Verrucous carcinoma of the vulva and pregnancy: case description and literature review

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ABSTRACT

Verrucous carcinoma is a very rare entity, accounting for less than 1% of vulvar neoplasms. Although a peak incidence in women of childbearing age has been documented, this entity is rarely found in pregnant women.

We present the first case published in English of a giant vulvar verrucous carcinoma, treated during the second trimester of pregnancy by surgical excision with margins free of disease. The pregnancy subsequently developed uneventfully and terminated at week 42. The patient gave birth by eutocic delivery to a male infant weighing 3765 g. At the first neonatal follow-up examination at two months of life, an oropharyngeal exudate culture was performed, which yielded negative results for HPV infection, and five years later the patient has not presented recurrences.

We conclude that active management of vulvar verrucous carcinoma during pregnancy is an acceptable and safe option, which allows for the treatment of the disease along with normal development of pregnancy and childbirth without posing extra risks to the mother or the newborn.

KEYWORDS

Verrucous carcinoma, vulvar neoplasms, vulva surgery, pregnancy.

Introduction

Verrucous carcinoma is a very rare entity, accounting for less than 1% of vulvar neoplasms. Although a peak incidence in women of childbearing age has been documented1, this entity is rarely found in pregnant women. Here we present the first case published in English of a giant vulvar verrucous carcinoma, treated during the second trimester of pregnancy, together with a review of the literature on the treatment of vulvar cancer in pregnancy.

Case description

A 29-year-old primiparous woman was referred to the Unit of Lower Genital Tract Pathology at week 23 of pregnancy due to verrucous lesions on the labia majora and inner thighs. She reported that the lesions had enlarged during the pregnancy and complained of pain when walking and at rest. Her medical background included onset of the lesions at the age of 15, but was otherwise unremarkable. Gynecologic examination of the vulva revealed a giant ketarinized condylomatous crazy-paving lesion of chronic appearance, extending over the labia majora and vulvar introitus. The inner thighs showed similar verrucous lesions, which ranged between 3 and 5 cm in diameter, accompanied by millimetric satellite lesions (Fig. 1). The vagina showed a normal appearance and the cervix was well epithelized. A cervical cytology study conducted five months before showed negative results for intraepithelial lesion.

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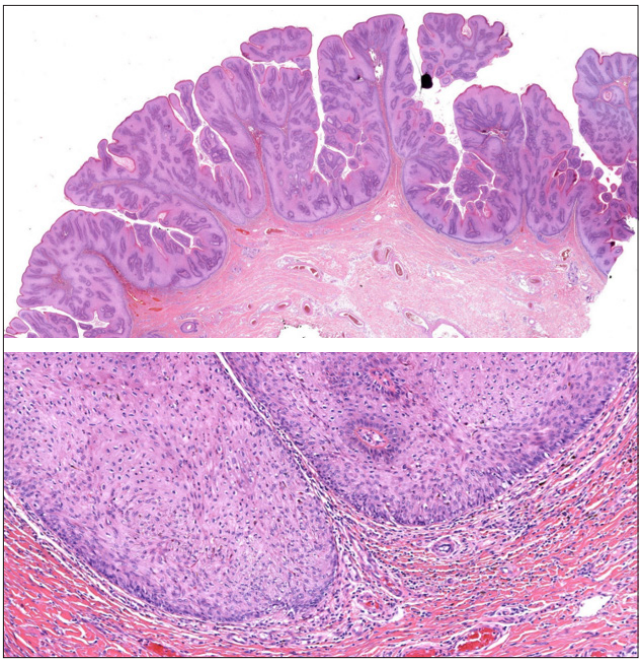
The lesions were excised under epidural anesthesia (first from the labia majora and subsequently from the thighs) by clamping and excision with an electric scalpel. Hemostasis was achieved with electrocoagulation and suture with loose stitches in two planes: subcutaneous fat and skin (Fig. 1). Blood loss was minimal. Fetal health and the absence of uterine contractions were verified after the intervention. During the postoperative period, dehiscence of some superficial suture stitches required local care and closure by secondary intention. The wounds healed correctly without affecting the pregnancy.

A histological study of the excised specimens evidenced verrucous carcinoma with signs of infection by human papillomavirus (HPV), no signs of invasion, and margins free of disease (Fig. 2). Analysis showed positive HPV-6 genotype.

The pregnancy developed uneventfully and terminated at week 42. Cervical ripening with E2 prostaglandins and induction of labor were necessary due to prolonged pregnancy. The patient gave birth by eutocic delivery to a male infant weighing 3765 g. She suffered a 2nd degree vaginal tear that was sutured (Fig. 3).

