

## Giant Condyloma Acuminatum – Buschke-Löwenstein Disease – a Literature Review

D. Spînu<sup>1</sup>, A. Rădulescu<sup>1</sup>, O. Bratu<sup>1,2</sup>, I.A. Checheriță<sup>3</sup>, A.E. Ranetti<sup>4</sup>, D. Mischianu<sup>1,2</sup>

<sup>1</sup>Department of Urology, “Dr. Carol Davila” Central Military Emergency University Hospital, Bucharest, Romania

<sup>2</sup>Department of Urology, Clinical Department No. 3, “Carol Davila” University of Medicine and Pharmacy, “Dr. Carol Davila” Central Military Emergency University Hospital, Bucharest, Romania

<sup>3</sup>Department of Nephrology and Dialysis, Clinical Department No. 3, “Carol Davila” University of Medicine and Pharmacy, “Sf. Ioan” Clinical Emergency Hospital, Bucharest, Romania

<sup>4</sup>Endocrinology Ward, “Dr. Carol Davila” Central Military Emergency University Hospital, Bucharest, Romania

### Rezumat

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

**Premiză/Scop:** Boala Buschke-Löwenstein sau condilomatoza gigantă este o afecțiune rară, cu transmitere sexuală, evoluție lentă și cu tendința de a infiltra țesuturile adiacente, care netratată poate avea un prognostic sumbru. Elementul definitoriu este dezvoltarea uneia sau mai multor formațiuni tumorale vegetante, de mari dimensiuni, cu tendința la ulcerare.

**Material și Metodă:** Lucrarea de față tratează atât aspecte de etiopatogenie, cât și formele de abordare terapeutică folosite în managementul actual al acestei afecțiuni.

**Rezultate:** Chirurgia minim invazivă împreună cu terapia locală și sistemică este adecvată în cazul pacienților cu leziuni de dimensiune mică sau în cazul celor care prezintă comorbidități asociate importante. Tratamentul principal rămâne în continuare chirurgia extensivă, cu rezecții largi și de multe ori repetate.

**Concluzii:** Condilomatoza gigantă reprezintă o provocare din punct de vedere chirurgical, necesitând intervenții chirurgicale laborioase care trebuie să respecte atât principiile oncologice, cât și o refacere cât mai anatomică a structurilor. Raritatea afecțiunii face ca, în prezent, existența unui protocol standardizat de tratament să fie un lucru greu de atins. Chirurgia radicală cu exereza largă a zonelor implicate rămâne încă „gold standard-ul” terapeutic. Alte forme de tratament oferă rezultate contradictorii și nu prezintă încă importanță statistică, fiind aplicate unor grupuri mici de pacienți. Dată fiind rata mare de recurență, o urmărire îndelungată și atentă a pacienților este imperios necesară.

**Cuvinte cheie:** boala Buschke-Löwenstein, excizie largă, carcinom verucos

---

Corresponding author:

Arsenie Dan Spînu, MD  
“Dr. Carol Davila” Central Military  
Emergency University Hospital  
Bucharest, Romania  
88 Mîrcea Vulcanescu Street, District 1  
Bucharest, Romania  
E-mail: dan.spinu@yahoo.co.uk

### Abstract

**Aim:** Buschke-Löwenstein disease or giant condyloma acuminatum 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).



**Figure 1.** *Buschke-Löwenstein* disease: inguinal localization – exophytic tumor development (photo collection of the Department of Urology, “Dr. Carol Davila” Central Military Emergency University Hospital)



**Figure 2.** *Buschke-Löwenstein* disease: peno-scrotal localization – the adjacent tissue infiltration (photo collection of the Department of Urology, “Dr. Carol Davila” Central Military Emergency University Hospital)

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 c, 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).

