CASE REPORT

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Surgical pathology, management and outcome in the vulvar melanoma associated with abdominal mass – a case report

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Abstract

Vulvar malignant melanomas are extremely rare neoplasms, representing less than 3% of all cancers in women, 9% of all external genital tract malignancies and 9% of all primary vulvar malignancies. We present the case of a 60-year-old Caucasian patient, who has been admitted in the Clinic of Obstetrics and Gynecology with polymorphic, vulvar local, pelvic-abdominal, genitourinary and general symptoms, being diagnosed with nodular and superficial spreading vulvar melanoma and multiple voluminous uterine leiomyoma with various degenerations. Our study presents the approach of this case in terms of surgical pathology, management, prognosis and outcome. Surgical treatment is the central element of therapeutic management. Vulva melanomas are in general a relatively unpredictable unfavorable prognosis. The sizes of the tumor, the thickness and micro-staging are essential factors for prognosis.

Keywords: genital cancer, abdominal tumor, immunohistochemistry, diagnosis, prognosis.

Introduction

The melanomas of the genital area on the one hand, and the vulvar melanoma in particular is an extremely rare pathology. Vulvar melanoma is 8–10% of all malignant disorders of the vulva [1]. Vulvar malignant melanoma is approximately 5% of the melanomas diagnosed in women [2, 3].

As distinct entity, melanoma is a malignant tumor resulting from the transformation and proliferation of melanocytes, arising from the neuroectoderm and are located in the basal cells of the epidermis. The etiology of the melanoma involves the genetic susceptibility, the pre-existence of a benign lesion (30% of melanomas), the risk being significantly high in the white race, compared to the black race, Asian women or originating from other races with increased pigmentation [1, 4].

Malignant vulvar melanoma occurs most commonly in the labia minora, labia majora or clitoris [1].

The microscopic features of vulvar melanomas typically include one of three recognized growth patterns and a variety of cellular variants. Vulvar melanomas can usually be classified as nodular, superficial spreading or mucosal and acral lentiginous [2, 5, 6].

Although the morphological pattern of the clinical examination is suggestive, the vulvar melanoma requires a complex differential diagnosis, which may include benign pigmented lesions such as lentigo simplex, vulvar melanosis, acathosis nigricans, seborrheic keratosis, intradermal, junctional or compound nevi, as well as the pigmented vulvar intraepithelial neoplasia, vulvar squamos carcinoma, Paget's disease [1, 2, 7–9].

In this paper, we present a case of vulvar melanoma associated with a voluminous abdominal pelvic tumor in a Caucasian patient with polymorphic, local vulvar, pelvic-abdominal, genitourinary and general symptoms.

Case presentation

We present the case of a 60-year-old Caucasian patient, who has been admitted in the Clinic of Obstetrics and Gynecology with complex genital, urinary and digestive symptoms.

The genital symptoms included the vulvar tumor (Figure 1), local painful discomfort, vaginal discharge, local itchiness and discreet local bleeding. The whole clinical picture also included discreet dysuria and frequent urination, pelvic and abdominal pain, enlarged abdomen, episodes of constipation as well as significant weight loss.

During the clinical examination of the patient, the vulvar tumor was identified in the right labia minora and

majora, also involving the lower urethra and the external urethral meatus by infiltration, with sizes of 4/5 cm (Figure 2).

The macroscopic examination in terms of surgical pathology proves the presence of a right labial vulvar tumor located medially, which implicates the mucosal-keratinized epithelial junction, involving the vulvar vestibule, the clitoris and the urethral region. The tumor has irregular edges, is elevated and non-hairy, having a polypoid polymorphic, nodular aspect or as a hyper-pigmented extended placard with minimum ulcerations.

The genital examination identifies the presence of a voluminous pelvic-abdominal tumor in the uterine body, with irregular contour and increased, hard consistency, minimum relative mobility, smooth and non-infiltrating edges, with overall dimensions in the uterine body of 16/19 cm. No adnexal masses are individualized upon the physical examination.

Patient had bilaterally clinically negative inguinal lymph nodes.

The transabdominal ultrasound examination describes a tumor of the uterine body in terms of an irregular and uneven consistency, with irregular calcifications disseminated throughout the tumor, which occupies the pelvis, with sizes of 18.5/15.27/12.04 cm, with the possibility to individualize from the remaining pelvic organs. The ultrasound description is suggestive for the diagnosis of uterine leiomyoma and adenomyosis.

