

CASE REPORT

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Vulvar melanoma: A rare case report from the department of obstetrics and gynecology

Meriem Nouri, Oumaima Baloul, Hajar El Borgi, Abdillah Kouchih, Safae Ammouri, Abdellah El Farouqi

ABSTRACT

Introduction: Approximately 3% to 5% of all cancer cases in women are caused by vulvar cancer, a rare tumor compared to other gynecological tumors. It is a particularly aggressive tumor originating from melanocytes and accounts for only 2.9% of all vulvar malignancies.

Case Report: A 56-year-old woman, single, menopausal for five years, presented with chronic left-sided vulvar pruritus evolving for approximately five years. Gynecological examination revealed a large erythematous lesion involving both labia majora, with a central erosive area and peripheral induration, associated with an irregular pigmented plaque centered on the left labium majus, extending posteriorly to the perineum and to the inner surface of the buttocks. Multiple excoriations due to scratching were noted, as well as several nevi, with no palpable inguinal lymphadenopathy. Bilateral inguinal ultrasound demonstrated lymphadenopathies of variable sizes, including nodes showing loss of fatty hilum, the largest measuring 10 × 9.4 mm on the left and 7 × 6 mm on the right, without abnormal fluid collection. Pelvic magnetic resonance imaging (MRI) revealed a vulvar tissue process located in the posterior aspect of the left labium majus, without signs of deep extension. Thoraco-abdomino-pelvic computed tomography (CT) showed no evidence of metastatic disease. The patient underwent partial vulvectomy combined with bilateral inguinal lymph node dissection followed by reconstruction using a flap procedure. Surgical margins were clear on frozen section.

Final histopathological examination confirmed an invasive superficial spreading vulvar melanoma, associated with an extensive in situ component. Breslow thickness was 1 mm, with invasion limited to the superficial dermis (Chung level I). Mitotic activity was 6 mitoses per 10 high-power fields, with no ulceration, no lymphovascular invasion, and no perineural invasion. The invasive component was located more than 10 mm from all surgical margins; however, the in situ component involved the external and internal margins and was 6 mm from the superior margin. Bilateral inguinal lymph node dissection showed no metastatic involvement.

Conclusion: Vulvar melanoma is a rare and particularly aggressive tumor with a poor prognosis. Prognostic factors include tumor size, depth of invasion, tumor differentiation, surgical margins, patient age, involvement of adjacent structures, and especially lymph node status.

Keywords: Ainguinal lymphadenopathy, Case report, Vulvar melanoma

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INTRODUCTION

Vulvar cancer is a rare tumor compared to other gynecological tumors and accounts for approximately 3% to 5% of all cancer cases in women [1]. It is estimated that 2 to 3 cases per 100,000 women occur each year, and it mainly affects women who are post-menopausal, typically between

the ages of 50 and 70 [2]. The most prevalent cancer in men is squamous cell carcinoma, adenocarcinoma, basal cell carcinoma, malignant melanoma, sarcoma, and metastatic carcinomas. Among these tumors, vulvar melanoma (VM) ranks second after squamous cell carcinoma, representing 5% to 6% of all vulvar cancers [3]. Its occurrence seems to be increasing gradually [4]. It is a particularly aggressive tumor, originating from melanocytes, and accounts for only 2.9% of all vulvar malignancies. It most often occurs after menopause, usually around the sixth decade of life [1]. Clinically, its presentation is not very specific: bleeding and chronic itching are the most observed symptoms, with a wide variation in severity. Vulvar melanomas are rare tumors, often associated with a poor prognosis. On the molecular level, they are clearly different from cutaneous melanomas: while the latter commonly have a BRAF mutation, VMs are more often characterized by c-KIT mutations [5]. To confirm the melanocytic nature of the lesion, diagnosis requires a thorough histopathological examination. To treat, a multidisciplinary approach is necessary, which includes surgery, lymph node evaluation, and potentially targeted therapies or immunotherapies based on the molecular profile. The high risk of metastatic spread is the main reason why the prognosis remains poor despite these strategies [6].

