ISSN No:-2456-2165

Descriptive Study of Buschke-Lowenstein Genital Tumors: A Series of 18 Cases

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Abstract:- The Buschke-Löwenstein tumor is a rare tumor. It is a tumor linked to a sexually transmitted viral infection by the human papillomavirus (HPV) that develops on the external genitalia and the ano-rectal region.

Objective: To describe the clinical, anatomopathological and management characteristics through a series of 18 observations in a North African population.

Methods: We have retrospectively analyzed data from 18 patients in our prospective database since 2010. This work is based on the exploitation of clinical records, the interpretation of the radiological balance, the analysis of therapeutic methods, as well as short- and long-term developments.

Results: This includes 18 men whose average age is 52.4 years, 12 of whom have risky sexual behaviors with two men who have sex with men (MSM), chronic smoking, cannabis addiction, and HIV-positive human immunodeficiency virus (HIV) for eight patients with Buschke-Lowenstein tumors treated with full surgical resection, which remains the reference treatment. All patients were sexually active. In all patients, the tumors were exophytic, cauliflower-shaped ulcers dotted with outbreaks of infection. Most of the shapes seen were bulky with an average size of 11cm. The location on the genital area was constant within 9 cases of an invasion on the thighs and the peri-anal region. No surgical complications were noted, particularly infectious. A relapse was noted in one patient, and it was treated with radiotherapy and surgical recovery. Due to its rarity, the management of this type of tumor remains uncodified and a multidisciplinary consultation meeting and network management in an expert center guarantee a better therapeutic strategy.

Conclusions: There seems to be a consensus that the surgical option should be as radical as possible with organ preservation. Prevention of this tumor is based on the treatment of acuminate condylomas and the fight against sexually transmitted infections.

Keywords:- *Buschke-Lowenstein Tumor, Surgery, Human Papillomavirus, Radiotherapy, Relapse.*

I. INTRODUCTION

The Buschke-Löwenstein tumor (BLT) or giant acuminate condyloma is a rare nosological entity [1]. It is a viral, sexually transmitted infection that develops on the external genitals and the anoctal region [2]. It differs from acuminate condylomas by its more marked proliferation and deep penetration in the underlying tissues that can then be repressed and from an epidermoid carcinoma by the absence of histological invasion and metastases, characterized by its degenerative potential and its recurrence after treatment [3]. The causal agent is the human papillomavirus (HPV), which exclusively infects the skin and mucosal epithelia [4]. The replication cycle is linked to the proliferation and differentiation of the infected epithelial cell. It can remain quiescent and reactivate during immunosuppression. The risk factors are poor rectal hygiene, pregnancy, multiparity, MSM population, immunosuppression, smoking, alcohol, and sexually transmitted infections (STIs) [4]. Care is often controversial: therapeutic abstention, surgical exeresis, electrocoagulation-exeresis, CO2 laser, and immunotherapy. The consensus seems to be emerging for the surgical option [5, 6, 7].

BLT is a rarely curable disease. If not treated early, it can have a dramatic evolution involving mutilating surgery without the possibility of organ preservation with the impact on the quality of secondary life.

We report clinical, anatomopathological, and management characteristics through a series of 18 observations in a North African population. We analyzed retrospectively the data of 18 patients in our prospective database since 2010 who completed the follow-up to the date of the latest news.

II. MATERIALS AND METHODS

Our work consisted of a retrospective study with 18 cases of Buschke-Lowenstein tumor collected at the FES Hassan II Hospital Urology Department over nine years (January 2010 to January 2018). This work is based on the exploitation of clinical records, the interpretation of the radiological balance, the analysis of therapeutic methods, as well as short- and long-term developments. All patients were hospitalized in the urology department during this

ISSN No:-2456-2165

period. We included in this study all patients who had consulted at the urology department of the Hassan II Hospital in Fez and whose clinical and paraclinical examinations revealed a buschke-lowenstein tumor. The collected parameters were evaluated from the register of incoming patients, the clinical records of the patients, the pre-anesthetic consultation sheets, the register of the operative records, the computer system Hosix.