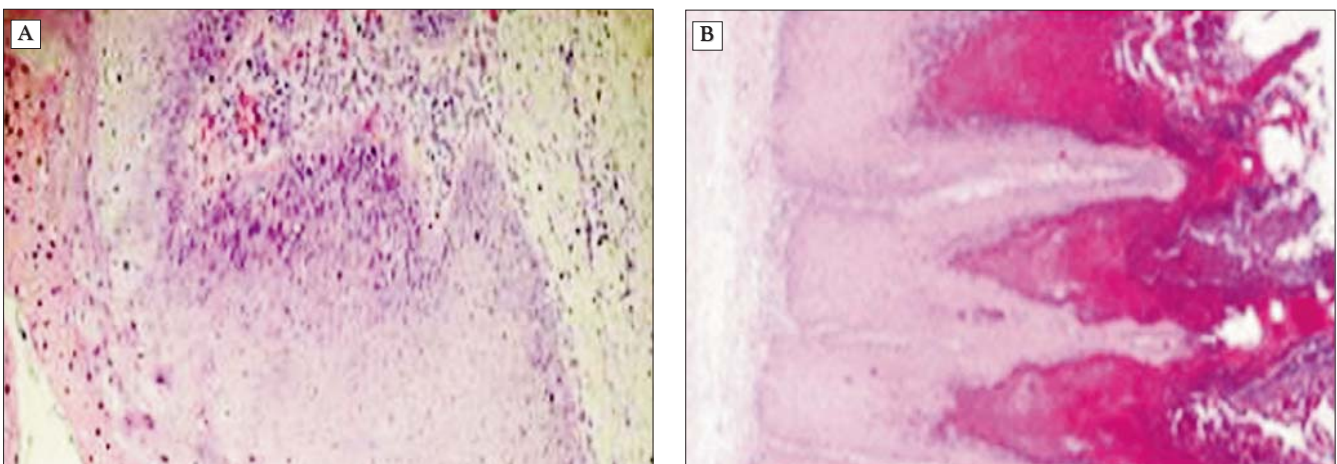
Preoperative imagistic investigations (CT, MRI) are required in order to evaluate the local and systemic disease extension, and to select the best treatment approach (Figs. 6, 7). Some studies recommend temporary colostomy followed by reintegration in cases of rectum involvement (18).

### **Discussions**

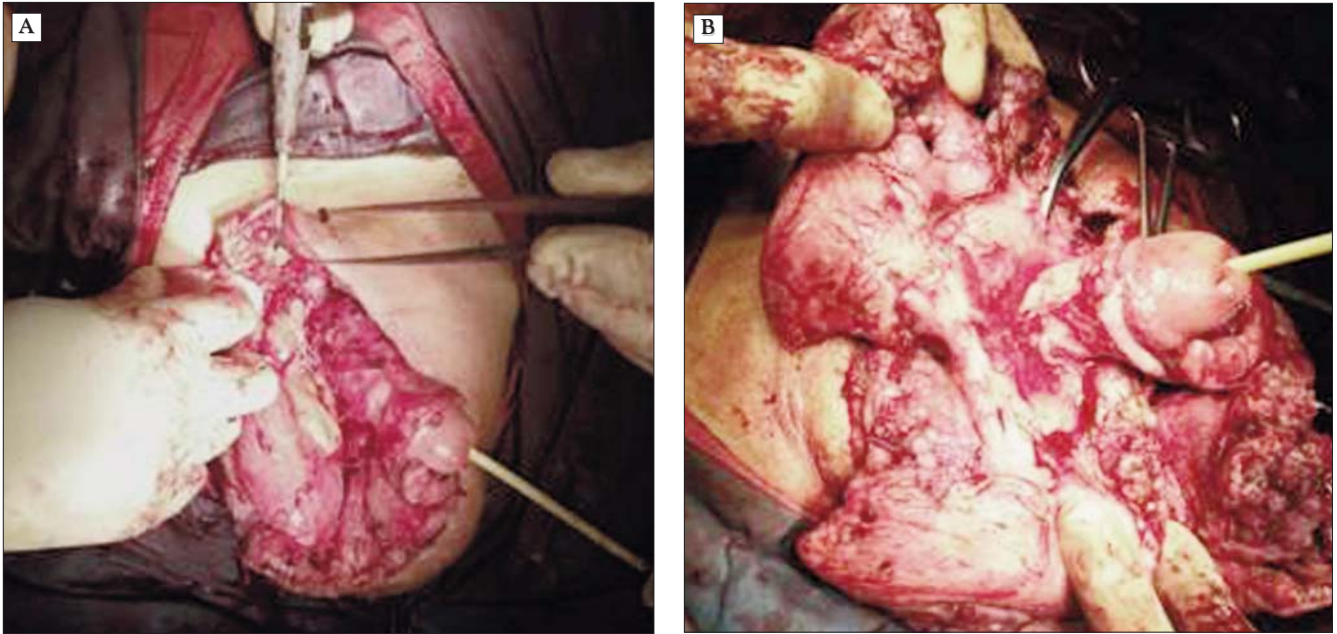
Minimally invasive surgery along with local and systemic therapy is adequate in patients with small-sized lesions or high intraoperative risk. Thus, cryotherapy (liquid nitrogen, nitric oxide) associated with topic chemotherapy proved efficient in patients with small-sized tumors (16,19,20). Carbon dioxide, 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 bichloride 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).