CASE REPORT

A 56-year-old woman, single, nulligravid, and menopausal for five years, with a medical history of type 2 diabetes mellitus treated with oral antidiabetic agents, presented with a chronic left-sided vulvar pruritus evolving for approximately five years, refractory to medical treatment and without associated symptoms. Two years prior to consultation, the patient noticed the appearance of a darkly pigmented vulvar lesion, which prompted evaluation by a dermatologist. A vulvar biopsy was performed, revealing VM, after which the patient was referred to our department for further management.

On physical examination, the patient was in good general condition. Vital signs were stable, conjunctivae were normally colored.

Gynecological examination revealed a large erythematous lesion involving both labia majora, with a central erosive area and peripheral induration, associated with an irregular pigmented plaque centered on the left labium majus, extending posteriorly to the perineum and to the inner surface of the buttocks. Multiple excoriations due to scratching were noted, as well as several nevi (Figures 1 and 2). A speculum and bimanual examination were deferred due to the presence of an intact hymen. No palpable inguinal lymphadenopathy was detected. The remainder of the systemic examination was unremarkable.

Histopathological examination of two vulvar biopsy specimens revealed distinct findings. The first biopsy demonstrated a superficial spreading vulvar mucosal

melanoma in situ, without any evidence of stromal invasion. The second biopsy showed an invasive superficial spreading vulvar mucosal melanoma, characterized by focal superficial stromal infiltration measuring approximately 1 mm, corresponding to Chung level I. The tumor thickness (Breslow depth) was 1 mm. No vascular emboli or perineural invasion were identified. An extensive pagetoid spread was also noted.

Bilateral inguinal ultrasound demonstrated bilateral lymphadenopathies of variable sizes, including nodes showing loss of fatty hilum. The largest nodes measured 10 × 9.4 mm on the left and 7 × 6 mm on the right without any abnormal fluid collection (Figure 3).

Pelvic magnetic resonance imaging (MRI) revealed a vulvar tissue process located in the posterior aspect of the left labium majus, without signs of deep extension (Figures 4 and 5). Thoraco-abdomino-pelvic computed tomography (CT) showed no evidence of metastatic disease.

The patient underwent a partial vulvectomy combined with bilateral inguinal lymph node dissection (Figures 6–9), followed by reconstruction using a flap procedure (Figure 10). The surgical margins were clear on frozen section.

Final histopathological examination of the surgical specimen confirmed an invasive superficial spreading VM, associated with an extensive in situ component. The



Figure 1: Extensive erythematous lesion of the bilateral labia majora with central erosion and peripheral induration.



Figure 2: Extensive erythematous lesion of the bilateral labia majora with central erosion and peripheral induration.



Figure 3: Bilateral inguinal ultrasound showing bilateral lymphadenopathies.

Breslow thickness was 1 mm, with invasion limited to the superficial dermis (Chung level I). Mitotic activity was 6 mitoses per 10 high-power fields, with no ulceration, no lymphovascular invasion, and no perineural invasion. The invasive component was located at a distance greater than 10 mm from all surgical margins; however, the in situ component involved the external and internal margins and was located 6 mm from the superior margin.

Bilateral inguinal lymph node dissection showed no metastatic involvement:

- Left side: 6 lymph nodes negative (0/6).
- Right side: 4 lymph nodes negative (0/4).

The case was discussed at the multidisciplinary tumor board (MDT) meeting after the final histopathology results were available. The MDT decision was not to perform re-excision, as further surgery was not feasible. The patient is a candidate for adjuvant (complementary) treatment.