III. RESULTS:

The average age of our patients was 52.4 years (39; 63), all our patients were married males, with two MSM and 10 have risky sexual practices. Eight (8) cases of chronic smoking and one case of cannabis use. Only one patient was HIV-positive, and another had been treated for type II diabetes for 20 years under insulin. The appearance of the cauliflower-looking tumor was the primary reason for the consultation (Figure 1). Pruritus was reported by 2 patients, and the urinary burns were found in only one patient. The lesions found in our series all had a vegetative aspect, burgeoning in cauliflower with over infection seats and a bad smell. They were large in all cases, with an average diameter of 10-11cm. Localization at the external genitals was constant (Figure 2). We did not find any fistulae or inguinal lymphadenopathies in our patients. The tumor had invaded the thigh in 4 cases and the peri-anal region in 5 patients. The pre-and sub-pubic region was invaded in two cases. In 3 cases, both the thighs and the anal region were flooded. All the patients reported an interruption in their sexual activity, as well as an alteration in the quality of life identified by IIEF 15 (International index of Erectile Function), translated into an Arabic dialect.

In all our patients, the treatment was surgical. It had consisted of a large experiment at first with organ preservation, and recovery was done at a second stage in five cases **(Figure 3).**

The accurate diagnosis of Buschke-Lowenstein's tumor is based on a broad, surgical, rather than a circular bistoury, histological examination, so as not to incorrectly conclude that a seborrheic condyloma or keratosis is present.

The anatomopathological study of the surgical room confirmed the diagnosis of TBL in all cases with the presence of an outbreak of squamous cell carcinoma in a patient. In one case, TBL was associated with Bowen's disease **(Figure 4, 5).**

It can also be manifested by a burgeoning exophytic keratinized epithelial tumor with papillomatosis and marked acanthosis and regular cytology. It is associated with parakeratosis and many mostly superficial koilocytes. In some cases, intra-epidermal corneal cysts may be present, simulating seborrheic keratosis. The proliferation is initially exophytic but can extend in-depth in the form of cytologically regular keratinocyte buds with the presence of many koilocytes but the basal membrane remains continuous.

The verification of compliance with the basal membrane is crucial since otherwise, the diagnosis of Buschke-Lowenstein tumor is discarded in favor of the diagnosis of micro-invasive or invasive squamous cell carcinoma (EC) occurring on Buschke-Lowenstein tumor [8,9,10].

On a macroscopic scale, the Buschke-Lowenstein tumor is a large-sized (up to 10 cm wide axis) papillomatous, irregular tumor, with a heroic surface of keratotic vegetation, burgeoning, cauliflower, often whitish or yellowish, often with superficial ulcers and over added infectious lesions. The volume is variable, the consistency is firm, hard, and resistant to cardboard roof. The presence of bleeding, infiltration of the base, or the presence of lymphadenopathies should lead to suspicion of malignant degeneration.

In optical microscopy, BLT is a perfectly limited Malpighian tumor, characterized by considerable epithelial hyperplasia, sometimes pseudo-epitheliomatous, whose basal membrane is still intact, hyperacanthosis, hyperpapillomatous hyperplasia, and koilocytes are pathognomonic markers of HPV infection, however, their presence is not constant. The basal membrane remains intact, which proves the benignity of the tumor despite its malignant behavior.

In electron microscopy, the examination shows a widening of intercellular spaces, the cell edges are well defined, but irregularly. The cells form well-developed desmosomes with their neighbors. The cytoplasm contains a well-developed Golgi apparatus, ribosomes, and dispersed glycogens. The oval or round mitochondria, whose ridges appear curved, a granulated endoplasmic reticulum. Tone filaments, high in some cells and reduced or rare in others. Lysosomes are in small numbers. The nuclei are round or oval. Chromatin is dispersed and tends to agglomerate in the periphery. Sometimes we find intranuclear annular bodies. The basal layer cells rest on a single intact basal membrane. In addition, electron microscopy of Buschke-Lowenstein Tumor fragments did not detect viruses, even with a peroxidase immunomarker.