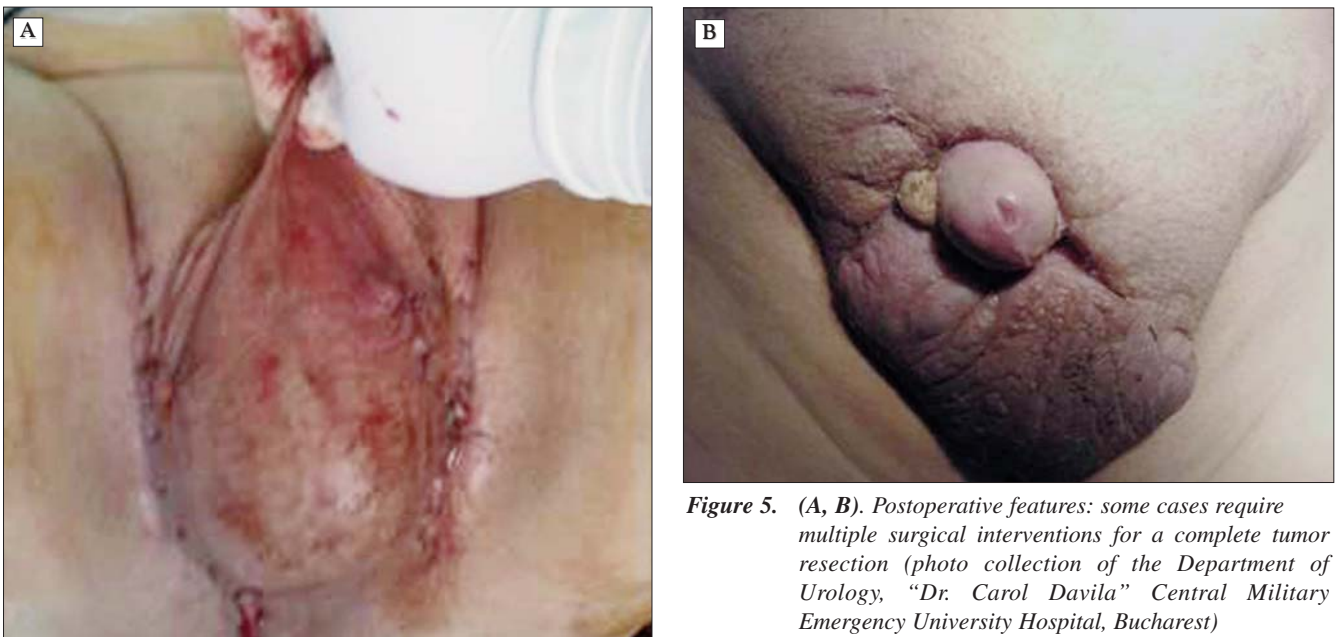
Systemic immunotherapy with alpha interferon or imiquimod has had remarkable results. Abcarian et al study, conducted on 200 patients treated with interferon after surgical excision, reported an 84% resolution rate (28-30).



