

## Vulvar Metastases from Colorectal and Gynecological Tumors: Two Case Reports and A Literature Review

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### ABSTRACT

**Introduction:** Squamous cell carcinoma is the most common histological type of primary vulvar tumor. However, when vulvar tumors are secondary, investigation for the primary site should include the rectum, colon, anus, cervix, ovary, endometrium, vagina, skin, breast, lung and bladder. These secondary lesions may be single or multiple and may vary macroscopically, presenting as maculae, ulcers, papules, nodules, plaques, inflamed lesions or even telangiectasias. Diagnosis is histological, with immunohistochemistry being helpful in clarifying cases. Prognosis tends to be poor and treatment is palliative because of the advanced stage of the primary tumor.

**Case:** The present report describes two clinical cases and discusses their rarity, clinical diagnosis, histopathology findings and the treatment of patients with metastatic vulvar lesions. The data were collected at a hospital in Vitória, Espírito Santo, Brazil.

**Conclusion:** In the female genital tract, the vulva is the least likely site of skin metastasis. However, when present, prognosis tends to be poor, since this finding is an indication of the advanced stage of the primary disease. Therefore, inspection of the vulva is mandatory. If lesions of any morphological type are present in this region, histology should be performed.

### Keywords

Cervical cancer, Colorectal cancer, Skin metastasis, Vulva.

### Introduction

Primary carcinoma of the vulva is responsible for approximately 3.6% of all gynecological cancers [1]. The risk of developing primary vulvar cancer is associated with behavioral factors such as smoking, as well as hormonal, reproductive and genetic factors. Other types of genital neoplasia, inflammatory diseases of the vulva, a history of verrucous lesions, immunosuppression and vulvar intraepithelial neoplasia may all contribute towards increasing the risk of vulvar cancer [2].

Squamous cell carcinoma is the most common histological type

involved in cases of primary vulvar cancer, accounting for over 90% of cases. In almost two-thirds of cases, squamous cell carcinoma develops in women over 60 years of age, although it may present in young women and adolescents [3].

Melanoma is the second most common histological type. Vulvar adenocarcinoma, however, is extremely rare and in such cases, investigation should be made for metastases, since the primary site may be the rectum, colon, anus, cervix, ovary, endometrium, vagina, skin, breast, lung or bladder [1,2].

Except for choriocarcinoma, metastatic tumors of the vulva are also rare [3]. This report describes two patients with metastatic vulvar lesions in which the primary disease was colorectal and

cervical cancer, respectively. The internal review board of the School of Sciences of the Santa Casa de Misericórdia de Vitória (EMESCAM) approved this case report under reference CAAE 95100718.9.0000.5065. Informed consent forms were signed granting permission to publish the report of these two cases.

### Case 1

A 32-year old multiparous woman whose latest child had been born three months previously presented at a gynecology department in the city of Vitória, Espírito Santo, Brazil with complaints of intense pain in the vulvar region, weight loss of 5 kilograms over a two-week period, adynamia and moderate dyspnea over the preceding thirty days. At admission, she reported no change in bowel or urinary habits.

The patient was jaundiced, dehydrated and swollen. She presented with reduced vesicular murmur in the right hemithorax and mild dyspnea. Abdominal examination revealed hepatomegaly. Inspection of the vulva showed a hypochromic, vegetative nodular lesion in the clitoral region and on the upper part of the left labium majus, in addition to bilateral palpable inguinal lymph nodes (Figure 1). Speculum examination showed no abnormalities. Rectal examination performed under sedation revealed an infiltrating, stenosing, ulcerative, vegetating and friable tumor around 8 cm from the anal verge.

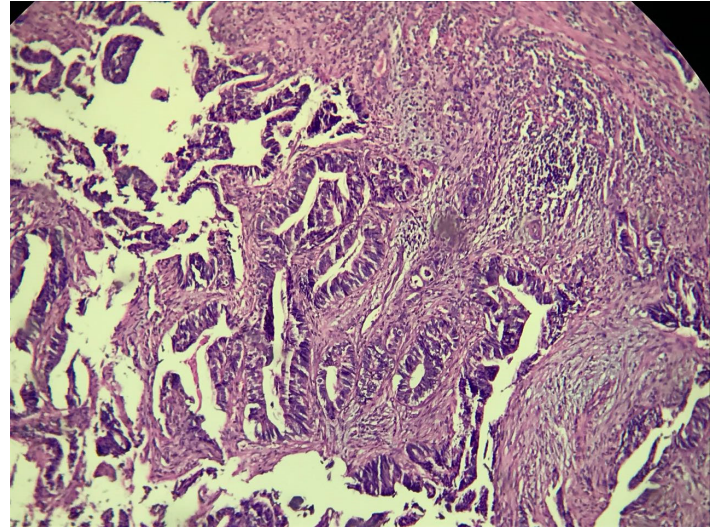


**Figure 1:** Hypochromic, vegetative nodular lesion in the clitoral region and on the left labium majus.

During hospitalization, tomography of the abdomen and pelvis revealed multiple diffuse secondary lesions in the liver and lymph nodes, and implants in the peritoneum and in the soft tissues of the abdomen, with no clear indication of the site of the primary lesion. Computed tomography of the thorax revealed multiple diffuse nodular lesions in the parenchyma suggestive of secondary lesions. Skull tomography showed no abnormalities.

