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Squamous Cell Carcinoma of perineal area developed from the Buschke–Löwenstein tumor

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Abstract: The Buschke–Löwenstein tumor is a rare disease associated with human papillomavirus infection. The condition manifests with an ulcerative, exophytic tumor localized in the perineal area. Generally considered as non-cancerous, the growth may develop malignant transformation. Our manuscript highlights the importance of early diagnosis with histopathological analysis.

Keywords: human papillomavirus, giant condyloma acuminatum, malignant transformation, HPV vaccination, Buschke–Löwenstein tumor.

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Introduction

The Buschke–Löwenstein tumor (BLT), also called a giant condyloma acuminatum (GCA), is a sexually transmitted disease caused by the human papillomavirus (HPV) (more than 90% of cases are associated with low-risk HPV types 6 or 11) infection [1–4]. The virus has a predilection for residing in the basal layer of squamous epithelium [2]. The viral oncoproteins E6, E7, which integrate into the human genome, alter cell cycle regulation and telomere maintenance, induce DNA damage and genomic instability. These pathological changes can lead to malignant transformation [2]. GCA manifests with an exophytic tumor localized in the genital area. Ulcerative, large growth with local extension and destruction is distinctive for this disease [3]. Tumor has a tendency to recur, estimated at 60–70% [5]. The patients may complain of discomfort, pain and bleeding from the perineal area [6]. Studies suggest that BLT has 30 to 56 percent risk of malignant transformation to squamous cell carcinoma [6, 7].

Case report

In February 2022 the 53-year-old female, of unknown sexual orientation, was moved from a psychiatric hospital, where the patient was treated due to depression and marasmus, to an emergency department of gastroenterology ward because of anemia and lower gastrointestinal bleeding.

The patient complained of progressive weakness and diarrhea — yellowish, loose stools, periodically with blood, lasting for 3 months. The patient said that she lost 20 kilograms in the last 6 months. The patient reported smoking for at least 25 years. There was no history of thyroid disease or diabetes. The patient was stated as immunocompetent.

The physical exam revealed dehydration, tachycardia, hypotension and asymmetrical oedema of lower extremities. The laboratory testing showed anemia (6.3 g/dl), elevated C-reactive protein level (111.1 mg/l) and neutrophils count (23000/mL). Intravenous fluids, noradrenalin, antibiotics and blood transfusion were administered. The perineal area and per rectum examinations revealed a protruding, massive, necrotic, cauliflower-like growth that was bleeding by touch (Fig. 1). It involved the labia majora. The Buschke–Löwenstein tumor was initially diagnosed.

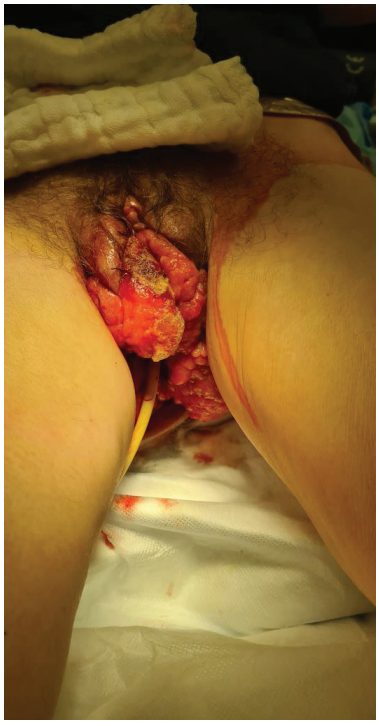

Fig. 1. Massive cauliflower-like tumor of the perineal area.

The endoscopic examination with biopsy couldn't be performed, thus after a consultation the patient was admitted to the general surgery department. The analysis of an additional patient's medical history, revealed that the perineal lesion was diagnosed 3-years before the patient administration to hospital, but the patient refused the treatment at that time. Control complete blood count analysis revealed deterioration of anemia which required blood transfusion. To assess the tumor localization and tissue destruction the MRI scans of pelvis were ordered. The MRI showed an extensive, irregular, inhomogeneous nodular/infiltrating mass, size about 105 × 45 × 100 mm (AP × TR × CC). The infiltration of tumor mass involved: the intergluteal cleft, subcutaneous tissue of medial parts of both buttocks in the area of intergluteal cleft, soft tissue of perineum, vagina, anal sphincters, circa 6 cm of rectum and puborectalis muscles. The invasion of the tumor was also found in soft tissue of the pelvis, around distal parts of the rectum and vagina (Figs. 2, 3).

