Buschke-Löwenstein Tumor: Case Report And Review With Focus On Therapeutic And Psychological Aspects

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Citation

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Abstract

Buschke-Löwenstein tumor (BLT) is a rare entity and less than 100 cases have been reported. These are slow-growing, cauliflower-like, destructive lesions that histologically have benign appearance. One of the hallmarks of the disease is the high rate of recurrence and malignant transformation. Human papillomavirus has been identified as contributory to its development as well as immunosuppressive factors. We report a new case of BLT and review current knowledge about the disease, emphasizing in therapeutic but also in psychological aspects, which have never been previously analyzed. Surgery is the only treatment with curative potential and adjuvant interpheron should be considered due to the high rate of recurrence. In unresectable cases, preoperative systemic treatment is warranted. Participation of a psychologist and/or psychiatrist in the management of these patients is essential to fully understand and adequately manage mechanisms that frequently lead to a negligent attitude that can interfere with adaptation and treatment adherence.

INTRODUCTION

In 1896 Buschke [1] described a disease as "verrucous carcinoma" for the first time. It consisted in a giant condyloma that microscopically had a differentiated squamous epithelium with papillary growing. Despite a benign histological appearance its local behavior was aggressive with infiltration and destruction of surrounding tissue due to compression. This disease is known today as Buschke-Löwenstein tumor (BLT). To our knowledge, less than 100 cases have been reported up to today in the English literature.

Usually located in perineal region it has also been reported in oral cavity, larynx and nasal cavity, characterized by slow growth with major local inflammation [2].

Sexually transmitted human papillomavirus DNA subtypes 6 and 11 is regularly found in these lesions, strongly suggesting its etiopathogenic role in tumor development. Still today, it is unknown which viral factor(s) or hostess features promote the replication of these generally indolent viruses leading to the progression of a plaque to a cawliflowerlike mass and later even to a carcinoma in about 30-50% of the cases [3,4,5].

Although surgical resection is potentially curative, the extension of these tumors usually limits its indications and makes radical treatment impossible. For that reason, immunotherapy, chemotherapy and/or radiotherapy are frequently considered.

Psychological features in these patients have not been assessed in the cases published up to now. It constitutes an extremely relevant aspect in the evaluation of this pathology that requires long-term treatments, mutilative surgeries and which involves the possibility of malignant transformation and death. Getting to know the psychological profile of these patients would help physicians to promote treatment adherence and, furthermore, get patients to consult in earlier stages of the disease.

In this paper we review the most noticeable clinical features of BLT on the base of a case report and emphasize the psychological features that have not been previously analyzed in medical literature.

CASE HISTORY

Seventy years-old, male, heavy smoker, homosexual, bad socioeconomic situation, without family support.

He presented at the Emergency Room with a perineal tumor that had been slowly growing for the previous 2 years. The mass was initially painless but at consultation it was extremely painful. In the evolution fecal incontinency arouses. Of notice on physical examination the patient has

regular general condition and the ano-perineal region was completely occupied by a cawliflowerlike tumor of 10 by 15 cm in major diameters with multiple fistulae with spontaneous discharge of semi-liquid stools (Figure 1). Digital rectal examination was impossible due to pain. No palpable lymph nodes were found.

Figure 1

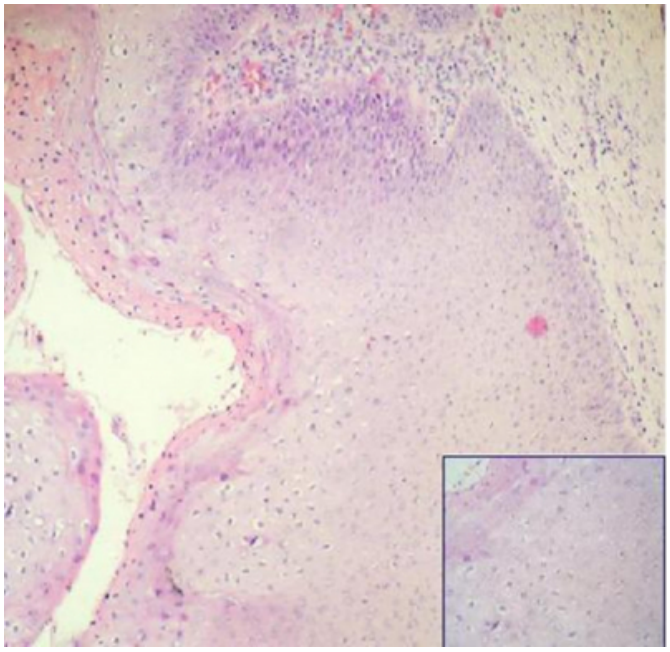
Figure 1: Cawliflowerlike and fistulized tumor, measuring 10 x 15 cm, located in the perineal region and extending from coccygeal region to scrotum.