The surgical management for the diagnosis of vulvar malignant melanoma and uterine tumor included: radical vulvectomy, distal urethral resection, distal colpectomy, bilateral superficial and deep inguino-femoral lymph-adenectomy and total bilateral abdominal hysterectomy with bilateral adnexectomy and bilateral pelvic lymph-adenectomy (Figures 3 and 4).

No intraoperative or postoperative complications were registered, the postoperative evolution was favorable. Adjuvant systemic therapy in process.

Surgical pathology description for the diagnosis of vulvar malignant melanoma includes the radical vulvectomy specimen with the vulvar tumor, distal urethra and posterior vagina (Table 1). The macroscopic description of the vulvectomy specimen is indicating a 5/4 cm tumor, of blackish color, ulcerated, areas of necrosis, cauliflower-like appearance, infiltrative.

Table 1 – ***Diagnosis, surgical management and pathology***

Clinical diagnosis	Surgical management	Surgical specimen	Pathology
Vulvar melanoma	Radical vulvectomy	Vulvectomy specimen Vulvar melanoma 5/4 cm	Nodular and superficial spreading vulvar melanoma. Vertical growth pattern. ↑↑↑ Fusiform cell. Pleomorphic nucleolus nuclei. (+) Intra- and extra-cellular melanin granules. Tumor emboli inside the vessels. ↑↑↑ Atypical mitoses. Mitotic index – 8 mitoses/mm^2. Clark level IV. Breslow Index > 2 mm Oncological safety limits.
	Distal urethral resection	Distal urethra	Chronic stromal inflammation. No tumor involvement.
	Distal colpectomy	Distal vagina	Wall coated by the stratified squamous epithelium. Chronic sub-epithelial inflammation. No tumor involvement.
	Bilateral superficial and deep inguino-femoral lymphadenectomy	Inguino-femoral lymph nodes: ▪ left – 2; ▪ right – 9.	Histologically reactive aspect. No tumor involvement.
	Bilateral pelvic lymphadenectomy	Pelvic lymph nodes: ▪ left – 10; ▪ right – 15.	Histologically reactive aspect and lipomatous dystrophy. No tumor involvement.
Uterine tumor	Total abdominal hysterectomy with bilateral adnexectomy	Uterus Uterine cervix Ovary Fallopian tubes	Leiomyoma with sclero-hyaline areas. Internal adenomyosis. Atrophic endometrium. Endometrial glandular polyp. Ovaries – corpus albicans and follicular cysts. Fallopian tubes – preserved structure.

The microscopic description of the vulvectomy specimen histologically presents nodular and superficial spreading vulvar melanoma, cutaneous tissue with medium sized cell proliferation and pleomorphic nucleolus nuclei, vertical growth pattern and predominantly fusiform cell, partially epithelioid, with necrotic areas, positive intra- and extra-cellular melanin granules, involving the deep dermis to the vicinity of the hypodermis. Frequent atypical mitoses. Mitotic index of 8 mitoses/mm^2. Clark level IV. Breslow Index >2 mm. Diffuse chronic inflammation. Tumor emboli inside the vessels. Peri- and intra-neural tumor involvement (Figures 5–7). The labia and clitoris present subtegumentary diffuse chronic inflammation, without tumor involvement. Fragment of vulvar tegument laterally of the main lesion and deep fibroadipose tissue without tumor involvement. Resection within oncological safety limits. The distal urethra with chronic stromal inflammation, without tumor involvement. The posterior vagina with the wall coated by the stratified suqamos epithelium with chronic sub-epithelial inflammation without tumor involvement.

The surgical pathology description for the diagnosis of uterine tumor and the analysis of the lymph nodes include the uterus, cervix, adnexes, bilateral pelvic nodes, inguino-femoral right and left nodes (Table 1).