Because of rectum invasion the interdisciplinary medical team decided to perform a laparoscopic surgery to form a loop colostomy before further oncological treatment. Additionally, intraoperative examination revealed the presence of rectovaginal fistula. During the surgical procedure the biopsy of tumor tissue was taken. The postoperative histopathological diagnosis revealed the *carcinoma planoepitheliale partim keratodes G2*. After the operation the patient was diagnosed with COVID-19 and she was moved to the department of internal medicine. After the patient finished a treatment of COVID-19, the patient was admitted to the oncological department for further radiotherapy and oncological treatment.

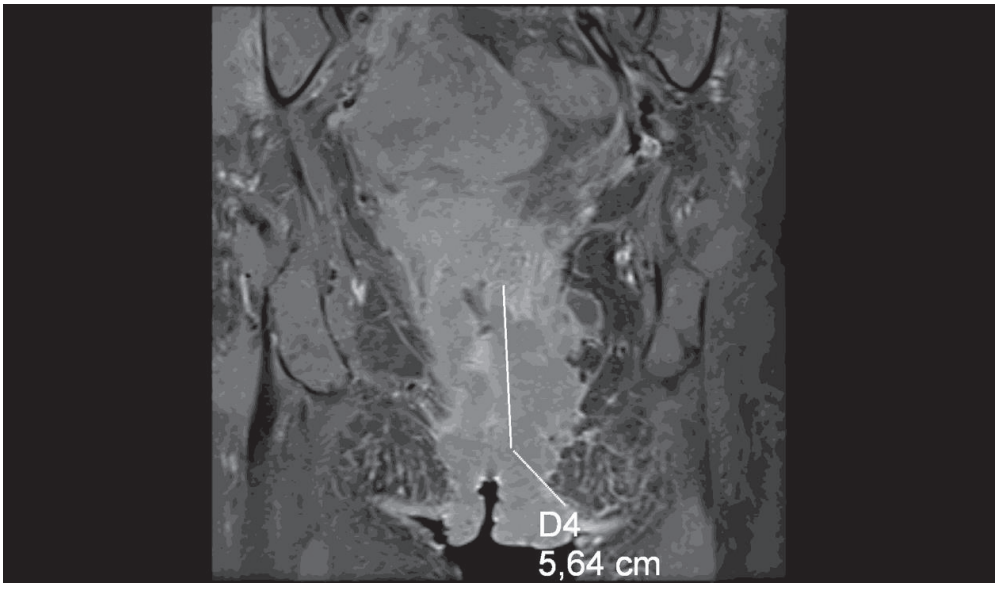

Fig. 2. An irregular, destructive mass invading the perineum. The coronal plane.

