

# A Multidisciplinary Approach To The Treatment Of Buschke-Lowenstein Tumor During Pregnancy

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## 1. URGENCY OF THE PROBLEM.

Buschke-Lowenstein tumor (verrucous cancer, verrucous carcinoma) is a disease of the anogenital area, with the human papillomavirus (HPV) as the causative agent, mainly of a low-oncogenic type 6 or 11. It is characterized by large cauliflower-type vegetation, progressive invasive growth and at the same time by a benign histological pattern [1-4]. It is a sexually-transmitted infection. This pathology is named after the authors A. Buschke and L. Lowenstein, who first described huge condyloma accuminatum of a penis in 1925. The progression of condyloma accuminatum to the size of a Buschke-Levenstein tumor (BLT) is very rare. This pathology occurs in about 0.1% of sexually active people [5]. Histologically, BLT reveals benign features of a typical condyloma accuminatum (acanthosis, papillomatosis, koilocytosis). Cases of BLT malignancy have been described, but they are extremely rare [6]. Usually BLT develops rather slowly, sometimes within several years, but there have been specified the cases of fast development of BLT with solitary condylomata during pregnancy [7, 8].

A surgical way of treatment is one of the leading methods [9], with the mandatory radical excision of condyloma foci with resection up to 1 cm from the edge of the tumor within healthy tissues. The surgical method is considered to be the "gold standard". Individually (if required), a decision is pending about rectal extirpation and protective colostomy. There are also methods of chemical and physical destruction of the pathological focus: condylomata can be treated with drugs of local necrotizing effect, also methods of laser vaporization, radio- and cryodestruction, electrocoagulation, argon-plasma ablation are used. Nowadays, effectiveness of chemotherapy or radiation therapy, as well as their combination, is disputable, although separate cases of their application have been reported [10, 11, 12, 13].

Given the viral etiology of the disease, the relapse rate after surgery can reach 62% [14]. An important problem arises for a surgeon to eliminate the defect, as the widest possible excision of BLT is recommended in order to reduce the relapse rate [15]. For this purpose, plastic reconstruction with a skin-fascial VY graft is used, with a double-stage plastic reconstruction by means of a split skin graft applied in the case of extensive defects [16].

Here is a clinical case of rapid development of Bushke-Levenstein tumor during pregnancy and its successful surgical treatment in the early postnatal period.

An 18-year-old woman, seven weeks pregnant, came to see her obstetrician-gynecologist at the place of her residence in the territory of Donetsk region, uncontrolled by Ukraine, complaining of 3-millimeter condyloma. In the first trimester, the doctor chose expectant treatment. By the 14<sup>th</sup> week, the condyloma had already reached 15 mm in diameter. The woman was treated with drugs of local necrotizing effect, but without any success.

Being 34 weeks pregnant, the woman was sent to the Institute of Pediatrics, Obstetrics and Gynecology named after Academician O. M. Lukyanova of the National Academy of Medical Sciences of Ukraine with a diagnosis of Bushke-Levenstein tumor (see photo 1). The woman complained of pain and discomfort in the perineum. During the medical examination, single pass petechiae of the tumor, mucus secretion, maceration of the skin, as well as foul smell, were revealed.

During the examination of the perineum (photo 1), the gynecologist revealed 2 symmetrical tumors of soft elastic consistency, with a size of 8x10 cm, in the perianal area with spread to the posterior wall of the vagina, labia majora and minora, as well as to anal derma.