A biopsy was performed as well as an abdominopelvic computed tomography (CT), and general bloodwork. Of notice, syphilis and HIV serology were negative.

Histology revealed a condyloma with areas of moderate dysplasia (Figure 2).

Figure 2

Figure 2: Microscopy showing squamous epitelium with achantosis, parakeratosis and basal cell hyperplasia. Some superficial koilocytes can be seen. These features (especially koilocytes) are characteristic of HPV infection. Inset: koilocytes. (Courtesy of MarÃa Luisa Musto M.D.)



A second biopsy was performed which had similar results and did not found malignant cells. The CT showed a heterogeneous and irregular solid tumor at the anal margin with thickening of the anal wall and low perirectal fat. On its anterior portion muscular planes and fat was involved up to the scrotum. A 1.5 cm left inguinal adenomegaly was identified.

Mild opioids were unable to relief pain so morphine had to be indicated. Antibiotics (metronidazol 500 mg iv tid), steroids and non steroidal anti-inflammatories contributed to infection and inflammation control.

A three-stages treatment was planned. Firstly, a left iliac colostomy was performed to relief pain, infection and local discomfort. After that, neoadjuvant combination chemotherapy was indicated and at last surgical resection was to be performed.

Effectively, the patient had colon derivation and received two cycles of induction chemotherapy with cisplatin (100 mg/m^2 iv D1) and bolus 5-fluorouracil (425 mg/m^2 D1-5). No objective response was obtained. The patient did not adhere to scheduled visits. Twenty days after the second cycle of chemotherapy patient was found dead at home.

Suicide was ruled out and no autopsy was performed.

DISCUSSION

ETIOPATHOGENY OF BLT

The cause of BLT is not known with certainty; the favored theory is that of viral origin. Co-localization with human papillomavirus (HPV) types 6 and 11 and less frequently with HPV types 16 and 18 have been shown [6]. Other risk factors are: local chronic inflammation, smoking, and immunosuppressant treatment.

These factors contribute as initiators and/or promoters to the development of BLT [7,8,9]. Probably, the sum of contributory factors (infection, smoking) leads to the secondary malignant transformation in up to 56% of the cases [3].

The implication of sexually transmitted HPV in the etiopathogeny of BLT highlights the need for an adequate prophylaxis of this entity in order to avoid its occurrence.

It is also evident that any immunosuppressive maneuver or disease can contribute to HPV replication and eventually to BLT development [10,11]. Quitting smoking should be specifically emphasized in patients with known HPV infection in an attempt to avoid the associated chronic immunosuppression that may facilitate the tumorigenicity of HPV [12].

In consequence, it can be hypothesized that the sequence condyloma-BLT-cancer is the result of the sum of cell changes induced by HPV colonization (especially HPV 6 and 11) and the secondary contribution of local and general factors with immunosuppressive effect.

CLINICAL AND PATHOLOGIC DIAGNOSIS

Gross examination of BLT, condyloma and squamous carcinoma can be very alike: big cauliflowerlike tumors that may have been growing for several years [3]. Histologically, BLT and condylomas share microscopic benign aspect, what differentiates these entities from squamous carcinoma.

Despite its benign histologic appearance, BLT has a locoregional malignant behavior. Infiltration and destruction of contiguous tissue is frequently seen at debut. Sometimes, differential diagnosis with anal carcinoma can not be excluded after CT or Magnetic Resonance Image (MRI), since involvement of deep structures can be present in BLT as well as in anal cancer [2].

TREATMENT APPROACHES

Untreated or inadequately treated BLT has a relentless progression and is fatal by direct spread to pelvic organs. The ‘contradiction' between the histological benignity of these lesions and their aggressive behavior is evidenced by the fact that most initially radical approaches turn out be palliative due to the inability to effectively control the locoregional spread of the disease.

Many therapeutic approaches have been attempted in these patients: topic, radiant, systemic and surgical strategies will be analyzed.

LOCAL MODALITIES

Topic treatments, including weekly hyperthermia [13], trichloroacetic acid [14], 5-fluorouracil [15] and thiotepa [16], have been reported in these patients but resulted in most cases in poor results. Podophyllin applications, usually effective for condylomas, induce acute histologic changes that can make BLT resemble an in situ carcinoma, and have posed problems to pathologists who sought to differentiate between these entities [17].

According to some reports, radiation therapy may contribute to the malignant transformation of BLT [18,19]. Besides, although small superficial lesions may be effectively controlled using radiotherapy, poor outcomes are obtained when treating more advanced lesions [20]. Other local treatments like CO2 laser [21], electrotherapy [22], and local resections [23] have been used with limited success.