The macroscopic description of the radical total

hysterectomy specimen with bilateral adnexectomy and pelvic and bilateral inguino-femoral lymph node dissection, which presents a uterus of 18/15 cm, when sectioning, a uterine leiomyoma of 9/9 cm is emphasized, arranged subserosally and another one 5/5 cm arranged submucosally. Endometrial intracavitary polyp. Cervix of 2/2/1 cm, which shows superficial ex-ulcerations. Ovaries of 2/1 cm, which upon sectioning, they have small cysts containing serous fluid in the stroma. Fallopian tubes of 4.5 cm length and resilient wall.

The microscopic description histologically presents uterus with leiomyomas with sclerohyaline areas and areas of internal adenomyosis. Atrophic glandulo-cystic endometrium. Atrophic glandular endometrial, glandulo-cystic polyp. Superficial ex-ulcerations. Non-specific chronic cervicitis with glandulo-cystic hyperplasia.

Ovaries with corpus albicans and follicular cysts. Right and left Fallopian tubes with a preserved structure.

Lymph nodes: right pelvic (15) histologically presenting a reactive aspect and lipomatous dystrophy. Left pelvic nodes (10), left inguino-femoral (2) and right inguino-femoral (9) histologically presenting a reactive aspect (Table 1).

The immunohistochemical study included the following panel of antibodies: Mart-1 (Melan A) (mouse monoclonal, A103, Cell Marque), melanoma cocktail [HMB-45 + MART-1 (Melan A) (A103) + tyrosinase (T311)]; vimentin (rabbit monoclonal, SP20, Cell Marque), S100 (mouse monoclonal, 4C4.9, Cell Marque), Ki67 (rabbit monoclonal, SP6, Cell Marque). The antigenic retrieval and working systems were used according to manufacturers. Also, in order to validate the immunoreactions, internal and external negative controls were used for each marker.

The immunohistochemical analysis indicated the following aspects: melanic cell proliferation characteristics, positivity for vimentin, pS100, Mart-1 and HMB-45. Ki67 immunostainig revealed a 70% high proliferation index (Figures 8–12).

The presence of the lymphatic and vascular tumor emboli is also highlighted.

Depending on the oncological evaluation, testing for BRAF gene mutations might be required. Unless V600E mutation is negative, immunohistochemical assessment of CD117 is to be evaluated.

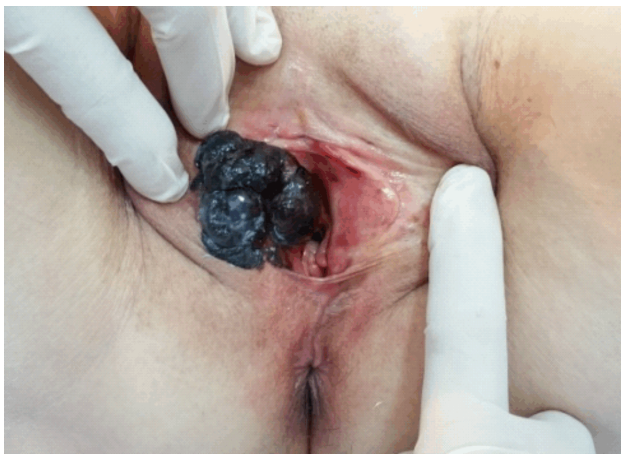

Figure 1 – ***Vulvar melanoma. The macroscopic examination in terms of surgical pathology proves the presence of a right labial vulvar tumor located medially, which involves the mucosal-keratinized epithelial junction, involving the vulvar vestibule, the clitoris and the urethral region.***

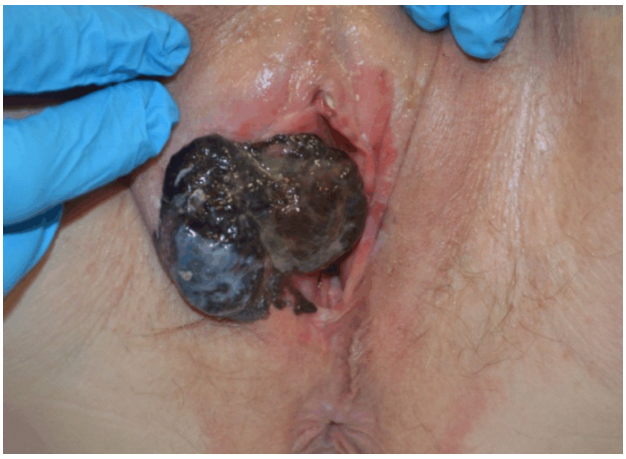

Figure 2 – ***Vulvar melanoma. Reexamination prior to surgery. The tumor has irregular edges, is elevated and non-hairy, having a polypoid polymorphic, nodular aspect or as a hyper-pigmented extended placard with minimum ulcerations.***

