Giant condyloma acuminatum (Buschke-Lowenstein tumor). Series of seven cases and review of the literature

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Introduction
Giant condyloma acuminatum (Buschke-Lowenstein tumor) is a rare presentation of the Human Papilloma Virus (HPV) infection that is seen mainly in immunocompromised patients(1). It greatly affects the quality of life of patients as a result of its high rate of malignant transformation to squamous cell carcinoma, frequent recurrence and high mortality(2). Because of its low incidence there are no specific guidelines on how to manage this condition once diagnosed, its treatment is mainly surgical(1,3,8). Therefore, it is not certain how and when to monitor patients after undergoing surgery. Radiology plays an important role in both cases, as it determines what type of surgery is best for each patient and opportunely searches for complications and recurrences in postoperative controls(9-11). Following are 7 cases observed between the years 2009-2013, as well as a review of the literature regarding this disease.

Case 1:
26 years old male patient, diagnosis HIV (+) a year ago, has no CD4 T lymphocyte count, neither...
viral load nor antiretroviral therapy. Without any other relevant history, consults for a perianal mass of 5 months evolution. Physical examination revealed a cauliflower-like tumor protruding from the anal canal, with a verrucous surface. Giant condylomata acuminata is diagnosed and the patient is admitted for study and management, a pelvis MRI with contrast is requested to evaluate the extent of the lesion. The examination shows a lesion that originates from the anal canal with apparent anal sphincter compromise, maximum diameter 12 cm, isointense on T1, slightly hyperintense on T2, with significant restricted diffusion and quick/early heterogenous contrast enhancement, maintaining said enhancement in the late phase at 5 minutes (Figures 1 and 2). Miles’ operation with colostomy was performed, extracting the lesion, which showed on histological examination hyperplasia, acanthosis and keratinization of the perianal skin, inflammation of the rectal mucosa associated with hyperplasia of the muscle layers, without atypia foci and with signs of HPV infection, compatible with perianal condylomata acuminata (Figure 3).

Figure 1. Pelvis MRI. Axial T1-weighted sequence (a) and T2 (b). Lesion originating in the anal canal and which compromises the sphincter complex (arrows), isointense on T1, slightly hyperintense on T2.

Figure 2. Pelvis MRI. Axial diffusion-weighted sequence with b = 800 (a) and fat-saturated T1 in porto-venous phase after injection of paramagnetic contrast medium (b). The lesion (arrows) is seen with significant restricted diffusion and heterogenous contrast enhancement.

Case 2:
19 year old male patient, newly diagnosed HIV (+), HBV (+), without anti-retroviral therapy, viral load of 57,000 RNA copies/ml, CD4 T lymphocytes: 418. Consultation for a mass in the anal region of 10 months evolution, pain associated with defecation, bleeding and foul-smelling, in the last month. Physical examination revealed a cauliflower-like tumor, which appears to originate from the edge of anal canal, has verrucous surface, with blackish tinted bloody discharge, bad odor. Giant condylomata acuminata is diagnosed and a pelvis MRI is requested. The examination shows a mass originating from the outer edge of the anal canal, without deeper compromise, maximum diameter 6 cm, isointense on T1, slightly hyperintense on T2, with significant restricted diffusion, without contrast enhancement in the arterial phase, but with heterogeneous enhancement at 5 minutes (Figures 4 and 5). The decision was taken to perform surgical excision of the lesion with extended edges. Histological analysis shows hyperplasia and acanthosis of the perianal skin, with inflammatory reaction of the adjacent rectal mucosa, without atypias, compatible with perianal condylomata acuminata.

Figure 3. Histological slice of the lesion at 10x magnification with hematoxylin and eosin stain showing classical findings for the lesion: Acanthosis, hyperplasia and keratinization of the cells that form the tumor, associated with signs of HPV infection (arrow). Inflammatory reaction of the rectal epithelium and hyperplasia of the muscular layer, without infiltration by the lesion, was observed.

Figure 4. Pelvis MRI. Axial T1-weighted sequence (a) and T2 (b). Lesion originating from the outer edge of the anal canal (arrows), without deeper compromise, of 6.0 x 3.6 x 3.0 cm in the transverse anteroposterior and craniocaudal axes respectively, isointense on T1, slightly hyperintense on T2.
Case 3:

40 year old male patient, HIV (-), VDRL (-), HBV (-), treated for tuberculosis twice, the last time 20 years ago. Consults for a left inguinal mass of 5 years evolution, to which is added bleeding and odor two months ago. Physical examination revealed a pedunculated tumor in the third medial of the left inguinal fold, has verrucous surface, bad odor. MRI of pelvis is requested for its evaluation. The examination shows a mass in the medial third of the left inguinal fold, near the base of the penis, without compromising it, measuring about 8.5 cm maximum diameter, isointense on T1, slightly hyperintense on T2, with large restricted diffusion and quick/early heterogenous contrast enhancement, maintaining said enhancement up to 5 minutes (Figures 6 and 7). It was decided to perform surgical excision of the lesion with extended edges. The biopsy showed acanthosis and hyperplasia of the dermis cells with mild inflamed infiltration, without atypias, compatible with perianal condylomata acuminata (Figure 8).