In the treatment project, electrocoagulation was performed in a single patient with small penile condylomatous lesions associated with the primary BLT. Radiotherapy was performed in two patients, the first case had presented a trivial giant condyloma to the biopsy, while the histological study of the surgical room showed a malignant transformation of the tumor, the second case had presented a local recurrence, and the radiotherapy was therefore administered by neo-adjuvant before the surgical resumption to decrease the tumor volume. Follow-up was possible in twelve patients with an average setback of 44 months. One patient died of myocardial infarction while in hospital and five patients were lost sight of it. The only recidivism was noted, the patient had received neo-adjuvant radiotherapy before the surgical resumption.

IV. DISCUSSION

The Buschke-Lowenstein tumor is a rare tumor [11]. In our series, the frequency is about 0.003% by estimating the number of hospitalizations in the urology department during the period of our study at 5252 patients. This tumor occurs at any age with a predominance between the 4th and the 6th decade.

Infection can occur in both sexes and is more common in males (77%). Transmission of BLT occurs primarily through sexual transmission and also through dirty water, linen, gloves, and other materials. The virus is resistant to environmental conditions.

Lack of hygiene, risky sexual behaviors, the HRSM population, and chronic HIV infections contribute to HPV infection remain the contributing factors to this tumor [12, 13]. The persistence, development, and recurrence of these condylomas depend on the immune status of the affected person [4, 14].

Several papillomavirus serotypes, including 6 and 11, appear to be involved in the genesis of the Buschke-Lowenstein tumor, but the oncogenic potential remains low compared to serotypes 16 and 18 [5,12].

BLT is most often located at the external genitals and mainly at the yard level. Ano-rectal localization is less frequent but not uncommon.

In humans, TBL is found in 81-94% of cases in the penis and 10-17% of cases in the anoctal region. In women, localization is essentially vulvar in 90% of cases, unlike the anoctal localization, which is less frequent. In our series the location at the external genitals was constant, the tumor had invaded the thigh in 4 cases and the peri-anal region in 5 patients or 31%. The pre-and sub-pubic region was invaded in two cases.

In two patients, the lesion involved the anal margin, buttocks, perineum, scrotum, and rod. In 5 other patients, all-male, the lesion sat downstream of the navicular dimple and emancipated in cauliflower at the urethral meat.

The tumor is always preceded by grayish or pink condyloma lesions, evolving gradually to take on a papillomatous, irregular aspect.

It evolves in surface and depth, which marks its difference from ordinary acuminate condylomas. The scrotum or vulva, the inter-buttock groove, the buttocks, even the rectum, and the pelvis can be extended. On the surface, it can give birth to a huge tumor of about ten centimeters. Deep the tumor evolves by destroying and repressing nearby structures without infiltrating them [5, 8, 12, 15].

The symptoms are linked to deep infiltration: pain, bleeding, pruritus, and the formation of fistulas, which can become over-infected and lead to bacteremia. The clinical examination must include the examination of the external genitals and the inguinal ganglionic areas (inflammatory and non-metastatic lymphadenopathies frequent due to the superinfection of the tumor). Examination of the perineal and anal region is necessary, in search of condylomas, and must be completed by anoscopy in case of anal reports. The clinical examination of the partner(s) should be proposed, in search of induced anogenital or oral HPV lesions.

The accurate diagnosis of BLT is based on a histological examination of a broad surgical biopsy rather than a circular bistoury, so as not to incorrectly conclude that a seborrheic condyloma or keratosis is present. This histological examination shows a burgeoning exophytic keratinized epithelial tumor with marked papillomatosis and acanthosis and regular cytology. It is associated with parakeratosis and numerous koilocytes (keratinocytes clarified as evidence of the cytopathogenic effect of HPV virus) mostly superficial. In some cases, intra-epidermal corneal cysts may be present, simulating seborrheic keratosis.

The proliferation is initially exophytic but can extend in-depth in the form of cytologically regular keratinocytes buds with the presence of many koilocytes but the basal membrane remains continuous. The verification of compliance with the basal membrane is crucial since otherwise the diagnosis of BLD is discarded in favor of the diagnosis of micro-invasive or invasive squamous cell carcinoma (EC) occurring on BLD [8, 9, 15].

In our series, the histological study of the surgical room confirmed the diagnosis of BLT in all cases, with the presence of an outbreak of squamous cell carcinoma in a patient.

