgical excision. Skrining GCA dengan menggunakan PCR bukanlah pemeriksaan yang

rutin dilakukan, namun pemeriksaan PCR ini mempunyai sensitivitas dan spesifitas tinggi untuk menentukan tipe HPV yang berguna untuk menentukan prognosis serta terapi GCA dan disarankan untuk deteksi keganasan serta deteksi kemungkinan rekurensi GCA.

Kata kunci: *giant condylomata acuminata, HPV, rekurensi, HIV, LSL*

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INTRODUCTION

The incidence of anogenital condylomata acuminata (CA) has increased in the past decades and is, to date, the most common sexually transmitted disease in Western countries. Condylomata acuminata is correlated with low-risk human papillomavirus (HPV) type 6 and 11 infections, whereas high-risk HPV type 16 is frequently present in anogenital malignant lesions.¹

Perianal giant condyloma acuminatum (GCA) is a rare clinical condition related to HPV infection and characterized by a circumferential, exophytic, cauliflower-like mass with an irregular warty surface localized in the anal region.¹

The giant form of this disease has a rare event rate, no more than 0.1% genital warts. Most of the incidence attacks middle-aged men, with a male-to-female ratio at 3:1.² Risk factors for GCA include anoreceptive intercourse, Human Immunodeficiency Virus (HIV), and immunosuppression.³ Human Immunodeficiency Virus infection is a predisposition that increases the CA incidence and spread caused by HPV.⁴

Many examination techniques are used to detect HPV infection. To mention one is polymerase chain reaction (PCR) technique. By PCR, it is now possible to amplify enzymatically specific target Deoxyribonucleic acid (DNA) sequences to higher levels so that they are now readily detectable by additional methods to detect the type of HPV.⁵ Detection and subsequent HPV types have a profound role in assessing the prognosis and therapy of genital lesions and evaluation of efficacy therapy.⁵ Classification of HPV infection types is important for the identification of patients at risk of developing

malignant transformation and for the detection recurrence rates of GCA.^{5,17}

A case of giant condylomata acuminata caused by HPV types 6 and 11, identified by PCR techniques in a 28-year-old male patient with HIV-infected who had sex with men (MSM).

CASE REPORT

A man, 28 years old, came to dermatovenereology's outpatient clinic of Saiful Anwar Regional General Hospital (RSSA) Malang with a complaint of cauliflower-like mass on his anal and perianal since 2 months ago. It initially appeared as a small bump that got bigger in both anal and perianal, and some reddish and some brownish-gray in color. There was no itching or pain in the bumps. The cauliflower-like mass was rapidly enlarged. Three days before his visit, the patient felt difficult to defecate due to the mass getting bigger and bled after defecation, accompanied by an unpleasant odor.

The patient had a history of similar complaints 2.5 years ago, initially obtained small bumps around the anal, enlarged within a year. The bump in the anal was also getting bigger, and the patient complained often of bleeding after defecation. He checked to the private hospital and was diagnosed as "giant condylomata acuminata." He was referred to the surgical department in RSSA and performed surgery in August 2017 (6 months ago). The complaint reappeared 4 months later.

The patient had been diagnosed with HIV since March 2017, and routinely taking antiretroviral (ARV), Efavirenz 600 mg daily, from Internal Department's outpatient clinic of a private hospital in Malang. He was also diagnosed

At the follow-up, five weeks after the patient back from abroad, mass in the anal region grew larger by 6 x 3 x 3 cm (Figure 2). Therefore, the patient agreed to be referred to the surgical department with an extensive surgical excision plan.