**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)



**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)

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).

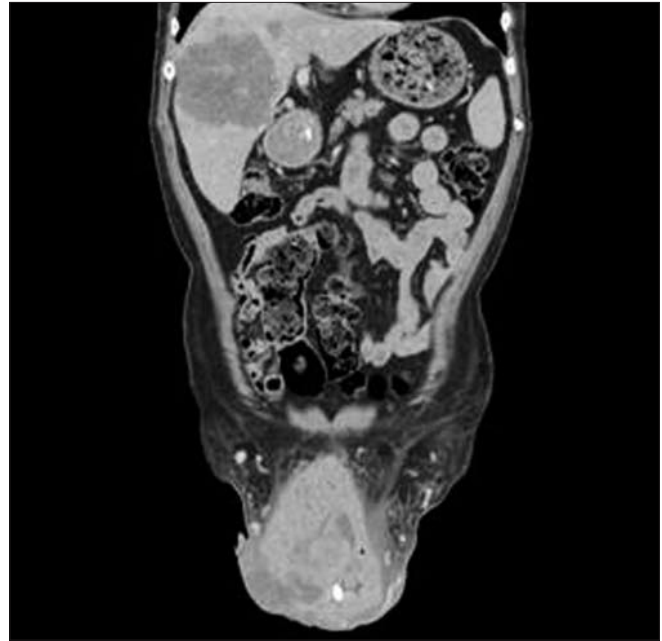
Mohs micrographic surgery represents one of the minimally invasive surgery alternatives, but with poor results and a significant recurrence rate (32%) (33). In addition, it is a time-consuming technique and not accessible in all Centers

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 6.** Preoperative CT features: giant peno-scrotal tumor apparently limited to the penile anatomy structures (photo collection of the Department of Urology, “Dr. Carol Davila” Central Military Emergency University Hospital, Bucharest)



**Figure 7.** Preoperative CT features: giant peno-scrotal tumor presenting hepatic secondary lesions (synchronous cancer considered the primary lesion) (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. Checheriță and A.E. Ranetti consultant on nephrological and endocrinological aspects.

### Acknowledgements

This paper is supported by the Sectoral Operational Programme Human Resources Development (SOP HRD)

2007-2013, financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/107/1.5/S/82839

## References

1. Steffen C. The men behind the eponym – Abraham Buschke and Ludwig Lowenstein: giant condyloma (Buschke-Loewenstein). *Am J Dermatopathol.* 2006;28(6):526-36.
2. Schwartz RA. Verrucous carcinoma of the skin and mucosa. *J Am Acad Dermatol.* 1995;32(1):1-21.
3. Gole GN, Shekhar TY, Gole SG, Prabhala S. Successful treatment of *Buschke-Löwenstein* tumor by surgical excision alone. *J Cutan Aesthet Surg.* 2010 Sep;3(3):174-6.
4. Rosemberg SK. Sexually transmitted papillomaviral infection in men. An update. *Dermatol Clin.* 1991;9(2):317-31.
5. Wiedemann A, Diekmann WP, Holtmann G, Kracht H. Report of a case with giant condyloma (*Buschke-Löwenstein* tumor) localized in the bladder. *J Urol.* 1995;153(4):1222-4.
6. Boshart M, zur Hausen H. Human papillomaviruses in *Buschke-Löwenstein* tumors: physical state of the DNA and identification of a tandem duplication in the noncoding region of a human papillomavirus 6 subtype. *J Virol.* 1986;58(3):963-6.
7. Ambriz-González G, Escobedo-Zavala LC, Carrillo de la Mora F, Ortiz-Arriaga A, Cordero-Zamora A, Corona-Nakamura A, et al. *Buschke-Löwenstein* tumor in childhood: a case report. *J Pediatr Surg.* 2005;40(9):e25-7.
8. Tinsa F, Gharbi A, Essit A, Driss M, Bousnina S. Giant condyloma acuminatum in an infant. *Pediatr Dermatol.* 2009; 26(4):488-9.
9. Schneider A, Lacreuse I, Moog R, Kauffmann I, Becmeur F.