Magnetic resonance imaging (MRI) of the penis and scrotum, or MRI or pelvic scanner are indicated to assess local tumor invasion and to guide surgical action [14, 16].

Other sexually transmitted infections include HIV serologies (Human Immunodeficiency Virus), HBV (Hepatitis B Virus), HCV (Hepatitis C Virus), TPHA-VDRL (Syphilis Serology), Chlamydia trachomatis and even Neisseria gonorrhoeae in the first urinary jet, sometimes in the oropharynx and anus depending on sexual practices, in our series, only one patient was HIV positive and an MRI was requested in two patients who had been exposed to sites of squamous cell carcinoma to assess infiltration and local invasion [5,6,14,16].

BLT poses the problem of differential diagnosis with other pathologies. Among them, the acuminate condyloma [9], especially in its beginner or recurrent form, also with Bowen's disease [12,14,15,16], in its dyskeratotic condylomas form that affects subjects over 45 years and also the pseudo-balanitis Keratotic and micaceous epitheliosclerosis [16], and the spinocellular epithelium which is characterized by a collapse of the basal membrane with cellular atypia, infiltration, and invasion of the underlying tissues and finally wart carcinoma, syphilis, Nicolas-favreou lymphogranuloma venereum, wart

tuberculosis, inguinal ulcerative donovanosis or granuloma, anogenital amebiasis which may confuse with BLT [6,14,15]. The scarcity of BLT explains the lack of consensus regarding its treatment [10]. However, surgical exeresis appears to be more effective than medical treatment.

BLT surgical treatment is based on full-scale, but uncodified, exeresis of the lesion, to reduce the risk of local recurrence, which remains significant even with clinically and histologically complete exeresis.

CO2 laser vaporization, less mutilating than conventional surgical exeresis, was reported only through a few clinical cases, some with no recurrence after a 10-year decline [17]. If the rate of recidivism after CO2-laser spraying has not been compared to that of conventional surgical exeresis, the absence of histological control of the entire lesion may disregard areas of transformation into micro-invasive or invasive EC. The other therapeutic modalities (chemotherapy and alpha-interferon intra-lesion or systemic, acitretin or isotretinoin, topical imiquimod, radiotherapy) can be discussed in a multidisciplinary consultation meeting on a case-by-case basis and can be used in isolation or combination with surgery, in particular, to reduce the lesion volume in preoperative [17].

The completeness of the surgical exeresis of the giant acuminate condyloma must be confirmed by the anatomopathological examination of the operative part. The incomplete surgical exeresis must indicate the surgical recovery [11].

The surgical procedure varies according to the extent of the lesions, the existence of infectious and hemorrhagic complications, the possibility of degeneration of the tumor, and the topography of the tumor and its extension to a possible organ (penis, anus).

Natural evolution can be to a local invasion, a recurrence, or a malignant transformation, it can be encumbered by several complications including dermatitis, infection, fistulation to neighboring organs, necrosis, anal stenosis, and hemorrhage. Spontaneous regression cases are exceptional, the malignant transformation into invasive epidermoid carcinoma varies from 5 to 42% in the literature and exposes the risk of ganglionic and visceral metastatic evolution [18].

Patient Consent: Note that our patients were informed of the diagnosis and they all agreed to the treatment with consent from them or their companions before all the actions were taken.

V. CONCLUSION

TBL remains a rare tumor, and its reduced incidence depends on informing the general population and improving national plans to prevent sexually transmitted infections, particularly in developing countries.

All data in the literature are derived from isolated cases or series of cases with insufficient levels of evidence to make general recommendations.

Treatment is often based on the formalized consensus of experts, hence the interest of a dedicated multidisciplinary network in expert centers to increase the specific surgical volume for better management.

Conflict of interest:

The authors do not declare any conflict of interest.

Contributions by authors:

Mr. Mzyiene and Mr. Ahsaini have had full access to all data from the study and they take responsibility for the integrity of the data and the accuracy of the analysis of the data.

