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Case report: Buschke-Löwenstein tumor in a non-immunosuppressed patient

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ABSTRACT

The present work aims to report a case of Buschke-Löwenstein tumor (BLT), which is a mass of genital warts that usually affects immunosuppressed people. The reported case was diagnosed in a young patient with no known immunosuppression. Several tests were performed to confirm the diagnostic hypothesis, including immunohistochemistry, histological, molecular and imaging analysis. The results obtained were confirmatory in all analyses, except in the molecular one. Because BLT is a rare condition, there is still great literary heterogeneity regarding the ideal treatment, but some options can be considered, such as excision and radiotherapy.

Keywords: *Buschke-Löwenstein tumor; HPV; Immune system*

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INTRODUCTION

The Buschke-Löwenstein tumor (BLT) is a rare entity characterized by large genital warts, which can invade adjacent dermal structures and form fistulas and abscesses, in addition to presenting metastatic potential[1]. BLT is considered a type of giant condyloma acuminatum and was first described in 1925 by German dermatologists Abrahan Buschke and L. W. Löwenstein[2]. It is a sexually transmitted infection mostly associated with low-risk human papillomavirus (HPV) types 6 and 11. More than 150 strains of HPV have been identified, but their risk of causing serious illness is different. Thus, HPV strains are classified into high-risk HPV and low-risk HPV[3]. The highest rate of HPV infection is seen in adults aged 18 to 28 years[4], associated with immunosuppression. poor hygiene, infection with the human immunodeficiency virus (HIV), and anal sex[5]. This report exhibits an unusual case of an HIV-negative man who developed BLT.

CASE PRESENTATION

A 18-year-old black man with male sexual partners sought the Dermatology Service complaining of a voluminous lesion in the perianal region over the last 11 months. Initially, he also complained of proctalgia and minor local hemorrhage, which became more intense in the last 2 months. He denied any incontinence, and also denied diabetes mellitus. The results for HIV and other sexually transmitted infections tests were negative. Proctological examination revealed a verrucous and infiltrative lesion measuring 13 cm in its longest axis and exteriorized by the anal canal (Figure 1-A) which was biopsied. The patient was referred to the surgery service to remove the tumor with preservation of the anal sphincter. During the clinical visit, four specimens of the lesion were collected for later histopathological and molecular investigation.

Macroscopic analysis and histological

The macroscopic analysis showed that the specimens (Figure 1-B) consisted of four irregular fragments. They were brown, firm-elastic and measured together 2.1 cm × 1.8 cm × 0.6 cm. When cut, the specimens had a white inner surface and papillomatous conformational outline.

Histological sections from the lesion were subjected to hematoxylin-eosin (HE) staining (Figures 1-C and D). For immunohistochemical analysis, the biotin free method was used and then conjugated with horseradish peroxidase (HRP). Mouse monoclonal antibodies against the p16INK4a protein, dilution 1:100 (Zeta Corporation; Clone G175-405) were used. For negative controls, we used known negative cervical samples, without using the primary antibody. For positive control, we also used a cervical sample known as positive for p16INK4a. A qualitative analysis of reactivity was performed by immunohistochemistry, considering the intensity and location. The results were described as negative when in the absence of reactivity and positive when reactivity was present in more than 10% of the field. The reaction was qualified by the detection of the protein in the nucleus and in the nuclear membrane (Figures 1-E and F).