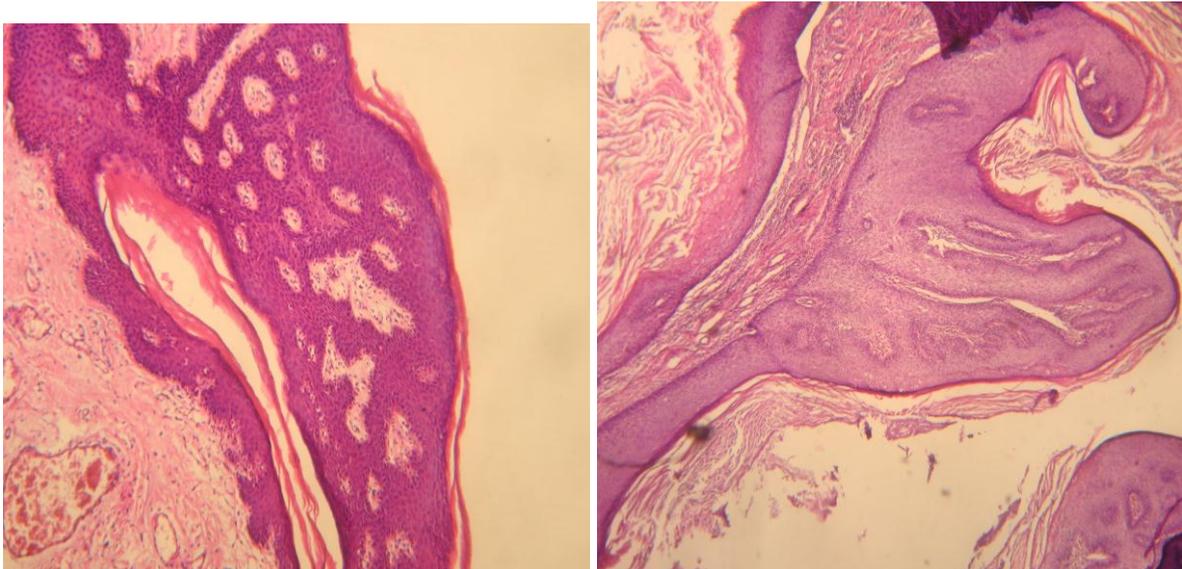
Photo1. Image of the perineum with a tumor (condyloma accuminatum).

The tumor, formed by condyloma accuminatum with areas of necrosis of black and brown color, as well as with single pass petechiae, was constantly infected during defecation and had a foul smell, as appropriate hygiene procedures were impossible due to the loose structure of tissues. During the vaginal examination, using a speculum, it was revealed that the tumor affects the labia majora and minora, as well as the posterior wall of the vagina at a distance of 2 cm from the vulva ring. No condyloma was revealed on the uterine cervix, as well as on anterior and lateral walls of the vagina. Given the huge size of the tumor, there was a high risk of infection of the baby during the passage of the birth canal and the risk of

excessive bleeding, so we decided to choose the abdominal delivery with subsequent resection of the tumor.

A tumor biopsy was performed with a subsequent histological examination for atypia. The results of the examination showed a typical condyloma without signs of any atypia (Photo 2,3). High oncogenic (16, 58, 66) and low oncogenic (6, 11) types were revealed during human papillomavirus gene typing. Conclusion on cytological examination of cervical smear was CIN 1.

Given the increased risk of infection of the fetus and a poor quality of life of the women, in the gestation period of 35 weeks +4 days, delivery was performed by



Photos 2,3. Image of histological examination . Typical genital condyloma.

cesarean section. A premature boy of 2,950 grams and 50 cm was born, with the Apgar scale of 6-7 points.

During the postnatal period the woman was treated with antibiotics (ofloxacin, metronidazole), without any complications. Taking into account the necessity of a further treatment, at the request of the woman, lactation was broken off.

On the 8th day after the delivery, the woman was taken to the surgical department of Oleksandrivska Central Clinical Hospital in Kyiv.

During the stay of the women in hospital, the skin was pale pink and clean, the mucous membranes of the oral cavity were without changes, temperature was 37.2<sup>0</sup>C, blood pressure was 110/60 mm Hg, and the heart rate was 80 beats per minute. The abdomen was soft, moderately painful in the area of the wound (after the cesarean section), with negative peritoneal symptoms, active peristalsis and normal bowel and bladder habits. Postoperative wound healed by primary intention.