Figure 1 A giant ketarinized condylomatous crazy-paving lesion of chronic appearance, extending over the labia majora and vulvar introitus. The inner thighs showed similar verrucous lesions, with diameters of between 3 and 5 cm, accompanied by millimetric satellite lesions. B Post-surgical appearance.

Figure 2 A histological study of the excised specimens evidenced verrucous carcinoma with signs of infection by human papillomavirus (HPV), no signs of invasion, and margins free of disease.



On the first neonatal follow-up examination at two months of life, an oropharyngeal exudate culture was performed, which yielded negative results for HPV infection. No signs of relapse of were observed.

Discussion

Vulvar cancer is a rare form of neoplasia, accounting for less than 1% of malignant neoplasms in women and 3-5% of neoplasms of the female genital tract. The estimated incidence is 1-2 cases per 100,000 women/year worldwide [1]. This entity affects

Figure 3 Delivery.

both young women (15% of cases; 40 years mean age) and women in the sixth or seventh decade of life (85% of cases) [1-3].

The most common histological types include: squamous cell carcinoma (86%), melanoma (4.8%), sarcoma (2.2%), basal cell carcinoma (1.4%), and adenocarcinoma (1.2%). Most cases of squamous cell carcinoma of the vulva are associated with HPV, while a smaller proportion of vulvar lesions develop from an area of lichen planus or lichen sclerosus et atrophicus and are not related to HPV infection [4].

Published incidence rates of vulvar cancer during pregnancy are 0.1-0.5 cases per 100,000 pregnancies, with only 38 cases reported in the literature up to 2019. In those cases, the treatment consisted of radical surgical excision plus lymphadenectomy or selective sentinel node biopsy. Vulvar radiotherapy is contraindicated during pregnancy [2]. Verrucous carcinoma of the vulva is a variant of squamous cell carcino-

ma, accounting for less than 1% of all vulvar neoplasms [1-3]. Ackerman used the term verrucous carcinoma for the first time in 1948 to describe an unusual variant of squamous carcinoma of the mouth [5]. Other locations have been described such as the skin, male or female external genitalia, uterine cervix, anal canal, bladder, renal pelvis and esophagus [6]. HPV infection was verified, by PCR detection of viral RNA, in about 27% of verrucous carcinomas [7]. In our patient, a relationship between the lesion and the HPV-6 type was found.

Macroscopically, the verrucous carcinoma showed a friable, exophytic surface that may become ulcerated and bleed, as happens in giant condyloma acuminatum (or Buschke-Löwenstein tumor) [8]. Histologically, it was an exophytic neoplasm with a broad attachment base, neatly separated from the underlying stroma. The papillae were lined with hyperplastic squamous epithelium with low cell atypia and reduced mitotic activity [9].

Verrucous carcinoma is a locally aggressive tumor characterized by expansive rather than infiltrative growth, which may involve nearby organs such as the vagina or the uterus. The risk of regional lymph node metastasis is very low. This is a radioresistant type of tumor; it has been reported to become more aggressive and to metastasize after radiotherapy9. On this basis, the treatment should consist of local excision with free margins of at least one centimeter. Margin involvement is associated with high recurrence rates [10]. Other treatments such as local podophyllin applications, bleomycin therapy or cryosurgery are ineffective to treat verrucous carcinoma [11].

Increased vulvar blood flow during pregnancy can lead to increased blood loss during the procedure. Such a risk can be reduced by careful electrocoagulation of the surgical site [2]. In our patient, clamping the vessels in the lesion allowed for correct hemostasis with minimal blood loss.

The American College of Obstetricians and Gynecologists (ACOG) recommends examination of the amniotic fluid and fetal heart rate before and after surgery. In patients with a pregnancy of more than 24 weeks' gestational age, continuous fetal monitoring is advised [12]. In the present case, fetal monitoring was conducted before and after surgery, and normal fetal heart rate was found at all times. Abdominal ultrasound showed a normal amniotic fluid maximum column. Perioperative prophylactic tocolytic agents are not recommended due to the lack of studies to support their use. Furthermore, there is no evidence that this intervention is associated with higher rates of preterm delivery [12]. A relevant issue to be considered in this treatment is the fact that the risk of blood loss increases as the lesion size and vascularity increase with gestational age. Consequently, it is advisable to perform this intervention as early as possible.

The European Society of Medical Oncology (ESMO) recommends cesarean section as the route of delivery in patients with recent surgery, because vaginal delivery increases the risk of surgical wound dehiscence. However, with small or well-healed surgical wounds, vaginal delivery is safest and therefore recommended [2]. In the present case, complete resection of the lesions and good wound healing allowed for vaginal delivery without risk of contagion for the newborn.

We conclude that active management of vulvar verrucous carcinoma during pregnancy is an acceptable and safe option, which allows for the treatment of the disease along with normal development of pregnancy and childbirth without posing extra risks to the mother or the newborn.

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