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Giant Condyloma Acuminatum (Buschke-Lowenstein Tumor): A Case Report and Review of the Literature

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Abstract

Giant condyloma acuminatum (GCA) commonly known as Buschke-Lowenstein tumor is a rare, aggressive, slow growing; fungating variant of condyloma that is usually found in the genital and perianal regions but may affect any portion of the anogenital region. Although clinically malignant, its histology is benign without distant metastases. The incidence is 0.1% in the general population and while the prognosis is generally good with early diagnosis and proper treatment, mortality rates as high as 20% have been reported. Human papilloma virus (HPV) types 6 and 11are implicated as etiologic factors in the development of GCA. Radical surgical excision with clear histologic margins and plastic reconstruction remains the cornerstone treatment of choice, while preventing the incidence of recurrence. Topical agents and local destructive methods can be helpful for smaller lesions and immunotherapy as an alternative for widespread and relapsed cases. The authors report the case of a 51-year-old male patient with a perianal 8 × 7 cm Buschke-Lowenstein tumor who underwent total excision and plastic reconstruction with V-Y flap technique.

Keywords: Giant condyloma acuminatum; Buschke-Lowenstein tumor; V-Y flap technique; Case report; Review

Introduction

Surgery, Condyloma acuminata is the most common sexually transmitted disease found in young, sexually active population and mostly seen in the colorectal practice. Condylomas have been well known in history with physicians of ancient Roman Empire calling them as "figs" which were thought to result from excessive sexual exploits [1]. The term "acuminatum" means "pointed" and was used to distinguish condyloma acuminatum from condyloma lata, the "broad" condyloma of syphilis [2].

Giant condyloma acuminatum or Condylomata gigantea (commonly known as Buschke-Lowenstein tumor) is a rare, aggressive, slow growing; fungating variant of condyloma that is usually found in the genital and perianal regions but may affect any portion of the anogenital region.

While the tumor was first clinically described by Buschke in 1896, both Buschke and Lowenstein first discovered the histological features in 1932 and hence the name, Buschke-Lowenstein tumor. Although benign in nature, the GCA is also sometimes known as "verrucous carcinoma" because of its tendency to deeply invade the underlying tissues. It has been also described as a rare variant of genital warts [3]. Some authors, however, consider GCA as an intermediate form between benign condyloma acuminata and malignant verrucous carcinoma [3].

While there is no standard treatment due to its biological behavior, surgical excision remains the method of choice to achieve local control of the disease. Most of the authors recommend radical excision with clear histological margins and eventual abdominoperineal resection for perianal and anal canal invasion or malignant transformation [4-6]. The use of a temporary loop colostomy before excision, to avoid a possible contamination of the wound is rarely applicable. On the other hand, skin reconstruction can be performed with the use of different plastic procedures. S-plasty grafts (right or left gluteus and posterior leg flaps) and V-Y advancement flap technique have been commonly used [7,8]. We represent a case report of a perianal and anal GCA treated by radical local excision and reconstruction with the V-Y plasty technique and a review of the literature.

Case Report

A 51 years old homosexual man was admitted to the surgical department in October 2010 for a lesion located in the perianal and anal region. The patient was complaining of a painful palpable mass for the last year and also of itching and constipation. The last month he noticed a foul smell, bleeding and mucopurulent perianal discharge.

On physical examination an enormous, exophytic, cauliflower-like tumor was found with irregular surface, eventually exceeding 10 cm in length and 8 cm in diameter. All the patients" blood tests were normal, while he was found HIV negative and HbsAg positive. The tumor was totally excised. The entire specimen was sent for histological examination to ensure clear margins and the absence of a malignant verrucous carcinoma.