DISCUSSION

Giant Condylomata Acuminata (GCA) is a slow-growing, large, cauliflower-like tumor with locally destructive behavior that typically appears in the anogenital region.^{3,6,8} Originally described as a penile lesion by Buschke in 1896 and Löwenstein in 1925, it is a genital infection caused by Human Papillomavirus (HPV) types 6 and 11.⁷ The first description of anorectal GCA was by Dawson et al. in 1965. Giant condylomata acuminata is a rare lesion tending to present in the fifth decade with a 2.7:1 male: female ratio. For patients under 50 years old, this ratio increases to 3.5:1.^{3,8} In some cases, series of these lesions have a high recurrence rate of between 18% and 67%, with an overall mortality rate of 21%.⁹ According to some literature, GCA is a low-grade and well-differentiated squamous cell carcinoma. Giant condylomata acuminata or verrucose carcinoma should be considered as a differential diagnosis in lesions larger than 1 cm.⁷

Risk factors of GCA include anoreceptive intercourse, HIV and immunosuppression. The prevalence of HPV infection in the anal is very high, around 57% in men with Human immunodeficiency virus (HIV)-negative who have sex with men (MSM); and among people, with HIV-positive infections, the incidence rate is about 60 times higher than in the general male population.⁹

In this case report, the patient is experiencing an MSM for approximately 8.5 years, acted as a “bottom” and rarely used condoms. There were lesions in the form of stemmed vegetation with the largest size of 3 x 1.5 x 2 cm in the perianal and anal region. The patient was also diagnosed with HIV-positive and took ARV daily.

The anal disease is a common disease in patients with HIV infection, especially in

MSM patients.¹⁰ Anal HPV infection and anal intraepithelial neoplasia (AIN) are more common in HIV-positive compared to HIV-negative MSM.¹¹ Recurrent anal condylomata are stronger with HIV and CD⁺4 lymphocytopenia compared to HPV persistence indicating that people with HIV-negative can clear the virus more easily.¹²

Presumably, there is a complex interaction between HIV, HPV and local mucosal immune mechanisms. HIV increases HPV transcription and resets HPV E7 which affects cellular differentiation, leading to higher amounts of HPV DNA in the tissue.⁹ Furthermore, HPV causes a decrease in the number of local macrophages, Langerhans and CD⁺4 cells and decreases local cytokine production, which results in impaired local immunity control against HPV infection.⁹

Since HIV appears to increase HPV replication, one would expect that antiretroviral therapy initiation with future suppression of HIV viral load should lead to a decrease in the amount of HPV in the infected mucosa, followed by clinical improvement. It has been reported that a paradoxical case illustrates the impairment of GCA as a consequence of immune reconstitution syndrome after ARV, in patients with low CD⁺4 counts at the beginning of treatment (50 / mm³).¹³ A study of HIV positive women showed that antiretroviral drugs could reduce the incidence of genital warts and vulvar intraepithelial neoplasia and this effect was mediated through an increase in CD⁺4 count and HIV viral load reduction.¹⁴

Histologically, GCA appears to be similar to condyloma, but grows both upward and downward and indicates a local invasion.¹⁵ In a limited biopsy, the pathologist may only see hyperkeratotic benign epithelium, but the fully developed lesions exhibit an exophytic and endophytic growth pattern.¹⁵ Knowledge of HPV is obtained through several examinations such as cytological examination, histopathology, immunohistochemistry, molecular hybridization, and PCR.¹⁶

Polymerase chain reaction techniques have high sensitivity and specificity. They can be used to amplify and sequence DNA viral processes and to determine the type of HPV that is defined as DNA sequence homology. PCR

with pulmonary tuberculosis (TB) at the same time, received complete TB treatment for up to 6 months and was declared cured in September 2017.

The patient has had sex with men (MSM) since his age of 17 years. The patient acts as a “bottom”. He claimed to have had a pair of 7 men known through social media applications. The Patient and his couple rarely use condoms during intercourse. The last time he had sex was around 2.5 years ago. Currently, the patient works as an entrepreneur.

A general examination of the patient showed mild illness. Vital signs were within normal limits. Venereological examination of the corpus penis, glans penis, ostium urethra external, and scrotum was within normal limits. Preputium has been circumcised. The perianal and anal region revealed stemmed vegetation and erythematous to grayish papules, verrucous surfaces, multiple, well defined, varying in size with the largest size at 3 x 1.5 x 2 cm (Figure 1).