- Buschke-Löwenstein* anal tumor in children: two case reports. *Eur J Pediatr Surg.* 2009 Oct;19(5):330-2.
10. Li AL, Walsh S, McKay DR. Surgical management of a giant condyloma of *Buschke-Löwenstein* in a patient with Netherton syndrome using the pedicled anterolateral thigh flap – a case report. *J Plast Reconstr Aesthet Surg.* 2011;64(11): 1533-6.
  11. Chu QD, Vezeridis MP, Libbey NP, Wanebo HJ. Giant condyloma acuminatum (*Buschke-Löwenstein* tumor) of the anorectal and perianal regions. Analysis of 42 cases. *Dis Colon Rectum.* 1994;37(9):950-7.
  12. Bertram P, Treutner KH, Rübber A, Hauptmann S, Schumpelick V. Invasive squamous-cell carcinoma in giant anorectal condyloma (*Buschke-Löwenstein* tumor). *Langenbecks Arch Chir.* 1995; 380(2):115-8.
  13. Knoblich R, Failing JF Jr. Giant condyloma acuminatum (*Buschke-Löwenstein* tumor) of the rectum. *Am J Clin Pathol.* 1967;48(4):389-95.
  14. Trombetta LJ, Place RJ. Giant condyloma acuminatum of the anorectum: trends in epidemiology and management: report of a case and review of the literature. *Dis Colon Rectum.* 2001; 44(12):1878-86.
  15. Papiu HS, Dumnici A, Olariu T, Onita M, Hornung E, Goldis D, et al. Perianal giant condyloma acuminatum (*Buschke-Löwenstein* tumor). Case report and review of the literature. *Chirurgia (Bucur).* 2011;106(4):535-9.
  16. Della Valle A, Heguaburu M, Fresco R, Roldán G, Della Valle M. *Buschke-Löwenstein* tumor: case report and review with focus on therapeutic and psychological aspects. *The Internet Journal of Surgery.* 2007; 9(2):doi:10.5580/29a7.
  17. Ilkay AK, Chodak GW, Vogelzang NJ, Gerber GS. *Buschke-Löwenstein* tumor: therapeutic options including systemic chemotherapy. *Urology.* 1993; 42(5):599-602.
  18. Gholam P, Enk A, Hartschuh W. Successful surgical management of giant condyloma acuminatum (*Buschke-Löwenstein* tumor) in the genitoanal region: a case report and evaluation of current therapies. *Dermatology.* 2009;218(1):56-59.
  19. Carson TE. Verrucous carcinoma of the penis; successful treatment with cryosurgery and topical fluorouracil therapy. *Arch Dermatol.* 1978;114(10):1546-7.
  20. Hughes PS. Cryosurgery of verrucous carcinoma of the penis (*Buschke-Löwenstein* tumour). *Cutis.* 1979;24(1):43-45.
  21. Frega A, Stentella P, Tinari A, Vecchione A, Marchionni M. Giant condyloma acuminatum or *Buschke-Löwenstein* tumor: review of the literature and report of three cases treated by CO<sub>2</sub> laser surgery. A long term follow-up. *Anticancer Res.* 2002;22(2B):1201-4.
  22. Renzi A, Bruscianno L, Giordano P, Rossetti G, Izzo D, Del Genio A. *Buschke-Löwenstein* tumor. Successful treatment by surgical electrocautery excision alone: a case report. *Chir Ital.* 2004;56(2):297-300.