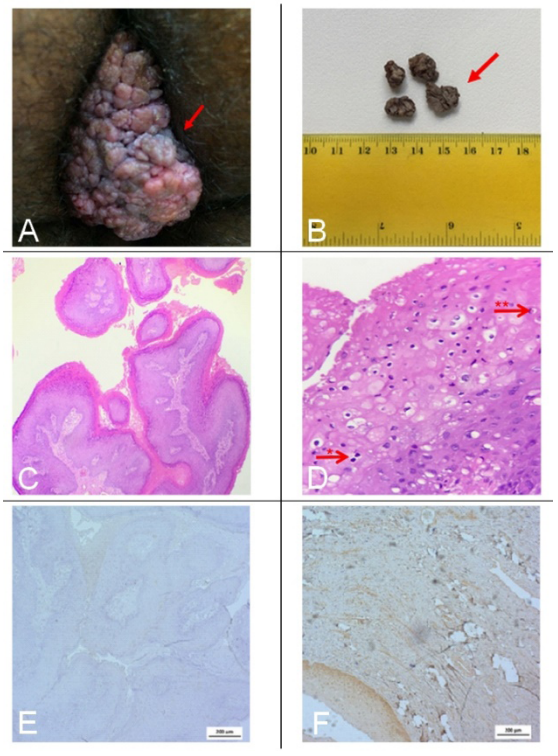

Figure 1: A: Gross view of the Buschke-Löwenstein tumor. Note the huge vegetating lesion in the perianal region; B: Specimens removed from the lesion for macroscopic analysis. For the histopathological analysis, hematoxylin and eosin (HE) staining were used (Figure 1-C e 1-D); C and D: Histopathologic examination of biopsies of the perianal lesion. The cuts showed an acanthotic, papillomatous architecture, hyperkeratosis, paraceratosis (3A). Intracytoplasmatic vacuolizations with hyperchromatic and irregular nuclei, binucleations, disceratosis, and coarse keratohyalin granules (3B) were noted. The histological analysis was compatible with condyloma acuminatum. *: coilocytic alteration; **: discereratosis. HE staining at 100x; E and F: Immunohistochemical study of p16INK4a expression. Pictures representing the absence of expression (E) and diffuse nuclear epithelial expression (F).

Molecular analysis

For the detection of HPV DNA, polymerase chain reaction (PCR) was used with the set of consensus and degenerate MY09/11 primers. MY09/11 primers were used in the present study, since they amplify a highly preserved 450PB partial sequence of the L1 gene of 47 papillomaviruses. The analysis of the samples was negative for DNA-HPV according to Table 1.

Table 1: Primers used in the detection of HPV.

		Size (BP)	
Primer	**Sequence of oligonucleotides (5'-3')**	**Oligo**	**Fragment**
MY09	CGTCCMARRGGAWACTGATC	20	
MY11	GCMCAGGGWCATAAYAATGG	20	445
GP05	TTTGTTACTGTGGTAGATAC	20	
FOLDING	METHOD		
GP06	GAAAAATAAACTGTAAATCA	20	170

Image analysis by magnetic resonance imaging (MRI)

MRI evidenced a perianal tumor lesion with exophytic, expansive formation, with no signs of invasion of adjacent structures or of inflammatory impairment of the fatty tissue that borders the lesion, as well as without compromising the penile components. The patient was referred to the surgery service to remove the tumor with preservation of the anal sphincter.

DISCUSSION

BLT is a rare and sexually transmissible disease associated with HPV infection[6]. Its clinical manifestations include pain, bleeding, pruritus, and appearance of fistulas[7]. Such manifestations are present in this case, since the patient complained of rectal pain and bleeding. The most frequently affected site is the penis in men and the vulva in women, with perineal involvement being less common for both

genders[8]. The risk factor for developing BLT is immunosuppression caused by diabetes mellitus, HIV infection, chemotherapy, use of corticosteroids, herpes simplex virus infection, pregnancy, long-term alcohol and tobacco misuse, in addition to poor local hygiene[1]. Although non-immunosuppressed patients with verrucas resistant to treatment were identified in the literature[4], immunosuppression leads to a higher growth of condyloma and increases the risk of malignant transformation by benefiting from the oncogenesis mechanisms caused by HPV infection[9]. In this case, the fact that the patient were not immunosuppressed, even after exhaustive investigation, is to be noticed.

It is important to point out that there is a vaccination available against the HPV virus, which is recommended to be taken before the initiation of sexual life. Taking the vaccination at the correct time could avoid BLT, as well as others serious conditions such as cervix cancer in women[10].

It is not known whether BLT, simple condyloma acuminatum, and squamous cell carcinoma of the anus are a spectrum of evolution or separate entities. This controversy is based on the pattern of malignant growth, despite with benign histological features: a well-differentiated hyperplastic epithelium with minimal atypia. Hyperkeratosis and parakeratosis with prominent granular layer can also be observed[6]. The same characteristics were evidenced by the histopathologic analysis of the case reported in this study, corroborating the diagnosis. The giant condyloma acuminatum behaves as an intermediary, with its slow growth, and a malignancy potential of 30 to 56% of the cases.

The patient was referred for tumor removal with preservation of the anal sphincter through surgical excision. The cure rate for this condition is 61%, and surgical excision can be used to treat recurrences successfully.

Conflicts of Interests

The authors declare no conflicts of interest.

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