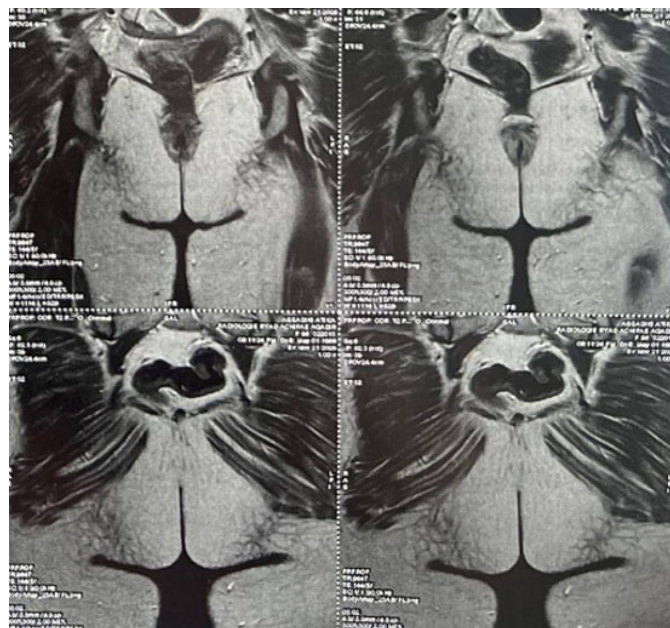


Figure 4: Pelvic MRI showing a posterior left labium majus tissue lesion without deep extension.

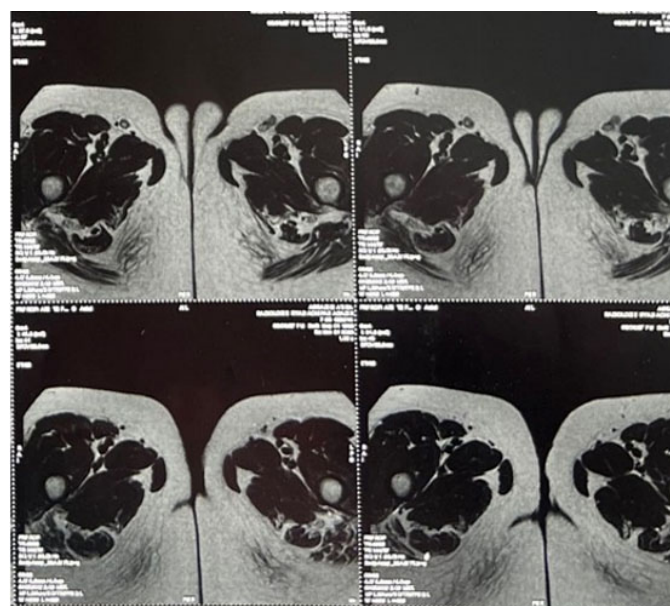


Figure 5: Pelvic MRI showing a posterior left labium majus tissue lesion without deep extension.

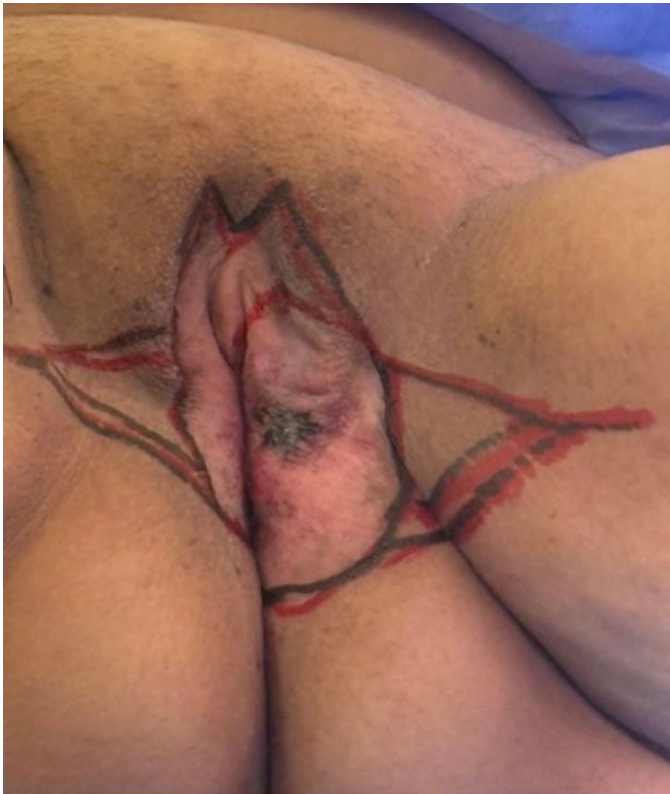


Figure 6: Preoperative image with marked resection margins and planned flap design.