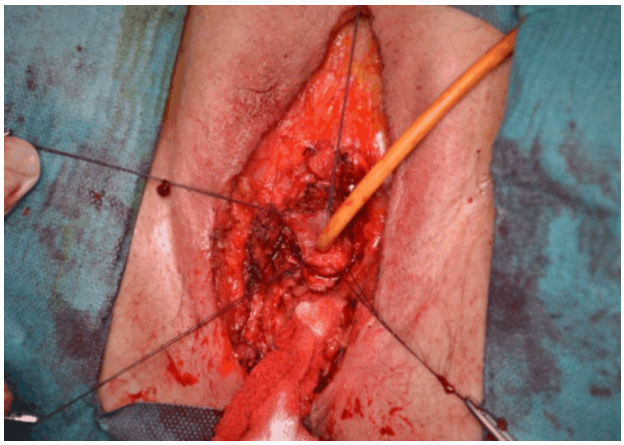

Figure 3 – ***Surgical management. Radical vulvectomy, distal urethra (1 cm) and a portion of distal vagina have been removed. Note the four sutures externalizing urethra after resection. Foley catheter is in place.***

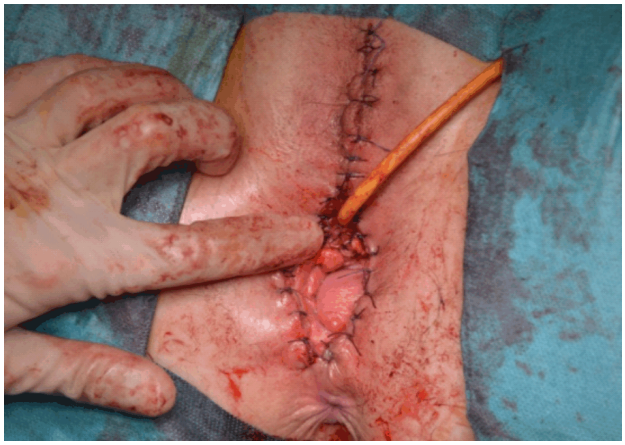

Figure 4 – ***Surgical management. Closure of the radical vulvectomy with the urethral and vaginal anastomosis.***

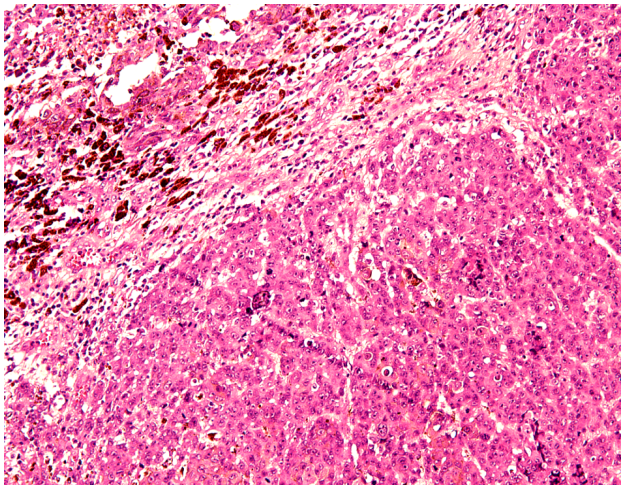

Figure 5 – ***Tumor surface. Nodular growth pattern and tumoral tissue ulceration. HE staining, ×100.***

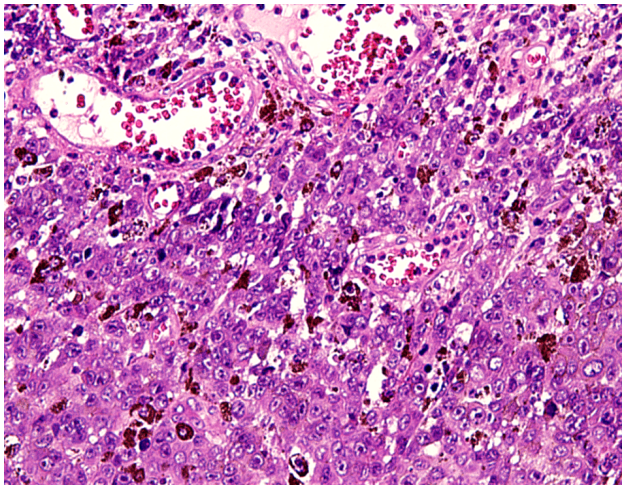

Figure 6 – ***Detail of the tumor surface. Round-oval cells, medium size, with solid-nodular arrangement, ulcerated areas. HE staining, ×200.***

