Rezumat

Boala Buschke-Löwenstein – Condiloma Acuminata Gigant - un review al literaturii

Premizã/Scop: Boala Buschke-Löwenstein sau condilomatoza gigantã este o afecåiune rarã, cu transmitere sexualã, evoluåie lentã şi cu tendinåa de a infiltra åesuturile adiacente, care netratatã poate avea un prognostic sumbru. Elementul definitoriu este dezvoltarea uneia sau mai multor formaåiuni tumorale vegetante, de mari dimensiuni, cu tendinåa la ulcerare.

Material şi Metodã: Lucrarea de faåã trateazã atât aspecte de etiopatogenie, cât şi formele de abordare terapeuticã folosite în managementul actual al acestei afecåiuni.

Rezultate: Chirurgia minim invazivã împreunã cu terapia localã şi sistemicã este adecvatã în cazul pacienåilor cu leziuni de dimensiune micã sau în cazul celor care prezintã comorbiditãå asociate importante. Tratamentul principal rãmâne în continuare chirurgia extensivã, cu rezeåii largã şi de multe ori repetate.

Concluzii: Condilomatoza gigantã reprezintã o provocare din punct de vedere chirurgical, necesitând intervenåii chirurgicale laborioase care trebuie sã respecte atât principiile oncologice, cât şi o refacere cât mai anatomicã a structurilor. Raritatea afecåiunii face ca, în prezent, existenåa unui protocol standardizat de tratament sã fie un lucru greu de atins. Chirurgia radicalã cu exereza largã a zonelor implicate rãmâne încã „gold standard-ul” terapeutic. Alte forme de tratament oferã rezultate contradictorii şi nu prezinã încã importanåã statisticã, fiind aplicate unor grupuri mici de pacienåi. Datã fiind rata mare de recurenåã, o urmãrire îndelungatã şi atentã a pacienåilor este imperios necesarã.

Cuvinte cheie: boala Buschke-Löwenstein, excizie largã, carcinom verucos

Abstract

Aim: Buschke-Löwenstein disease or giant condyloma acumina-tum represents a rare, sexually transmitted disorder, with a slow evolution and the tendency to infiltrate in the adjacent tissues; untreated, the outcome is unfavorable. The hallmark is the development of one or various prominent-sized vegetant tumors that usually ulcerate.

Material and Methods: The present article summarizes both the etiopathogenic features and the current approach of treatment management.

Results: Minimally invasive surgery along with local and
systemic therapy is adequate in patients with small-sized lesions or high intraoperative risk. The main treatment remains extensive surgery with wide resection and often reinterventions to complete the excision.

Conclusions: giant condyloma acuminatum represents a continuous surgical challenge, because of the need of exhaustive surgical procedures that should consider both the oncological principles and a better anatomical resolution. No standard treatment protocol can be established, because of the infrequency of the disease. Radical surgery including full thickness excision of the affected areas represents the “gold-standard” therapy. Other known forms of treatment present unsatisfactory results without statistical significance, the studies having been conducted on small groups of patients. An adequate, long-term follow-up of Buschke-Löwenstein patients is highly recommended, because of the increased recurrence rate.

Key words: Buschke-Löwenstein disease, large loop excision, verrucous carcinoma

Introduction

In 1925, Abraham Buschke and Ludwig Löwenstein described the disease and classified it as a potential malign condyloma acuminatum (1). In 1979, Mohs and Sahl included this disorder into the verrucous carcinoma category, along with oral florid papillomatosis and epithelioma cuniculatum (representing a squamous-cell carcinoma subgroup) (2).

The disease hallmark is characterized by the development and slow progression of exophytic, ulcerative and cauliflower-shaped tumors that infiltrate in the adjacent tissue. Men are most affected (ratio = 2.7:1), but some cases in women and children have also been highlighted (3). The anogenital region is the most affected and very seldom the urinary bladder and urethral area; when the last two mentioned regions are involved, the disease is correlated with severe immunodeficiency (Figs. 1, 2) (4,5).

Material and Methods

Etiopathogeny

The disease is considered to be sexually transmitted as human papillomavirus (HPV) (types 6 and 11 are the most common and 16, 18 and 33 are high-risk HPV types) and represents the causative factor (6). Buschke-Löwenstein disease development in children emphasizes the vertical or childbirth delivery transmission (7-9). Other possible risk agents are: smoking, multiple sexual relations, anaerobic infections, local chronic inflammation and immune deficiency (underlined by high frequency of recurrence events in transplanted patients or individuals diagnosed with HIV or other immunodeficiency syndromes – Netherton syndrome) (10).
The high recurrence rate (60–70% variation) (11), reduced metastasis tendency and 30 to 56% rate of malignant development (12) are essential features that should be taken into consideration by surgeons in the management of the disease.

Buschke-Löwenstein was histologically differentiated by Knoblich from simple condyloma; the first presenting increased mitotic activity, important papillomatosis, thickened tumor edges, acanthosis and the tendency to penetrate and infiltrate the adjacent tissues (Fig. 3) (13). The histological difference between Buschke-Löwenstein disease and squamous-cell carcinoma consists in the absence of basement membrane involvement (13).

