Buschke -Loewenstein tumor: identification of HPV type 6 and 11 *

Condiloma acuminado gigante de Buschke-Lowenstein: identificação dos HPV 6 e 11

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Abstract: The authors report a case of exuberant giant condyloma acuminatum of Buschke-Loewenstein in a male patient, slow-growing, progressive and with locally destructive behavior in the inguinal, body of the penis, scrotum, perineal and perianal regions. After surgery he showed no signs of recurrence in 20 months of follow-up. The identification of HPV types 6 and 11 was performed using ***in situ*** hybridization.
Keywords: Human papillomavirus 6; Human papillomavirus 11; In situ hybridization, fluorescence

Resumo: Os autores relatam um caso exuberante de condiloma acuminado gigante de Buschke-Lowenstein, em paciente do sexo masculino, de crescimento lento e progressivo e de comportamento destrutivo das regiões inguinal, corpo do pênis, escroto, perineal e perianal. Após tratamento cirúrgico, não apresentou sinais de recidiva em 20 meses de seguimento. A identificação dos HPVs, tipos 6 e 11, foi realizada através da técnica de hibridização *in situ*.
Palavras-chave: Hibridização in situ fluorescente; Papilomavírus humano 6; Papilomavírus humano 11

INTRODUCTION

The giant condyloma acuminatum of Buschke-Loewenstein (GCBL) or Buschke-Loewenstein tumor (BLT) was first described by Buschke in 1886, by Buschke and Loewenstein in 1925 and later on was named by Loewenstein "carcinoma-like condylomata acuminata" of the penis. It is considered a slow-growing verrucous tumor and reaches large sizes. Differently from condyloma acuminata, it has a large and infiltrative base, locally destructive behavior, a high rate of recidivism and possibility of malignant transformation. Ackerman (1948) considered the BLT a verrucous carcinoma with similar clinical and histopathological aspect, while to other authors BLT represents an intermediary lesion between the condyloma acuminatum and the verrucous carcinoma, that is, a pre-malignant condyloma-like tumor.[1,2] Its pathogenesis is not totally clear and several studies have tried to elucidate a possible oncogenesis mechanism of non-oncogenic HPV 6 and HPV 11 found in BLT.[3]

The present article describes an exuberant case of Buschke -Loewenstein tumor, an analysis of the clinical and laboratory diagnosis, as well as the chosen treatment approach.

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CASE REPORT

A 54-year-old male patient, white, heterosexual, alcoholic, refers that he has had a painful and foul-smelling tumor in the genital region for about five years. During this period he had appointments at several hospitals where the tumor site was thoroughly cleaned and treated with systemic antibiotics. After several treatment alternatives without improvement he came to our STD multidisciplinary outpatient clinic (dermatology, coloproctology and urology) of the Dermatology Clinic, Charity Hospital of São Paulo, for diagnostic elucidation and treatment.

The dermatological examination revealed an erythematous, exophytic, vegetative tumor with a multilobulated surface, friable, measuring 30 cm at the largest diameter, painful on palpation, with purulent secretion, foul-smelling and covering the entire inguinal region, body of the penis, scrotum, perineal and perianal regions. The scrotal region had increased volume, edema and was hard on palpation (Figure 1). The patient was malnourished, underweight and had cutaneous-mucosa paleness. The patient referred, as personal history, surgery to remove a moderately differentiated squamous cell carcinoma in the neck region and emptying of cervical lymph nodes due to metastasis five years before. Laboratory tests had shown normocytic and normochromic anemia (hemoglobin: 7.0 g/dL and hematocrit: 22.4%), liver and kidney functions normal. Serologies for B and C hepatites, HIV and syphilis had nonreactive results. Biopsy revealed a condyloma acuminatum without malignancy or atypia. Wide surgical excision of the entire area involved was carried out; 15 days later, with the presence of granulation tissue, a graft was performed with skin removed from the right thigh. After 30 days, complete epithelization could be observed. The patient continued to be monitored at the outpatient clinic and did not have any evidence of relapse 20 months after the surgery (Figure 1). The anatomopathological examination of the dried sample showed condyloma acuminatum with low-degree intraepithelial neoplasia. DNA analysis of the neoplasia by hybridization *in situ*, with a wide spectrum probe, revealed HPV types 6 and 11 (Figure 2).

DISCUSSION

The Buschke-Loewenstein tumor is more common in men, at a 3:1 rate, with mean age around 50 years. Differently from condyloma acuminata, BLT has a large and infiltrative base, locally destructive behavior, a high rate of recidivism and possibility of malignant transformation. [4,5,6]

Several authors mention only the presence of low-risk HPV (6 and 11) in BLT, while others report the importance of presence of high oncogenic risk HPV 16 or 18 in a condyloma that already contains HPV 6 and 11 for development of BLT.[1] BLT pathogenesis may be related to specific viral mutations responsible for oncogenesis. Some reports demonstrate the *in vitro* activity of an HPV 6 oncoprotein able to promote the exchange of protein E7 aminoacids, thereby being transformed in HPV type 16. Nevertheless, other authors were not able to reproduce these data.[7]

The underlying factors responsible for development of BLT are poor hygiene, uncircumcised patients, promiscuity, chronic irritation, immunosuppression by HIV or HTLV-1 infection and chronic, relapsing genital warts.[8,9] In the mentioned case the association of chronic warts was observed at onset. The presence of phimosis, immunosuppression acquired through alcoholism and personal history of squamous cell carcinoma probably contributed to the BLT progression.