The lesions in the rectum and clitoris were biopsied. Histopathology and immunohistochemistry findings led to diagnosis of a primary adenocarcinoma of the rectum. Pathology results of the vulvar

lesion were also compatible with adenocarcinoma, thus indicating that the vulvar lesion was the result of metastasis (Figure 2).



**Figure 2:** Poorly differentiated ulcerated adenocarcinoma, with extensive areas of tumor necrosis and signs of stromal desmoplasia.

The patient died due to cardiorespiratory failure on the third day of hospitalization prior to initiating the proposed palliative chemotherapy.

### Case 2

A 38-year old, brown-skinned, multiparous woman presented at a department of gynecology in Vitória, Espírito Santo, Brazil complaining of a painful nodular lesion in the vulvar region that had developed over the preceding three months. At admission, she reported no bowel or urinary symptoms. The patient informed that she had been diagnosed with stage 3B cervical cancer two years previously and was submitted to radiotherapy and chemotherapy, with the disease being considered under control at the end of the treatment.

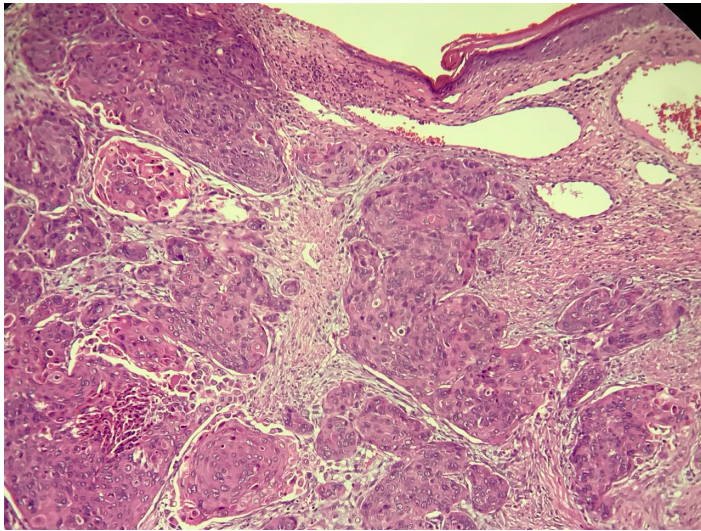


**Figure 3:** Hyperemic vulvar lesion measuring approximately 5 cm, with a central area of necrosis that presented the characteristic odor of a secondary infection. The lesion was located in the pubic region, extending as far as the clitoris.

Physical examination revealed a hardened, hyperemic lesion measuring approximately 5 cm, with a central area of necrosis and the characteristic odor of a secondary infection. The lesion was in the pubic region, extending as far as the clitoris (Figure 3). Speculum examination showed reduced vaginal rugosity, a shortened vaginal canal, and an atrophic, smooth cervix with no lesions.

The patient was submitted to computed tomography of the chest and abdomen, which showed no secondary lesions. Ultrasonography performed during hospitalization revealed a solid nodule in the vulva measuring 2.3 x 2.1 x 1.7 cm. Doppler revealed central and peripheral vascularization.

The patient was referred to the operating room for excisional biopsy of the vulvar lesion. Histopathology of the surgical specimen resulted in diagnosis of a well- to moderately-differentiated, ulcerative, vegetative, infiltrating epidermoid carcinoma (Figure 4). Angiolymphatic and perineural invasion were detected. Surgical margins were clear. Results were compatible with a metastatic lesion to the skin in the vulvar region from a primary cervical tumor. Immunohistochemistry showed positivity for vimentin, smooth muscle actin and pan-cytokeratin.



**Figure 4:** Well-to-moderately differentiated, solid epidermoid carcinoma with acantholytic, ulcerative, vegetative and infiltrating foci, measuring about 40 mm, reaching subcutaneous adipose tissue. Presence of stromal desmoplasia and areas of fibrosclerosis. Presence of angiolymphatic and perineural invasion.