Skin defect reconstruction was achieved with a bilateral V-Y fasciocutaneous advancement flap. The skin incision was closed with a stapler and the medial edge of the flap was sutured to the anal area by a 3/0 ploglactin material. The histological report of the specimen revealed the presence of a giant condyloma acuminatum (Buschke-Lowenstein tumor) with clear surgical margins and no evidence of malignant transformation. An HPV analysis was also performed by PCR technique, demonstrating the presence of HPV types 16 and 18, something less common in giant condyloma acuminatum. A non-fiber diet and loperamide (12mg/day) were administered for 4 days to avoid wound infection.

There were no postoperative complications and the patient was discharged. After 2 years the patient is doing well without any evidence of recurrence (Figures 1-6).

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Discussion

The incidence of GCA is probably 0.1% in the general population and about 2 to 3 million newly reported cases each year have been estimated [9]. While the prognosis is generally good with early diagnosis and proper treatment, mortality rates as high as 20–30% has been reported.

Most frequently, Human papillomavirus (HPV) types 6 and 11 are implicated as etiologic factors [10] in the development of GCA. However, an immunologic aberration of the cell-mediated immune system and/or the combined synergistic effect of viral or environmental carcinogens may all contribute to the formation of the tumor. In addition, one of more of the risk factors may have a significant contributory role in the development or aggravation of the disease process.

Gender: Buschke-Lowenstein tumor is much more common in males than in females. The ratio of males to females is approximately 2.3:1 [11].

Viral infection: The tumor has been found to be frequently associated with the presence of human papillomavirus (HPV) viral infection [11,12]. In fact, almost all cases of GCA are associated with contagious low-risk HPV types 6 and 11 [3].

Condyloma acuminatum: GCA is always preceded by condyloma acuminatum, and the immune system is probably suppressed.

Homosexual men: Common practice of anal receptive intercourse in the homosexual population is also considered a risk and GCA, therefore, is mainly seen in men.

Uncircumcised males: The tumor has also been frequently noticed in uncircumcised men between the ages of 18 and 86 years. According to an estimate, about 5% to 25% of all penile cancers are GCAs [10].

Age: While GCA can occur at any age after puberty, it usually affects young patients in the second and third decades of life. However, its development between the 4th and 6th decades of life is also not uncommon. Various studies have shown that the average age for the occurrence of disease among most patients is 43.5 years [13].

Immunocompromised patients: In some cases, GCA has also been found to be associated with chronic diseases or immunocompromised states such as congenital or acquired immunodeficiency (AIDS), alcoholism, diabetes, or chemotherapy with immunosuppressive therapy [9].

Other associated risk factors include numerous sexual partners (such as common in prostitution), poor hygiene, depression of immune system, smoking and anaerobic infections etc.

Although GCA is a highly differentiated squamous cell tumor of the genital region that is mostly benign, the characteristic thicker stratum corneum, marked papillary proliferation and its tendency to invade deeply displacing the underlying tissues are the histopathological features that differentiate the GCA from ordinary condylomas, and squamous cell carcinomas. It should also be noted that while squamous cell carcinoma and giant condyloma acuminata can coexist in 30% to 56% of patients [14], GCA only rarely presents with histological features of malignancy such as infiltration of the basement membrane, frequent mitotic figures, lymphatic or angioinvasion, and distant metastases. Granular vacuolization is present, and individual keratinocytes have large cytoplasm and a nucleus with prominent nucleolism [15]. The basal membrane is intact, and a lymphohistiocytic inflammatory infiltrate is present in the upper dermis [9].

The penis is the most common site for GCA development [3] although the perianal region, rectum, scrotum, perineum and bladder may also be involved. In women, however, the tumor usually occurs in the vulva, vagina, or cervix.

Most frequent symptoms include continuous perianal discomfort, anal itching, and painful defecation associated with bleeding and mucopurulent perianal discharge. A clinical study involving review of 51 patients with GCA showed the most frequent clinical features to due to tumor-effect: perianal mass (47%), followed by pain (32%), abscess or fistula (32%), and bleeding (18%) [11].