One of the characteristics of the giant condyloma acuminatum of Buschke-Loewenstein is a benign histopathological pattern that may progress to extensive papilloma proliferation that deeply penetrates

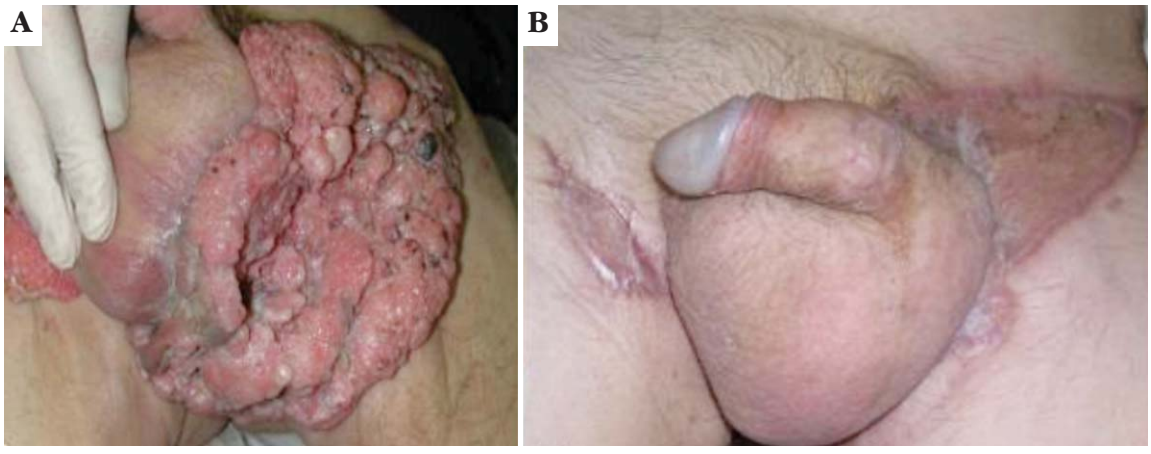

Figure 1: A. Exuberant exophytic tumor in the inguinal, scrotal, perineal and perianal regions; **B.** Cutaneous graft aspect

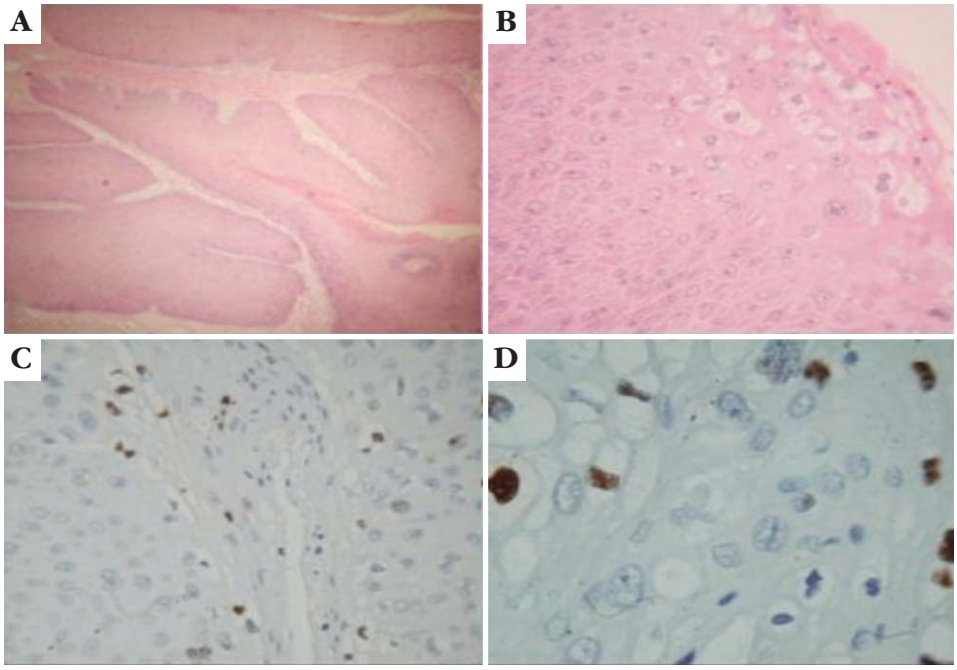

Figure 2: A. HE (10X) – Verrucous architecture with papillomatosis, acanthosis and minimal loss of epithelial cell polarity; **B.** HE (40X): koilocytosis and cellular binucleation. **C.** Hybridization for HPV 6 and 1 (40X) in situ: positive (brown) staining of superficial epithelial cells nuclei. **D.** Hybridization for HPV 6 and 11 (100X) in situ: detail: koilocytosis and cellular atypias, with brown staining of some nuclei

underlying tissues if not adequately treated. In the case reported, tumoral invasion reached the subcutaneous cell tissue; the sphincter muscles in the anal region were preserved and the resection at deeper planes permitted removal of the entire tumor.[7,10-11]

Malignant transformation of BLT has been reported in 30 to 56% of all cases and the risk of recidivism after surgical excision varies between 60-66% in up to 10 months after the treatment.[10] Distant metastases generally do not occur and the global mortality rate is 20-30% in up to five years.[12] In this case report, the anatomopathological examination of the surgical sample did not reveal presence of lesions with a high degree of malignant transformation, and a 20-month follow-up after the surgical procedure did not show clinical evidence of relapse. A long-duration follow-up is important to prevent, adequately treat recidivism of the clinical picture and avoid malignant transformation. ❑

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