Palliative chemotherapy was proposed, and the patient is being followed up at the oncology department. At the present time, she has been monitored for 13 months with no recurrence.

## Discussion

Squamous cell carcinoma is the most common type of primary vulvar malignancy. Typically, the tumor is associated with human papillomavirus (HPV) in women who have had multiple partners during their sexual life and who have a history of sexually transmitted diseases. Vulvar melanoma is the second most

common histological type, corresponding to 5-10% of malignant tumors of the vulva and may originate from an independent route of ultraviolet radiation [3,4].

The symptoms of vulvar cancer may include pruritus, pain, bleeding, dysuria and the presence of an unpleasant odor. Morphologically, the disease may present as maculae, ulcers, papules, nodules, plaques, inflamed lesions or even as telangiectasias [5]. Invasive squamous cell carcinoma presents as a nodular or verrucous vegetating polypoid lesion. Ulceration may also be present. Most cases consist of a single tumor, with multifocal disease being present in 10% of cases [3]. The two cases included in this report involved single nodular lesions. Differential diagnoses included benign dermatitis, mycosis fungoides and Kaposi's sarcoma [6]. Diagnosis is reached by histopathology, with immunohistochemistry providing further information on the case.

Vulvar intraepithelial neoplasia (VIN) is one of the most important risk factors. With the advancements in knowledge on vulvar carcinogenesis, precursor lesions have now been reclassified into two groups of different malignant potential: usual type VIN and differentiated VIN. Usual VIN is the most prevalent type of premalignancy and is associated with HPV infection. It can be further subdivided into basaloid VIN and warty VIN. Basaloid VIN occurs in younger women, has a greater potential for malignant transformation and a lower rate of spontaneous remission. Warty VIN is similar to condyloma acuminatum in appearance. Differentiated VIN is less common, has no association with HPV, and generally affects postmenopausal women over 65 years of age. The term differentiated refers to the squamous differentiation of the lesion. The lesion may be associated with lichen sclerosus [3].

Prognostic factors associated with vulvar tumors include size (prognosis is poorer with lesions over 2.5 cm in size), histologic type and grade, the depth of infiltration, negative or positive resection margins, vascular invasion and the presence of metastases to lymph nodes. Hematogenous dissemination may result in involvement of the liver, lungs and other organs. Perineural and vascular invasion have been correlated with a greater incidence of lymph node infiltration, which is the single most important prognostic factor of the disease [3].

Some of the most common sites of malignant skin metastases from tumors originating in the lower genital tract include the abdominal wall, vulva and thorax. In the case of vulvar neoplasia, the most common site affected is the labia majora in 66% of cases, followed by the labia minora, perineal body and clitoris [7].

Other histological types of vulvar cancer such as adenocarcinoma are rare. Vulvar adenocarcinoma is a rare malignant neoplasm that in most cases originates in the Bartholin's glands or skin annexes, principally the sweat glands. The epidermis may be infiltrated by individual cells or by groups of tumor cells, reproducing the histological appearance of Paget's disease of the breast [3].

Metastatic vulvar cancer is rare. A retrospective study conducted

in the United States evaluated 66 cases of metastatic cancer of the vulva and showed that the most common type of cancer responsible was cervical cancer (15 cases) followed by ovarian cancer (8 cases), endometrial cancer (6 cases) and colon cancer (3 cases) [8].

In the case of endometrial cancer, the principal metastatic route is hematogenous dissemination to the vulva. Nevertheless, the possibility of lymphatic dissemination cannot be ruled out in some advanced cases or in the case of type 2 endometrial cancer when behavior is similar to that found in cases of ovarian cancer, with dissemination to the round ligaments and to the pelvic lymph nodes [9]. In the case of cervical cancer, the tumor cells are metastasized by retrograde dissemination secondary to lymphatic obstruction [10].

The prognosis of metastatic cancer of the vulva is poor. In cases of metastatic cervical cancer, for example, only 20% of patients survive for more than one year. In cases of endometrial cancer with skin metastasis, the mean survival time is 3-6 months, with mortality rates of over 70% in the first year after diagnosis [6]. In the majority of cases, the time between diagnosis of the primary gynecological cancer and the development of skin metastasis is four years [9].

Up to the present time, no effective cure has been reported in the literature. Treatment is palliative and resources such as surgical resection, radiotherapy and chemotherapy have been used in combination or individually [6].

## Conclusion

Metastasis to the skin in the vulvar region from a distant carcinoma is rare; however, when present, prognosis is poor. The morphology of metastatic lesions of the vulva follows no specific pattern;

nevertheless, the present data confirm that the vulva is an important site to be monitored for the development of distant metastasis, particularly when the primary cancer is in the lower genital tract.

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