Figure 8: Surgical specimen from right and left inguinal lymph node dissection.

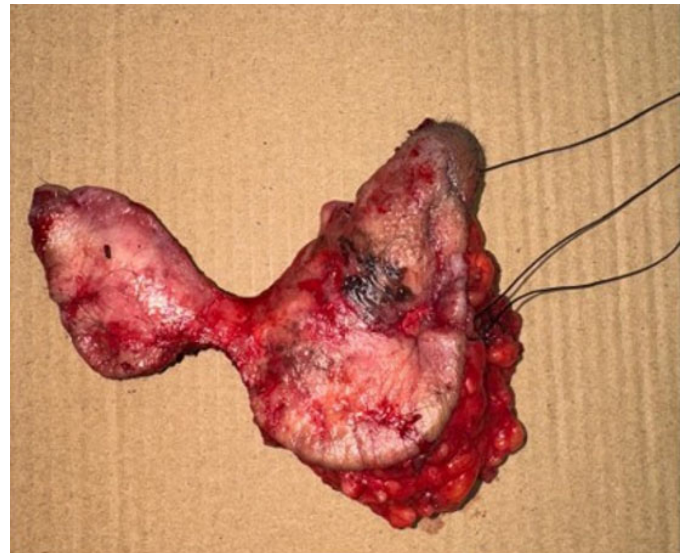


Figure 9: Oriented surgical specimen from vulvectomy.

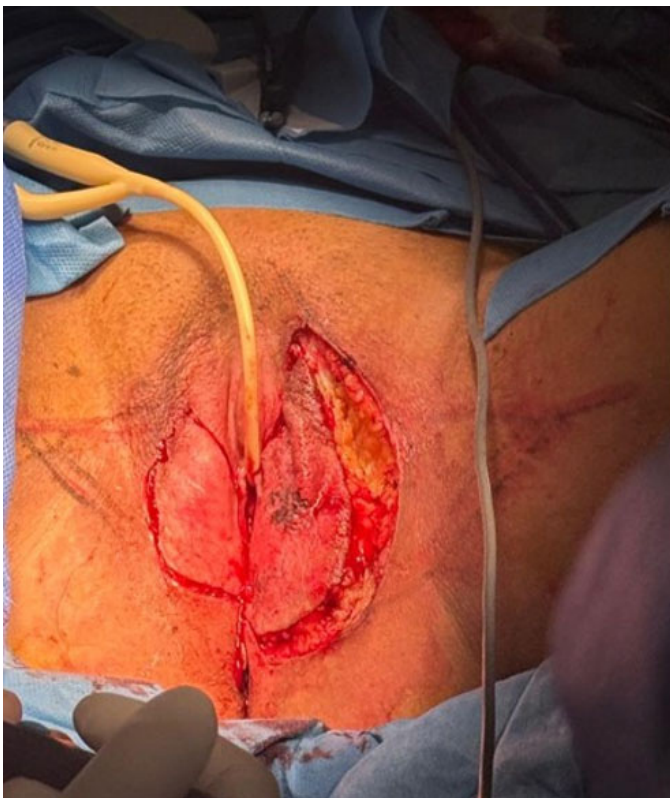


Figure 7: Intraoperative image of vulvar resection.



Figure 10: Partial vulvectomy combined with bilateral inguinal lymph node dissection and reconstruction using a flap procedure.

DISCUSSION

Primary malignant melanoma of the female genital tract is an extremely rare tumor. However, it is more commonly observed in the vulva than in the cervix and vagina [7].

Vulvar localization accounts for approximately 1% (all locations combined) of melanomas, followed in order of frequency by vaginal, uterine, and ovarian localization. These cancers have a poor prognosis if diagnosis is delayed. This late diagnosis is generally explained by a lack of knowledge about the symptoms of the disease, as well as modesty and a lack of expertise on the part of other clinicians [8].