The presence of neoplastic foci in various giant condyloma disorders (in situ carcinoma, squamous-cell carcinoma, basaloid carcinoma) has an uncertain role in the disease evolution (14).

Considering the decreased metastasis rate, the natural evolution of the disease is determined by tumor local control, and its tendency to infiltrate and “push” the adjacent tissue.

Clinical features

The clinical exam reveals: palpable tumor mass, bleeding, algic symptomatology, localized fistulas and pruritus, multiple necrotic foci abscesses, and sometimes important weight loss (15).

Treatment

The surgical treatment represents the “gold-standard” therapy and consists in full thickness excision and tumor-free margins control (Fig. 4) (16,17). Surgical reinterventions are often necessary to complete the initial resection up to the tumor-free margins (Fig. 5) (16,17). Depending on the patient’s clinical condition, exhaustive abdominopelvic surgery is recommended in cases of visceral involvement (pelvic exenteration, abdomino-

perineal amputation) (16,17).

Preoperative imagistic investigations (CT, MRI) are required in order to evaluate the local and systemic disease extension, and to select the best treatment approach (Figs. 6, 7). Some studies recommend temporary colostomy followed by reintegra-

case in cases of rectum involvement (18).

Discussions

Minimally invasive surgery along with local and systemic therapy is adequate in patients with small-sized lesions or high intraoperative risk. Thus, cryotherapy (liquid nitrogen, nitric oxide) associated with topic chemotherapy proved efficient in patients with small-sized tumors (16,19,20). Carbon dioxide, argon fluoride and Nd:YAG (neodymium-doped yttrium aluminum garnet) laser therapy is satisfactorily used in recurrence treatment (16,21). Additionally, some studies recommend minimally invasive surgery as first-line therapy with favorable outcome (22,23).

The topic treatment mainly consists in podophyllin, a substance successfully used in condyloma therapy, but in Buschke-Löwenstein disease there is an immediate recurrence rate and the lesions present tissue modifications resembling squamous-cell carcinoma (16,24). Other types of topic therapy have also been used with different degrees of efficiency (5-fluorouracil, bleomycin associated with cisplatin and methotrexate, trichloride and dichloride acetic acid, imiquimod and interferon) (16). These forms of treatment are either complementary to surgery or used in patients with limited biological resources. Recent reports underlined the beneficial effects of imiquimod and interferon as first-line therapy; therefore, nowadays, they are more often recommended (25-27).

Systemic immunotherapy with alpha interferon or imiquimod has had remarkable results. Abcarian et al study, conducted on 200 patients treated with interferon after surgical excision, reported an 84% resolution rate (28-30).

Figure 3. (A, B). Microscopic histological features: squamous epithelium presenting acanthosis, thickened tumor edges, koilocytosis and parakeratosis without basement membrane involvement (photo collection of the Department of Urology, “Dr. Carol Davila” Central Military Emergency University Hospital)
Furthermore, Eftaiha et al noticed a 94.1% recovery rate in 17 patients (31).

Photodynamic therapy consists in tumor cell absorption of 5-aminolevulinic acid, followed by a beam of pulsed light exposure (32). Paoli et al highlighted a 40% resolution rate in a small group of patients (32).

Mohs micrographic surgery represents one of the minimally invasive surgery alternatives, but with poor results and a significant recurrence rate (32%) (33). In addition, it is a time-consuming technique and not accessible in all Centers of Urology. The systemic chemotherapy is more often used both pre- and postoperatively as surgery complementary treatment; different drug schemes have proved their efficiency (cisplatin, mitomycin C, 5-fluorouracil, methotrexate, bleomycin, leucovorin) (16,34).

Radiotherapy represents one of the most controversial forms of treatment. There are cases that report postradiotherapy anaplastic lesions, even high-risk invasive squamous-cell carcinomas (35-37). Furthermore, the method has been successfully used both as neoadjuvant and salvage therapy (38,39).

Figure 4. (A, B). Intraoperative features: tumor mass invasion of scrotal and perineal regions (limited to the penile anatomic structures) (photo collection of the Department of Urology, “Dr. Carol Davila” Central Military Emergency University Hospital, Bucharest)

Figure 5. (A, B). Postoperative features: some cases require multiple surgical interventions for a complete tumor resection (photo collection of the Department of Urology, “Dr. Carol Davila” Central Military Emergency University Hospital, Bucharest)
Conclusions

Buschke-Löwenstein disease represents a constant challenge for the surgeon. The surgical excision remains the "gold-standard" treatment. The patient must be clinically and imagistically investigated to decide on the most appropriate treatment approach; exhaustive surgery is recommended to visceral involvement patients. A detailed histological exam of the lesion is mandatory, because microscopic excision (with tumor-free margins) presents a decreased recurrence rate compared to macroscopic resection (40). Chemo- and radiotherapy should be used as adjuvant treatments, because when used as single forms of therapy the results are not encouraging. Additionally, systemic immunomodulatory drugs have beneficial effects. Minimally invasive surgery can be successful in small-sized lesions and recurrence cases.

Authors’ contribution

D. Spînu conceived and drafted the study under direct supervision of Prof. Mischianu Dan and Assistant Prof. O. Bratu. A. Rădulescu, member of the surgery team, I.A. Checheriţă and A.E. Ranetti consultant on nephrological and endocrinological aspects.

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References