On physical examination, the tumor presents as an enormous, exophytic, cauliflower-like, white or yellow vegetative growth of papillomatous and irregular surface, eventually exceeding 10 cm [9]. It should be noted, however, that the gross appearance of GCA is not easily differentiated from ordinary condylomas or malignant squamous cell carcinomas as all of these masses appear as large cauliflower-like lesions.

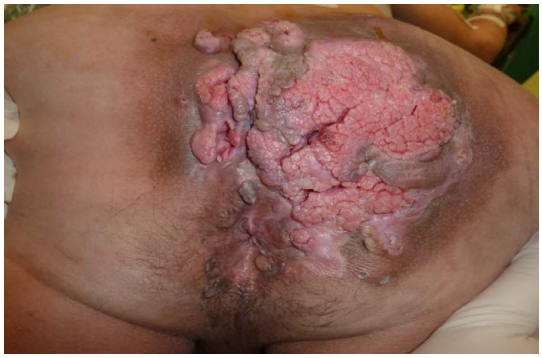

Figure 1: A Buschke-Lowenstein tumor in the perianal area.

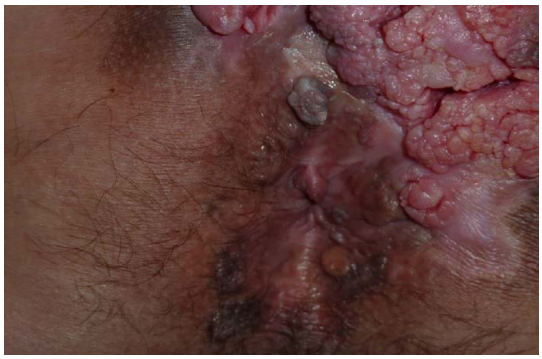

Figure 2: The tumor very close to the anus.

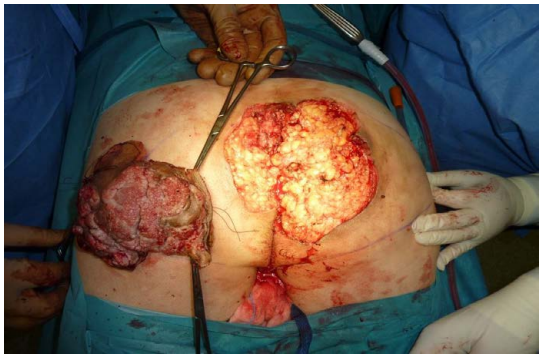

Figure 3: Circumferential excision is performed with wide margins, histologically negative for Condyloma acuminatum,

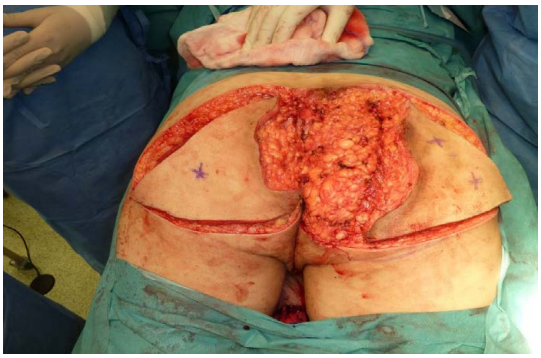

Figure 4: The residual defect will be closed by advancing surrounding V-shaped islands of skin and underlying tissue.

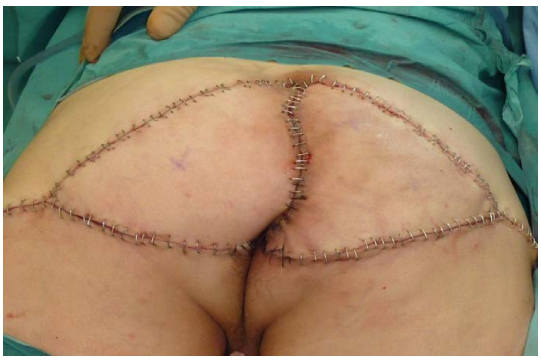

Figure 5: Closure of the flap wounds converts the V-shaped wounds to Y-shaped suture lines.