To determine the extent of the rectum damage, the patient was subject to rectoromanoscopy. The results of the examination showed huge condyloma in the perianal area from the outer anal ring. The tonus of the sphincters was preserved. In the anal canal there were small condyloma. There were no abnormalities of the inner anal ring, as well as of the rectal ampulla. The examination also revealed the single pass petechiae of condyloma.

Ultrasound examination of the abdominal organs revealed no abnormalities. MRT of the pelvis and soft tissues of the perineum did not show any condyloma areas ingrown into the tissue, deeper than 1 cm from the dermis, as well as into the external anal sphincter.

The laboratory research focused on the postnatal anaemia, as erythrocytes were  $3,15 \times 10^{12}/l$  and, with the indicator of hemoglobin of 90 g/l. Other indicators were within the reference values. HIV was not diagnosed in this patient.

Given the predicted blood loss during the removal of condyloma in the preoperative period, the patient was prescribed an iron (III) hydroxide sucrose complex intravenously.

The surgery included excision of condyloma with plastic reconstruction of the vulva, as well as perianal plastic reconstruction. By two enveloping incisions within visually healthy tissues, the tissues affected by condyloma were dissected out in the perianal area, as well as both labia majora, the lower third of the labia minora and the mucous membrane of the posterior wall of the vagina, 2 cm distally to the vulvar ring. Condylomata and hemorrhoid tumors were dissected out in the perineum and perianal area. The distally located area of the rectum (2 cm long) in the anal canal, affected by small condylomata, was circularly separated from the external anal sphincter and resected (photo 3).



Photo 3



Photo 4

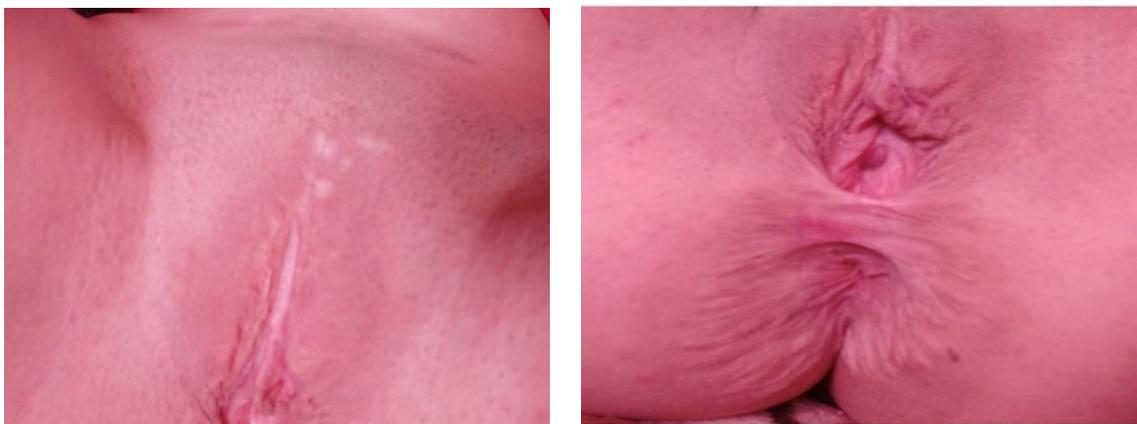
Photo 3. Image of the surgical wound after removal of genital condyloma

Photo 4. Plastic reconstruction of the wound of the perineum by moving dermic grafts

The labia were reduced with mobilized dermic grafts. The skin defect in the perineum was eliminated by moving the triangular skin-fascial grafts (Z-plasty). In the perianal area, the postoperative defect (2×3 cm) was eliminated by means of a triangular graft of the mucous membrane of the anterior wall of the rectum. The latter was pulled through and fixed to the dermic grafts with interrupted stitches (photo 4).

During the postoperative period, the patient received intensive antibacterial therapy (tigecycline, ornidazole), as well as anticoagulant therapy (low molecular weight heparin). To treat postnatal anemia and taking into account blood loss during surgery (700 ml), the maternity patient was subjected to blood transfusion by erythrocyte concentrate and intravenous infusion of Iron (III) hydroxide sucrose complex.