The majority of VMs are diagnosed in postmenopausal women, with a median age at diagnosis of 68 years [9].

Melanomas are cancers that originate in melanocytes. The pathogenesis of VM remains largely unknown. Unlike cutaneous melanomas, VMs are not linked to chronic sun exposure and damage caused by ultraviolet light. Chronic dermatoses such as lichen sclerosis have been discussed as potential risk factors based on the results of a population-based study, but this warrants validation in larger prospective studies [10, 11].

Clinically, VMs may remain flat or raised pigmented lesions that are oligosymptomatic or asymptomatic at the onset of the disease [9, 12]. Amelanotic melanomas account for only 2% of all VMs [9]. lesions at the time of diagnosis, lesions have an average size of 3 cm and may be associated with itching, ulceration, or bleeding, symptoms that generally occur in advanced stages of melanoma [13].

In younger women, Paget's disease, smoking, immunosuppression, or a history of cervical neoplasia. Extensive research shows the involvement of genetics. Indeed, the specific genetic profile of vulvar and vaginal melanomas justifies testing for mutations in the c-KIT and NRAS genes in addition to BRAF. The presence of c-KIT mutations could justify the use of c-KIT-specific tyrosine kinase inhibitors, and the presence of NRAS mutations could justify the use of MEK inhibitors [14].

The differential diagnoses for pigmented vulvar lesions include genital nevi, vulvar melanosis, post-inflammatory hyperpigmentation, low-grade and high-grade squamous intraepithelial lesions, differentiated vulvar intraepithelial neoplasia, and pigmented seborrheic keratosis [15–17]. Differentiating VM from benign vulvar lesions is often difficult and sometimes impossible to do based on clinical judgment alone. The “ABCDE” rule can be a simple guide for an initial assessment of pigmented lesions: “A” stands for asymmetry, and most melanomas are asymmetrical; “B” stands for border, as melanomas usually have an irregular border, while nevi usually have a smoother border. C is a reference to color. Although benign moles are often a single brown color, multiple colors, including different shades of brown, black, blue, white, or red, are usually signs of malignancy. “D” stands for diameter, and lesions larger than 6 mm should raise awareness. The term “E” refers to elevation or evolution,

and any alteration in shape, size, structure, color, or symptoms is potentially a sign of malignancy [18].

In contrast to cutaneous melanoma, mucosal melanoma is a rare and aggressive malignant tumor due to melanocytes located in the mucous membranes, and accounts for less than 2% of all melanomas. It is biologically and clinically distinct from cutaneous melanoma, with a different mutational profile, an advanced stage at diagnosis, and more mediocre clinical results [5, 19].

Overall, women with VM have a poor prognosis, with a 5-year overall survival rate of only 46.6% compared to 92% for cutaneous melanoma [7]. Previous studies suggest that age, ethnicity, stage at diagnosis, tumor thickness, lymph node status, histologic subtype, mitotic count, ulceration, lymphovascular invasion, perineural invasion, and microscopic satellitosis are predictors of outcome [12, 20–25].

If VM is confirmed on biopsy, staging should be based on the American Joint Committee on Cancer (AJCC) staging system rather than the FIGO staging system used for vulvar squamous cell carcinoma, as the AJCC has been shown to be a better predictor of survival in the prospective GOG-73 study and this has recently been confirmed by a large population-based study [9, 24, 26]. The AJCC staging system is currently in its eighth edition, and staging of the primary tumor is based on Breslow thickness and the presence/absence of ulceration [27]. Histological classification is not used in melanomas, but the lesion is classified into one of the histopathological subtypes: superficial spreading, nodular, lentigo maligna, acral lentiginous, and desmoplastic [27]. Women with superficial spreading VM appear to have a better prognosis than those with nodular melanoma [9].

Due to the often-advanced stages of the disease, preoperative imaging is recommended [13–18, 20–28]. Magnetic resonance imaging can be useful for determining the extent of the disease and for surgical planning. Computed tomography or positron emission tomography can be used to evaluate regional and/or distant metastases [13].