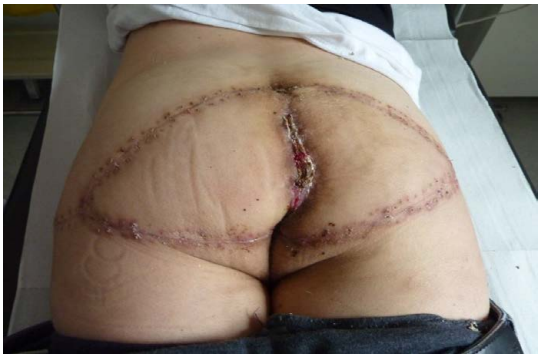

Figure 6: Follow up after 2 months.

GCA of the penis, for example, appears as a soft, pink, vascular, cauliflower-like warty growth that may be relatively small and localized initially but gradually enlarges to a size greater than 5 cm in diameter. The lesion begins on or around the prepuce and gradually becomes nodular [10]. In many cases, peripheral clinical signs such as inguinal lymphadenopathy have also been observed. The tumor often forms an ulcerating mass with abscesses and necrotic tissue [1].

Although GCA rarely metastasizes, its aggressive nature displaces deeper tissues by downward growth, causing multiple sinuses or fistula tracts that may invade deeply into the fascia, muscle, or rectum. In some cases, extension into the urethra, genitalia, and perineum can occur. This may result in inflammation, secondary bacterial infection, or hemorrhage. The lesion is also often complicated by several deep fissures discharging pus and blood. Improperly treated or unmanaged cases have been even found to be fatal in some cases [15]. One of the complications of GCA is its neoplastic transformation into fully invasive squamous cell carcinoma because of its highly malignant behavior which often conflicts with its benign nature and histopathological features. In fact, according to some estimates, GCA has a malignant transformation rate as high as 50% [3]. Therefore, while the GCA tumors do not metastasize, clinically they are nevertheless regarded as malignant [16]. Appropriate treatment of GCA provides very good prognosis and low rate of recurrence. Prognosis is specifically considered good with adequate surgical excision [10]. However, good prognosis does not necessarily affect the rate of recurrence of the tumor which is also considered relatively high. Initial diagnosis is based on a detailed clinical history and a thorough, carefully performed physical examination of the patient. In most cases, the pathologic analysis of the specimen confirms the diagnosis of condyloma acuminatum, with moderate degree of dysplasia of the epithelium with koilocytosis atypia, acanthosis, and parakeratosis. For a confirmatory diagnosis of GCA, however, deep biopsy from different points of infected tissue should be performed essentially involving the epidermal/dermal interface as the specimen usually shows presence of koilocytocic cells and the large hyperkeratotic cellular nests propagate deep into underlying stroma [15].

Although the lesion is generally benign, its management is often challenging due to the size, degree of local invasion, young age of the patients and high recurrence rate. In addition, as there are no universally accepted guidelines for the treatment of GCA, therapy is mainly based on individual case reports and degree of severity of the disease.

The following treatment modalities are generally implied in most cases:

Surgical excision: When possible, surgical excision with examination of histologic margins is considered as the cornerstone of treatment and is generally recommended as the treatment of choice in the early stages of the tumor for complete elimination of the tumor and prevention of recurrence. Excision must be wide and the Mohs technique is often used [9]. Lymph node dissection is indicated only in cases of suspected malignant transformation. However, evidence has shown that even surgically excised GCA cases tend to have a recurrence rate of about 50% [11]. In some cases, Cryosurgery has been also found to be successful but only in small, simple lesions.