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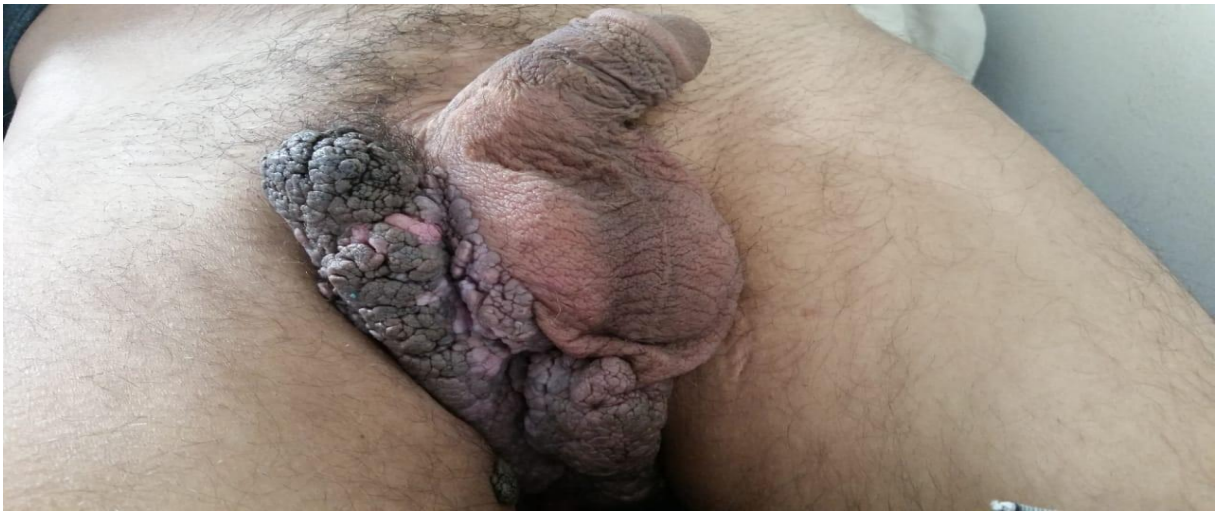

Figure 1: image of a 51-year-old patient with a large, one-sided genital lesion with typical cauliflower appearance, having undergone surgery without repetition.

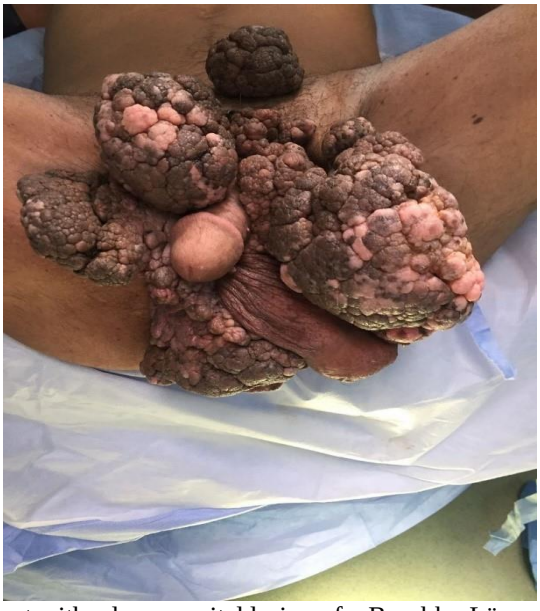

Figure 2: Image of a 45-year-old patient with a large genital lesion of a Buschke-Löwenstein tumor with a typical cauliflower appearance, having undergone surgery with healthy margins and organ preservation.

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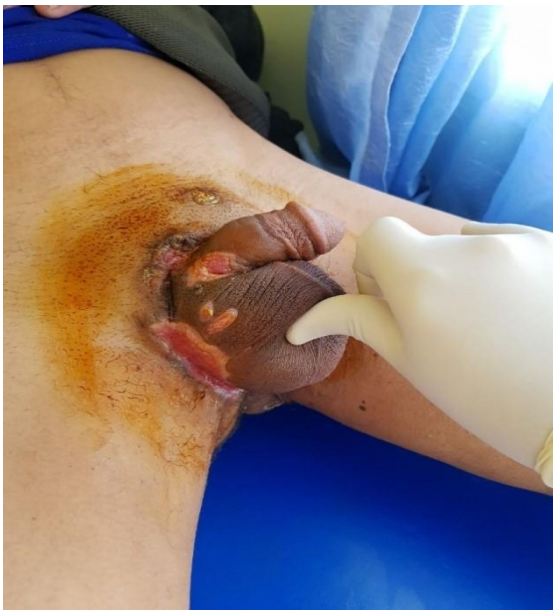

Figure 3: image of a 39-year-old patient who had undergone a healthy margin surgical procedure at 2 months post-operative.