Case 4:

40 year old female patient, no relevant history, consults for symptoms of perianal mass of 10 months evolution, bad odor. Physical examination revealed a large exophytic cauliflower shaped perianal tumor, with verrucous surface and smelly discharge, without being able to locate its origin (Figure 9). Computed tomography (CT) of the abdomen and pelvis with contrast is requested, observing a large dense mass of soft tissue, heterogeneous and vascularized, which affects the perineal skin, as well as the rectal mucosa and labia minora (Figure 10). Miles’ operation was performed.
preserving the functionality of the anal sphincter and rectal ampulla, obtaining a favorable postoperative outcome. Monthly outpatient follow-up were scheduled for three months, with no evident signs of relapse.

**Figure 9.** Cauliflower shaped perineal mass with heterogeneous and verrucous surface.

**Figure 10.** Computed tomography of the abdomen and pelvis. Perineal level axial slices (a) and in the proximal third of the lower extremities (b). The mentioned mass (arrows), of soft tissue density, heterogeneous, with contrast enhancement and the presence of blood vessels, is observed.

**Figure 11.** Pelvis MRI. Axial T1-weighted sequence (a) and sagittal T2-weighted (b). Lesion that originates from the perianal skin and does not affect the internal anal sphincter (arrows), of 5.1 x 2.0 cm on its maximum axes.

**Figure 12.** Pelvis MRI. Axial diffusion-weighted sequence with b= 800 (a) and fat-saturated T1 in porto-venous phase after injection of paramagnetic contrast medium (b). The lesion (arrow) shows significant restricted diffusion and heterogeneous contrast enhancement.

**Case 5:**

21 year old male patient, HIV (+), without antiretroviral therapy, without viral load, CD4: 252, no other relevant history, consulted for perianal mass that bleeds occasionally, of 15 months evolution. Physical examination revealed a verrucous tumor about 5 cm maximum diameter, which appears to rest on the anal verge. Buschke-Lowenstein tumor is diagnosed and a pelvic magnetic resonance is performed. The examination shows an exophytic, warty mass, of 5.1 x 2.0 cm that originates on the perianal skin and which does not compromise the anal sphincter. It is slightly hyperintense on T1, slightly hyperintense on T2, with large restricted diffusion and early heterogeneous contrast enhancement, maintaining said enhancement in late phase (Figures 11 and 12). Incisional biopsy of the lesion was performed, which shows papillomatous squamous epithelium with signs of HPV koilocytes compatible with Buschke-Lowenstein tumor. Taking into consideration the anal sphincter, a low anterior resection is performed, removing the lesion and preserving the functionality of the anal sphincter and rectal ampulla, obtaining a favorable postoperative outcome. Monthly outpatient follow-up were scheduled for three months, with no evident signs of relapse.

**Case 6:**

53 year old male patient, HIV (+), in antiretroviral therapy, without CD4 count, no other history, derived to surgical team from infectology polyclinic for presentation about 18 months ago of warty lesions that occasionally bleed, on inner thighs, perineum, inguinal folds, scrotum and penis. Physical examination revealed numerous small warty lesions, with two more prominent lesions, one in pubic region at the base of the penis and another in the scrotum. Condylomata associated to Buschke-Lowenstein Tumor is diagnosed, pelvis magnetic resonance is indicated to evaluate these last two lesions. The lesion at the base of the penis has the aspect of a verrucous blemish measuring 8.0 x 9.5 cm at its maximum axes on the coronal plane and has a thickness of 1cm. Moreover, the lesion at the scrotal level has a cauliflower-like appearance and measures 3.6 x 1.7 cm. The lesions are isointense on T1, slightly hyperintense on T2, have restricted diffusion and early heterogeneous contrast
enhancement, maintaining said enhancement in late phase (Figures 13 and 14). Excisional biopsy of the pubic lesion is programmed, which showed a papilliform microstructure with the presence of hyperkeratosis, acanthosis and HPV kliocytes binucleation, compatible with a condyloma. The remaining lesions were treated with regular cryoablation, firstly once a month for 6 months and then every three months for a year, reducing the controls and adding podophyllotoxin (0.5%) and podophyllin (20%) three times a week according to the response. This treatment to date has shown a slow improvement, but no signs of recurrence.