  23. Parise P, Sarzo G, Finco C, Marino F, Savastano S, Merigliano S. Giant condyloma acuminatum of the anorectum (*Buschke-Löwenstein* tumour): a case report of conservative surgery. *Chir Ital.* 2004;56(1):157-61.
  24. Machacek GF, Weakley DR. Giant condyloma acuminata of *Buschke* and *Löwenstein*. *Arch Dermatol.* 1960;82:41-7.
  25. Zachariae H, Larsen PM, Sjøgaard H. Recombinant interferon alpha-2a (Roferon-A) in a case of *Buschke-Löwenstein* giant condyloma. *Dermatologica.* 1988;177(3):175-9.
  26. Tsambaos D, Monastirli A, Kapranos N, Georgiou S, Pasmazi E, Berger H. Intralesional interferon alpha-2b therapy for *Buschke-Löwenstein* tumour. *Acta Dermatol Venereol.* 1994; 74(6):457-9.
  27. Gesau A, Heinz-Peer G, Volc-Platzer B, Stingl G, Kirnbauer R. Regression of deeply infiltrating giant condyloma (*Buschke-Löwenstein* tumor) following long-term intralesional interferon alfa therapy. *Arch Dermatol.* 2000;136(6):707-10.
  28. Abcarian H, Smith D, Sharon N. The immunotherapy of anal condyloma acuminatum. *Dis Colon Rectum.* 1976;19(3):237-44.
  29. Abcarian H, Sharon N. Immunotherapy in treatment of anal condyloma acuminatum. *Surg Forum.* 1976;27(62):127-9.
  30. Abcarian H, Sharon N. The effectiveness of immunotherapy in the treatment of anal condyloma acuminatum. *J Surg Res.* 1977;22(3):231-6.
  31. Eftaiha MS, Amshel AL, Shonberg IL, Batshon B. Giant and recurrent condyloma acuminatum: appraisal of immunotherapy. *Dis Colon Rectum.* 1982; 25(2):136-8.
  32. Paoli J, Ternesten Bratel A, Löwhagen GB, Stenquist B, Forslund O, Wennberg AM. Penile intraepithelial neoplasia: results of photodynamic therapy. *Acta Derm Venereol.* 2006; 86(5):418-21.
  33. Shindel AW, Mann MW, Lev RY, Sengelmann R, Petersen J, Hruza GJ, Brandes SB. Mohs micrographic surgery for penile cancer: management and long-term follow up. *J Urol.* 2007; 178(5):1980-5.
  34. Ilkay AK, Chodak GW, Vogelzang NJ, Gerber GS. *Buschke-Löwenstein* tumor: therapeutic options including systemic chemotherapy. *Urology.* 1993; 42(5):599-602.
  35. Drut R, Ontiveros R, Cabral D. Perianal verrucous carcinoma spreading to the rectum: report of a case. *Dis Colon Rectum.* 1975; 18(6):516-21.
  36. Netto NR Jr, Chade J, Camargo FP. Giant condyloma or *Buschke-Löwenstein* tumor. *Int Surg.* 1976; 61(2):105-7.
  37. Schwade JG, Warra WM, Dedo HH, Phillips TL. Radiotherapy for verrucous carcinoma. *Radiology.* 1976; 120(3):677-9.
  38. Marsh RW, Agalioitis D, Killeen R Jr. Treatment of invasive squamous cell carcinoma complicating anal *Buschke-Löwenstein* tumor: a case history. *Cutis.* 1995;55(6):358-60.
  39. Nigro ND, Vaitkevicius VK, Considine BJ. Combined therapy for cancer of the anal canal: a preliminary report. *Dis Colon Rectum.* 1974;17(3):354-6.
  40. Marchesa P, Fazio VW, Oliari S, Goldblum JR, Lavery IC. Perianal Bowen's disease: a clinicopathologic study of 47 patients. *Dis Colon Rectum.* 1997;40(11):1286-93.