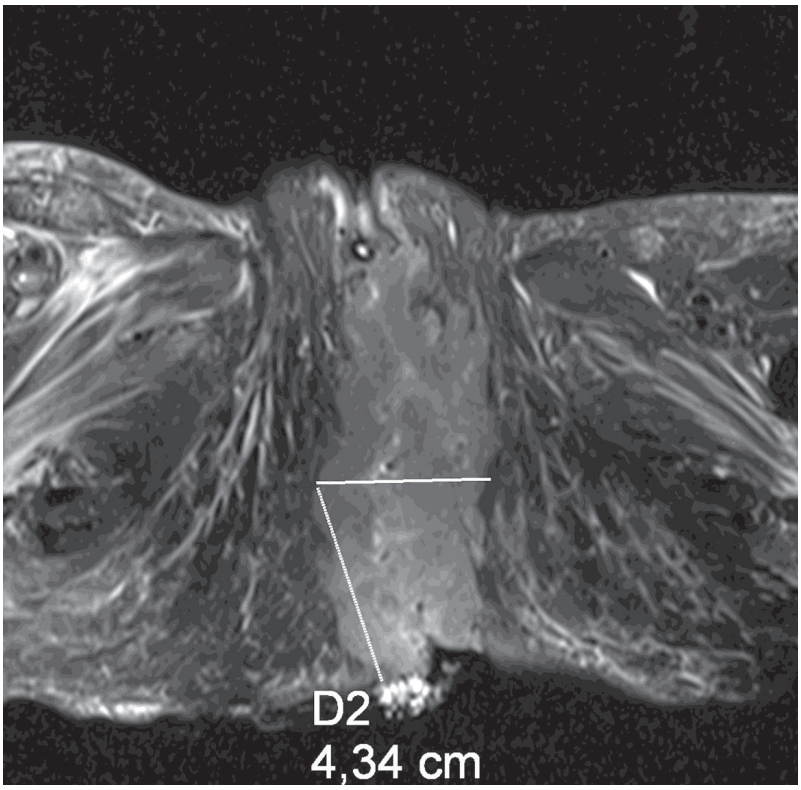

Fig. 3. An irregular, destructive mass invading the perineum. The transverse plane.

Discussion

The Buschke–Löwenstein tumor is a rare disease, prevalence is estimated at 0.1% in the general population [3, 8]. It is considered to be a locally aggressive lesion with benign histological appearance [8]. The female to male ratio is 1:3 [9]. Most patients present symptoms between the 4th and 6th decade of life [3]. Risk factors for BLT include: smoking, alcoholism, local chronic inflammation, immune deficiency (individuals diagnosed with HIV, transplant and diabetic patients), multiple sexual partners, poor hygiene [3, 5, 10, 11]. The overall mortality is 20% [6, 8].

The Buschke–Löwenstein tumor can become a life-threatening condition. There are controversies over histological classification of the tumor. Many authors suggest that it's an intermediate state between benign Condyloma Acuminata (CA) and Squamous Cell Carcinoma (SCC) [3, 11, 12]. It is possible to find a SCC component within the Buschke–Löwenstein tumor [6].

The patient requires appropriate diagnostics that involve the patient's history, detailed physical examination, MRI pelvis scans and tissue sampling. The malignant

transformation process is a continuum. Approximately 56% of Buschke–Löwenstein tumors develop malignant transformation [8]. Appropriate histopathological analysis enables classification of the tumor and is crucial for proper treatment implementation.

Because of the rarity of this disease, there are no particular guidelines on treating the patients. A multidisciplinary approach involving surgeon, gynecologist, oncologist, pathologist and radiologist is required. Every patient should be considered individually. The gold standard of BLT treatment is a complete excision with negative margins [3, 5, 6]. The complementary treatment consists of neoadjuvant or adjuvant chemotherapy and radiotherapy. In some cases the patients can benefit from immunotherapy with imiquimod [3, 6, 8, 11]. In addition, Wei, Zhen-Dong *et al.* reported that Mild Local Hyperthermia can successfully induce remission of GCA lesions [10].

The tumor develops from a persistent Condyloma Acuminatum that can grow within a couple of years (2.8–9.6 years, or longer) significantly [8]. For the best therapy results it is important to make a diagnosis as soon as possible. The case emphasizes a need for doctors to keep the oncological alertness. Promoting HPV prophylactic vaccination plays an important role in reducing infection rate, which is crucial for preventing HPV-associated conditions [4, 8]. It is important to plan follow-up visits, due to high recurrence of the disease.

Conclusions

The Buschke–Löwenstein tumor is a relatively rare disease manifested with an exophytic tumor of anogenital region. Fast diagnosis with histopathological confirmation is essential for the best therapy results. Due to the possibility of malignant transformation of BLT and its high tendency to recur, patients should receive radiation therapy or surgical excision with clear margins as soon as possible. It was mentioned that BLT can be an intermediate state between benign CA and SCC, thus it is advised to remove precancerous lesions preventively. Early diagnosis reduces morbidity, due to BLT and surgical procedures, and overall mortality [7]. Implementation of proper treatment plan in early stages of the disease is the most effective in local cases, it prolongs the survival of patients, decreases complications and improves quality of life.

Contributions

G.S. — writing—original draft preparation, data collection; J.W. — data collection, supervision, conceptualization; M.W. — supervision, conceptualization; Ł.D. — supervision, review. All authors have read the manuscript and approved its form.

Conflict of interest

All authors declare no conflict of interest.

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Informed consent

Informed consent was obtained from all subjects involved in this study.

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