Case 7:
30 year old male patient, HIV (+), HBV (+) without antiretroviral therapy, CD4 195, 207,000 copies/microlitre, no other relevant history, derived from infectology polyclinic for presentation 7 months ago of a pruritic perianal mass that has grown progressively, and that bleeds. Physical examination revealed a cauliflower-like verrucous tumor in the perianal region, approximately 8.0 x 5.0 cm on its maximum axes. Buschke-Lowenstein tumor is diagnosed and a pelvis magnetic resonance is performed. The examination shows an exophytic mass, verrucous, 7.9 x 5.2 cm on its maximum axes, which originates from the anal canal and compromises the anal sphincter. It is isointense on T1, slightly hyperintense on T2, with large restricted diffusion and early heterogeneous contrast enhancement, maintaining said enhancement in late phase (Figures 15 and 16). Patient does not return for follow-up.

Discussion
Buschke-Lowenstein tumor is a rare entity, with an incidence of 0.1% in the general population\(^1,2,3\). Predominantly affects men, with few reports in women, being more common during pregnancy\(^1,2,4,5,6\). Presents rates of up to 56% of malignant transformation to squamous cell carcinoma, 66% recurrence and 20% mortality, with fatal cases only in recurrences\(^1,3,7,8\). This disease has been considered an intermediate step between squamous carcinoma and condyloma.
acuminata or a benign entity in itself with malignant behavior\(^2,3,7,9\). There are little known clinical characteristics and imaging, and there is no agreement on handling/management. Risk factors described are HPV subtype infection\(^6,11,16,18\), immunosuppression (HIV infection, use of corticosteroids, immunomodulators, diabetes mellitus) sexual promiscuity and co-existence of condylomas\(^2,3,6\). The most frequent locations in males are the penis (81-94%) and in females the vulva (90%), secondly in both sexes is the perineum\(^3,8,10\). Lymphadenopathy associated with this lesion are mostly reactive to the lesion or superinfection, they rarely correspond to metastasis\(^3,8,10,11\).

In our series, only one patient was female and six were male. The age range of patients was between 19 and 53 years of age, with no clear age group preference. Five of the seven patients were HIV (+), of which only one was on antiretroviral therapy, also only three had CD4 counts the highest being 418 and the lowest 195 cells/mm\(^3\), reflecting the strong relationship between the existence of these tumors and immunosuppression. The most common site was the perianal area (five of seven patients), followed by the inguinal area (two patients) and then the scrotum (one patient).

Regarding the imaging examinations, their role is to determine the extent of the lesion and compromise of surrounding structures to establish the feasibility of surgical resection. There is no consensus on which examination to request, however the most common practice is to perform an MRI as a first examination\(^4,5,7,9,12,13\). In our series, MRI was requested in six of seven patients and only in one a CT scan, because there was not at the time access to a resonator. In cases of perianal condylomas, anal sphincter compromise must be established, as this determines the procedure of a local resection or low abdomino-perineal resection (Miles’ operation).

We recommend that the area study be performed with MRI, because of its greater sensitivity than CT scan to evaluate compromise of adjacent structures, taking into account the possibility of overestimation, due to the inflammatory reaction surrounding the tumor. In unclear cases, as in the first patient described, it is recommended to overestimate the lesion due to its high rate of recurrence and malignant transformation.

The imaging characteristics were those of a pedunculated tumor, verrucous, which on computed tomography shows soft tissue density and vascularization, whereas on MRI the lesions are isointense on T1, hyperintense on T2, restricted diffusion, with a heterogeneous enhancement on using intravenous paramagnetic contrast, that in 6 of the 7 cases was early and was maintained in late stages, whilst in the other enhancement was late.

As for imaging tests in the postoperative period, there is also no agreement on which examinations to perform nor how often\(^4,5,7,9,12,13\). In our cases, clinical controls were planned every three months for one year, then every six months for a year and then annually. Imaging controls are made with MRI at 6 months and then after a year, provided the biopsy shows no signs of malignancy and/or the physical examination doesn’t suggest a recurrence.

Treatment is usually surgical, without established rules. While localized treatments have been described (Podophyllin, cryotherapy, electrocautery, fluorouracil, CO2 laser and even radiation\(^15\)), the usual management is resection of the lesion with wide margins or more invasive procedures, according to the degree of local invasion of the tumor\(^2,4,5,6,12,15,16\). The use of adjuvant chemotherapy (bleomycin, methotrexate) has also been described\(^15\). None of these actions have achieved a lesser recurrence of the lesion. Our patients were managed with surgical excision, without reported recurrence to date in cases that have maintained controls.

**Bibliography**