Acetowhite test using 5% acetic acid revealed the mass changed becoming paler. Blood and urinalysis examination revealed normal limits, while CD⁴ was 230 sel/ μ L. HPV DNA

genotyping was performed using the PCR method, as tissue was taken from warts in the anal region. It found that the mass was due to types 6 and 11HPV infection.

Histopathologic examination taken from mucocutaneous lesions in the perianal region, found: acanthosis, papillomatosis, and hyperkerathosis epidermis. There were also koilocytosis cells, whereas in the dermis layer there was no abnormality. No malignancy was found in the tissues. The conclusion was a condylomata acuminata.

Having diagnosed as Giant Condylomata Acuminata, the patient was treated with electrodesiccation on genital warts in the perianal. Meanwhile, in anal warts due to extensive bleeding, electrodesiccation was done gradually. He was educated to routinely treat wounds and maintain hygiene.

The evaluation was done every two weeks. In the second week, evaluation for the rest of the electrodesiccation had dried up. After three times electrodesiccation, the mass in the anal region was getting bigger and bled easily with a size of 4 x 2.5 x 2.5 cm. Since the patient went abroad, the electrodesiccation was postponed.



Figure 1. Anal and perianal region revealed cauliflower-like mass.



Figure 2. Follow up of the 5th week, mass in the anal area grew larger by 6 x 3 x 3 cm.

examination requires only 10 copies of HPV.¹⁶ Because information on the type of HPV is clinically useful for prognosis and treatment of condyloma, molecular epidemiology of HPV using the PCR method has been widely used. Clinical classification of HPV types is important for identifying patients at risk of developing malignant transformation and detection risk of GCA recurrence.⁷

The result of the PCR examination of the patient showed that his GCA was caused by multiple infections, namely types 6 and 11 HPV. Cong X *et al.* (2015)¹⁷ conducted a study of HPV type correlation and clinical features in patients with CA in China and found out that multiple HPV infection results in the formation of larger-size of CA (GCA) and associated with higher recurrence rates, and extended disease course.¹⁷ This corresponds to a patient's history that 6 months ago the patient had undergone surgery at RSSA for his GCA in the anal region and then started growing again 4 months later.

The patient, in this case, was then referred to the surgical department for wide surgical excision. The treatment choice for the management of GCA is considered a wide surgical excision.¹⁸ Surgical excision alone has been shown to result in a disease-free state in up to 46% of cases.^{18,19} Oral and topical chemotherapeutic modalities can be used as an adjuvant, to surgery. Some factors that need to be taken into account during treatment choice include the size and thickness of the lesion, anatomic site, associated HPV subtype, and immune status.^{18,19,20,21}

The direct-applied modalities that are targeted to remove warts locally do not destroy all the very small or subclinical lesions in the surrounding healthy-looking skin and this may be the cause of recurrence.^{20,21,22}

The polymerase chain reaction was not a routine examination for GCA. Nevertheless, HIV-infected men with anal condylomatous lesions were at high risk of having high-grade squamous intraepithelial lesions and harboring multiple HPV infections involving high-risk HPV types in the canal anal in comparison to HIV-infected men without condylomata. These data emphasize the importance of screening and follow-up of

condylomata in the anal canal in HIV-infected men. One of the screenings is using PCR to determine the type of HPV.^{23,24,25}

CONCLUSIONS

The 28-year-old male patient, MSM, has been reported with recurrent giant condylomata acuminata and HIV positive. The patient was then referred to the digestive surgical department for wide surgical excision. Recurrent GCA in this patient may root in his immunosuppression condition due to HIV infection, multiple infections of some HPV types, or previous operations that were not completely clean. Polymerase chain reaction genotyping of HPV DNA obtained types 6 and 11 HPV. Screening of GCA using PCR is not a routine examination but it is very important to determine prognosis, therapy and possible of GCA recurrence.

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CONFLICT OF INTEREST

There is no conflict of interest of this study.

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