The postoperative period was without complications. The woman was discharged for outpatient treatment on the 7<sup>th</sup> day after surgery. The wound healed by primary adhesion, with the sutures removed on the 14<sup>th</sup> day. During the follow-up examination a year later, we revealed no relapse of the disease, no complaints of discomfort during sexual activity, as well as no poor quality of life (photos 5, 6).



Photos 5, 6. Image of the perineum and perianal area a year after removal of Buschke-Levenstein tumor.

In the future, plastic surgery is planned to correct scar changes in the perineal area.

## 2. DISCUSSION

Treatment of condyloma accuminatum remains controversial, however, surgery is the best option. Extended surgical or radical local excision with skin reconstruction is the basic method of treatment, with focus on minimally invasive surgery. These alternatives include CO<sub>2</sub> laser, electrocoagulation, radiation exposure and introduction of interferon-alpha or imiquimod locally. Cryotherapy with chemotherapy has been effective in patients with small tumors. Carbon dioxide, argon fluoride, as well as laser therapy, turned to be effective in treating relapses.

Treatment of BLT during pregnancy should be based on the condition of the mother and fetus. Buschke-Lowenstein tumor developed from condylomata accuminata (which the woman did not pay due attention) within 6-7 months. Some authors [7, 8] suggest removing the tumor as early as possible (in the second trimester of pregnancy), although the risk of complications for the mother and fetus is significantly high. Surgery in the affected area before delivery poses a risk of miscarriage, bleeding during the act of delivery, premature birth, low birth weight, etc. [17, 18, 19].

Therefore, it is usually recommended to postpone the operation until after delivery. It is necessary to take into account a relatively long duration of BLT surgery, which requires long-term general anesthesia with an increased risk of adverse effects on the fetal CNS. According to a recent US FDA warning, general anesthesia against the backdrop of a long-lasting non-obstetric surgery may impair fetal CNS development and function, whereas no relations have been identified between epidural anesthesia during Caesarian section and such complications [17, 18].

In cases where the tumor fills the natural birth canal, which increases the vertical transmission of human papillomavirus to the baby during its passage through the infected vagina, the selected method is abdominal delivery [19].

If the gestation period exceeds 34 weeks, the sequence of interventions should include Caesarian section followed by excision of giant tumors under general anesthesia. We should also take into account a high risk of intraoperative bleeding.

Based on the analysis of previously published results of BLT treatment by other researchers after assessing the condition of the mother and fetus, taking into account the period of 35 weeks + 4 days and a huge size of BLT of this patient, we decided to conduct abdominal delivery followed by BLT resection to prevent infection of the fetus, significant bleeding during the delivery act, reducing the drug load on the fetus during non-obstetric surgery and within the postoperative period.

Regarding the choice of the method of tumor removal and plastic reconstruction of the defect, we have applied the technique of wide excision of the tumor with plastic reconstruction of the defect by skin-fascial grafts, described by the majority of authors. It was expedient and successful to eliminate a small perianal defect with a graft of rectal mucosa.

BLT has a tendency to local relapse and transformation into dermoid cancellation, with the risk of relapse in the anorectal and perianal areas after excision of 60-66%, and the overall mortality of 20-30%. Malignant tumors have been reported in 30-56% of cases.

### **3. CONCLUSION.**

Nowadays, surgery is an appropriate way of treatment of Buschke-Lowenstein tumors. Removal of BLT diagnosed during pregnancy should be performed after abdominal delivery. Prenatal care of patients with this abnormality should be taken by a multidisciplinary group, consisting of obstetricians, gynecologists, surgeons, and, if necessary, internists. To date, there is no consensus on management of pregnancy of women with condyloma acuminatum. However, in our opinion, the expectant management in the first and early second trimesters turned out to be wrong, with ineffective methods of treatment with drugs of local necrotizing effect.

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