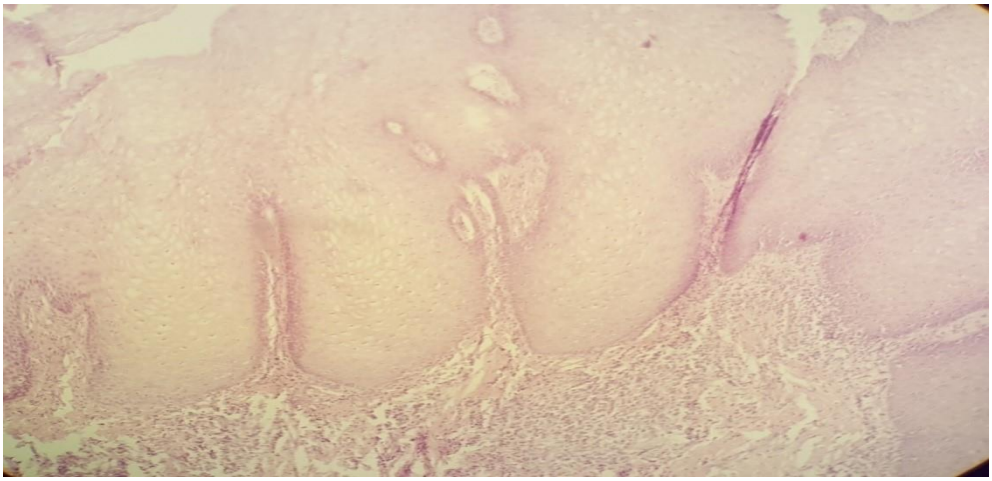

Figure 4: Histological study at magnification x 100, showing papillomatous, vegetative, ortho and parakeratotic epithelial proliferation, which invagines deeply in the dermis (hematein coloring - Eosine).

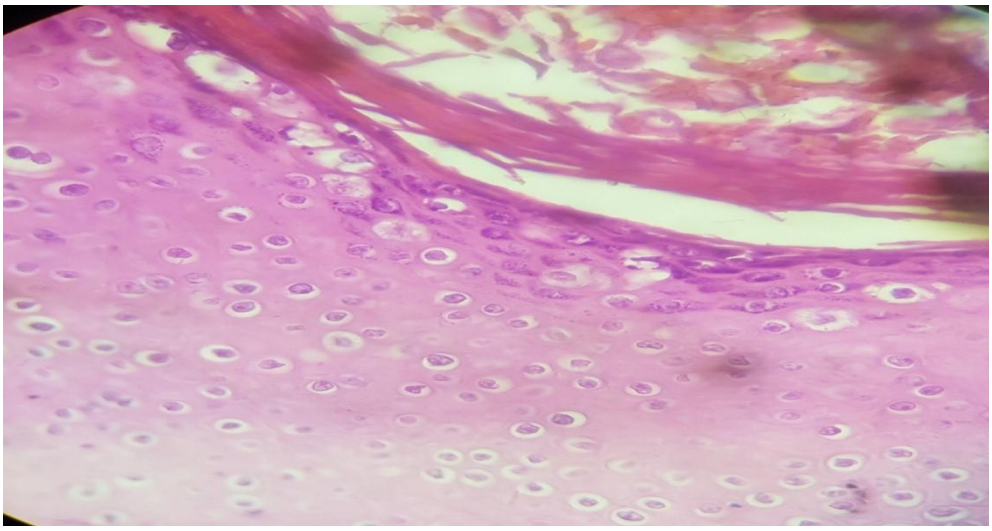

Figure 5: Histological study at magnification x 400, showing stigmata of human papillomavirus (HPV) infection in the form of koilocytes presenting an irregular nucleus with a clear peri-nuclear halo (hematein coloring - Eosine).