Surgery is the main modality of treatment and the only with potentially curative intent. Authors agree in the benefit of achieving a disease-free status (i.e. negative margins) and with this objective can be necessary to perform a pelvic exanteration [2], abdominoperineal amputation or other major surgery with high morbidity and mortality and major psychological impact. However, it must be considered that the rate of local recurrence in totally resected lesions can exceed 50-60% and that more than 20% of these patients die due to disease progression.

SYSTEMIC TREATMENT

Systemic immunotherapy with intramuscular interpheron has an objective response rate of 76% in advanced cases [12]. Some authors have reported cases of complete responses in patients with unresectable tumors in whom systemic or intralesional interpheron was used [24,25,26]. Therefore, induction treatment with interpheron should be considered in

patients with unresectable tumors or in cases in which mutilating surgeries (i.e. abdominoperineal amputation, hemi-pelvectomy) are necessary to achieve a complete resection.

Considering the high response rate in unresectable tumors, the use of adjuvant interpheron seems attractive and it has been explored by some authors [27,28,29]. One of the best therapeutic results has been observed in reports in which adjuvant interpheron have been used. Therefore we believe that, considering the high rate of recurrence, this treatment should be considered in every patient who undergone complete surgery for BLT.

Since the Abcarian et al reports [30,31,32] were they treated 185 patients with condyloma acuminatum or BLT with individually designed vaccines after radical surgery. They achieved excellent results with recurrences seen in only 7% of cases. Eftaiha et al [33] used the same approach and had similar good results. Unfortunately, we were unable to found more recent publications in which this modality is employed and its value is not clearly defined.

Finally, systemic chemotherapy is considered an alternative to immunotherapy in the postoperative setting. 5-fluorouracil, cisplatin, mytomicin, methotrexate and bleomycin are the most used drugs (alone or in combination) with dissimilar results in advanced tumors. Due to the low frequency of this disease, the lack of clinical trials and the fact that the current evidence derives mostly from case reports, no regimen can be considered as standard.

As previously mentioned, advanced and unresectable tumors are frequently seen at diagnosis. Therefore, neoadjuvant strategies can theoretically reduce tumor burden and facilitate surgical complete excision. Based on their own experience with only 2 patients, Ilkay et al [2] have proposed that neoadjuvant chemotherapy should be considered in cases in which surgery is not technically possible or patient refuses to it. They reported 2 cases in which systemic chemotherapy using bleomycin, cisplatin, methotrexate, and leucovorin led to complete responses, one of them a complete pathologic response. However, as well as adjuvant chemotherapy, neoadjuvant strategies have not been adequately explored and current recommendations are based on case reports.

PSYCHOLOGICAL CONSIDERATIONS

Like in the case reported by us, patients with BLT usually present, after prolonged intervals of neglect, with large and disfigurating lesions that are associated with pain, bleeding, infection and fetidness. Although ignorance, social isolation and low socioeconomic status can partially explain the neglection of these patients, other factors must be considered to fully understand this behavior. First, the delay in consultation (which can be of several years after the onset of the first symptoms) can be the consequence of a normal defense mechanism (i.e. negation) that in these cases can be abnormally prolonged due to the fear that a “hidden” homosexuality becomes known or to the fear of loosing a healthy status. When lesion progresses and grows, patient faces to the possibility of a cancer diagnosis and its implications (i.e. aggressive treatments, death), and this can also drive to a delay in consultation. A study showed that younger age, insensitivity to threat and low overall anxiety levels can explain the delay in consultation for cancer-related symptoms [34].

Once patient gets to a medical institution, he/she is faced to frequent examinations of the perineal region, invasive diagnostic procedures, and in some circumstances toxic systemic treatments and/or mutilating surgical maneuvers. Adherence to these strategies can be hampered by personal and psycho-social factors. In some patients, regression, a normal defense mechanism frequently seen in hospitalized patients, can lead to an excessively passive attitude with harmful effects (i.e. low level of involvement with treatment).

It must be emphasized that the role of the psychologist and/or psychiatrist and social worker, in the management of these patients is critical in an attempt to facilitate adaptation and increase treatment adherence. A case of suicide in a patient with BLT have been reported and the loss of follow-up or treatment abandon have been observed in 20% of cases [2,3].

In conclusion, we have reported a new case of unresectable BLT in which neoadjuvant chemoradiotherapy was proposed. BLT is a rare tumor usually found in the perineal region,characterized by its benign histologic appearance which contrasts with its malignant behavior characterized by the invasion of surrounding tissues and the frequent local recurrences after surgical excision. The optimal strategy for the treatment of this disease is not known. Surgery remains the mainstay of treatment and the only that can offer a chance for cure. Neoadjuvant and adjuvant approaches have been used but their role in not totally defined. Considering

the high rates of local recurrences after surgery adjuvant systemic therapies must be considered, and interpheron seems to be the most effective. For the fist time in medical literature, we have analyzed psychological aspects of these patients emphasizing the importance of their consideration in the standard management of this disease.

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