The main treatment modality for localized melanoma is surgical excision. In cutaneous melanoma, surgical margins are recommended based on the thickness of the tumor: 0.5 to 1 cm for melanoma in situ, 1 cm for invasive melanoma with a Breslow thickness ≤ 1 mm, 1 to 2 cm for Breslow 1.01–2 mm, and 2 cm for Breslow >2 mm. It should be noted that these are based on measured clinical margins taken at the time of surgery and not on gross or histological margins, as measured by the pathologist [29, 30]. The same margins should apply to VM. However, margins may be modified to consider individual anatomical or functional considerations, which may be considered in VM in terms of preserving continence and sexual function [13, 28, 29].

Regarding surgical treatment, more than five years ago, the trend was to perform a total vulvectomy and inguinal lymph node dissection extending to the pelvis.

Currently, surgery is limited to the affected area and superficial lymphadenectomy (bilateral or ipsilateral inguinal) is performed due to the morbidity associated with extensive inguinal surgery.

The GOG-73 trial, the only prospective study on VM conducted to date, and retrospective data indicate that more radical vulvar surgeries such as primary vulvectomy are not associated with better oncological outcomes compared to local excision using the above margins but are associated with an increased complication rate [31].

Sentinel lymph node biopsy should be offered to all women with VM and clinically non-suspicious lymph nodes or in the presence of ulceration [29, 30]. The multicenter Selective Lymphadenectomy Trial I validated the staging potential of sentinel lymph node biopsy but did not show an unequivocal survival benefit in terms of 10-year melanoma-specific survival related to treatment [32]. It should be noted that the study recruited patients between 1994 and 2002, before adjuvant treatment with checkpoint inhibitors was offered to node-positive patients. Sentinel lymph node biopsy has been extensively studied in vulvar cancer. A meta-analysis showed that the detection rate using blue dye in combination with a radiocolloid tracer is 97.7% (95% CI 96.6–98.5) if ultra-staging and immunohistochemistry are performed [33]. A similar detection rate of 98.3% was reported in a review of the literature on virtual machines [34].

Superficial lymphadenectomy (bilateral or ipsilateral inguinal) due to the morbidity associated with extensive surgery. The latter technique was used during this procedure. It has the advantage of reducing morbidity.

Selective lymphadenectomy is therefore likely to reduce morbidity by targeting samples to the lymph nodes draining the tumor area without risking the complications associated with inguinal dissection [35].

Before the arrival of immunotherapies and targeted therapies, the standard treatment for vulvovaginal melanomas (VM) relied on cytotoxic chemotherapy, such as dacarbazine and temozolomide. However, these treatments had low response rates and did not clearly improve survival [36]. The introduction of checkpoint inhibitors marked a major advance. Using PD-1 inhibitors alone or combined with anti-CTLA-4 drugs, response rates of about 33–37% were achieved in mucosal melanomas, which are slightly lower than those seen in cutaneous melanomas [37]. This difference may be due to the distinct biology of mucosal melanomas, including lower mutational burden and a less immunogenic tumor microenvironment [37]. Additionally, BRAF mutations are rare, so targeted BRAF/MEK therapies have limited use. However, mutations in c-KIT, especially in exons 11 and 13, may justify the use of tyrosine kinase inhibitors like imatinib in selected cases [38]. In the absence of robust trials focused on vulvovaginal locations, current guidelines generally recommend aligning adjuvant strategies for VM with those used for cutaneous melanoma, particularly using anti-PD-1 drugs for high-risk patients [39].

CONCLUSION

Vulvar melanoma is particularly aggressive and has a poor prognosis. Tumor spread mainly occurs through the lymphatic system, but it can also spread directly and through the bloodstream.

Prognostic factors include tumor size, depth of invasion, tumor differentiation, surgical margins, the patient's age, involvement of the urethra, vagina, perineum, and especially the lymph nodes.

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Author Contributions

Meriem Nouri – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Oumaima Baloul – Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Hajar El Borgi – Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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