Medical treatment & chemotherapy: Most of the published studies and documented evidence have shown highly variable response to the medical drug / chemotherapy. Topical application of podophyllin, for example, has shown to be helpful for ordinary condyloma acuminata but is not recommended for the treatment of condylomata gigantean because of its large size. Similarly, topical chemotherapy with 5-fluororacil has been used for the treatment of genital condylomata, but seems to yield poor outcome with giant lesions. However, administering interferon injection directly in the lesion is considered safe and has an eradication rate of 47% to 62%. It should also be noted that interferon chemotherapy is associated with high cost and a recurrence rate up often 40% [14]. Similarly, systemic interferon therapy may be considered for those very large lesions that cannot be excised surgically because of the immune-modulating, anti-proliferative and antiviral properties of GCA. It is expensive, however, with a high incidence of side effects and a variable response rate. Systemic chemotherapy with methotrexate, 5-FU, bleomycin, mitomycin C, cisplatin, and leucovorin may also be tried in extensive or recurrent GCA. On the other hand, long-term treatment with oral retinoids such as etretinate or acitretin has been reported to be effective in GCA because of their immune-modulating, anti-proliferative and proapoptotic properties. In addition, Imiquimod, a potent antiviral and antitumoral agent known for its protective cytotoxic immune response against HPV acts as a synthetic imidazoquinaline immune-response modifier. As Imiquimod also offers the valuable benefits of

less tissue damage, self-applicability on an outpatient basis and lower recurrence rates, its 5% cream has been approved by the US Food and Drugs Administration for the topic treatment of GCA. It is applied three times a week overnight for up to 4 months [3].

Immunotherapy: Immunotherapy with autologous vaccine from the patient's own condyloma has been reported with good success rates and, therefore, has been suggested for giant condyloma acuminata and recurrent lesions.

Radiotherapy: Evidence has shown radiotherapy as a controversial option (even contraindicated by some) for the treatment of GCA because of high rate of recurrence and appearance of anaplastic transformations in some cases [15]. It should be, therefore, reserved for non resectable or adamantly recurrent lesions [3]. However, there is some evidence that indicates the effectiveness of definitive radiation therapy as used in the Nigro Protocol when a patient with recurrent GCA after four surgical excisions, treated definitively with radiation therapy to 45 Gy, showed total regression, and was biopsy-proven to be disease-free 20 months after radiation [11].

Laser therapy: Recently, CO2 laser therapy as the next step after the surgical excision has been found to have some benefits such as a bloodless field, the least destruction of surrounding tissue, the lesser degree of scarring and hemostasis in a same time [15].

HPV vaccine: The available quadrivalent HPV vaccine which is frequently used in females aged 11 to 26 years for the prevention of cervical cancer has been suggested by some to be used in males as a preventive therapy against condylomas and extensive condylomatosis although, at present, no data is available to support this claim [13].

While the overall rate of recurrence of GCA is variable and depends on the on the modality of treatment, recurrence rates

as high as 67% and mortality rates of 20% to 30% have been reported. High rate of recurrence (over 60%) is characteristic for chronic disease [15].

Conclusion

Condylomata gigantean commonly known as Buschke-Lowenstein tumor or giant condyloma acuminatum (GCA) is a rare but highly aggressive tissue destructing lesion of genital or perianal region that is usually found in men but is also not uncommon in women. Because of its location, severity and high recurrence rates, the disease causes significant psychological morbidity and requires active treatment. However, with no universally defined treatment guidelines, GCA tumor remains a well-known, clinically challenging, entity. To date, surgical excision remains the treatment of choice for most of the cases but other treatment modalities such as chemoradiotherapy and laser have yielded mixed results with variable success and recurrence rates. The tumor also has a strong tendency to recur but is not frequently associated with metastatic potential and yet is known for "behaving in a malignant fashion" despite having no histopathological features of typical malignancy. Post-treatment clinical monitoring is highly recommended.

Conflict of interest

Authors have no conflict of interests to disclose

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