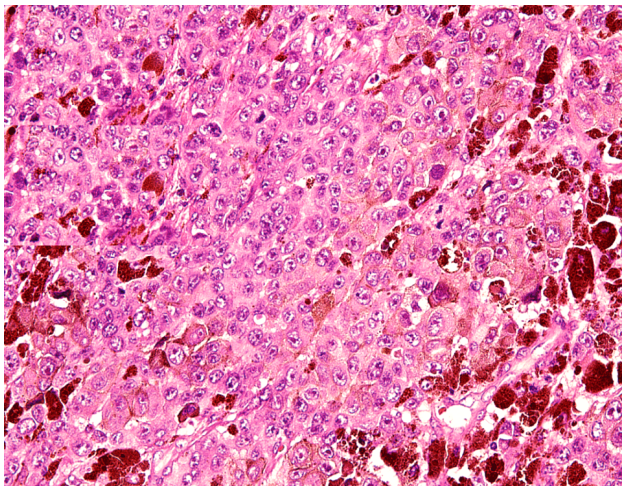

Figure 7 – ***Cellular details from the center of the tumor. Neoplastic proliferation with round-oval cells, medium size, with solid-nodular arrangement and ulcerated areas. HE staining, ×400.***

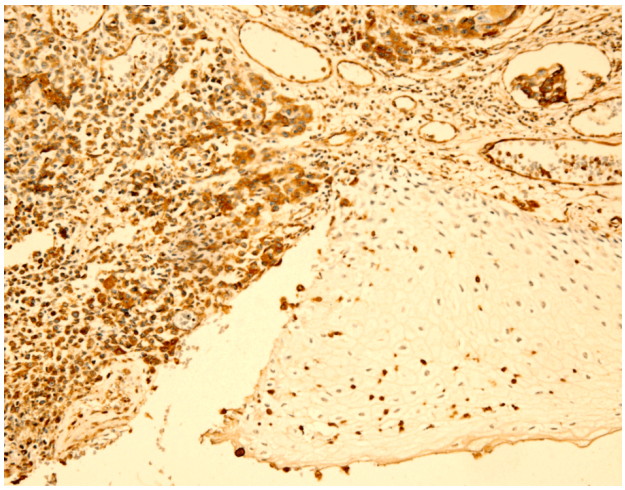

Figure 8 – ***Vimentin immunostaining (SP20 clone, Cell Marque) highlights the presence of vascular tumor emboli, ×100.***

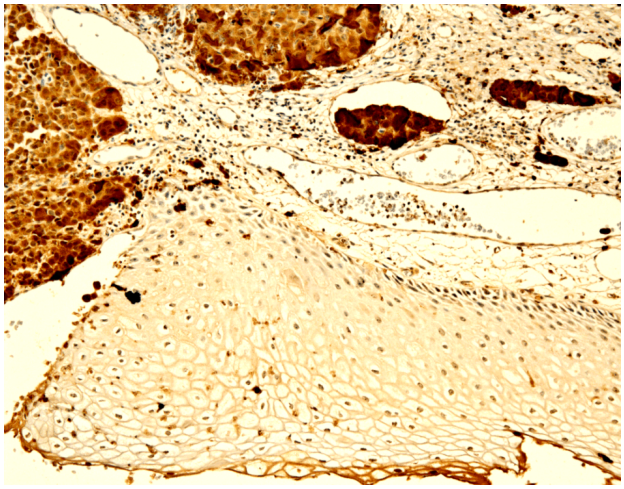

Figure 9 – ***S100 protein immunostaining (4C4.9 clone, Cell Marque). Lateral extension of the tumor highlighting the lymphovascular tumor emboli, ×100.***

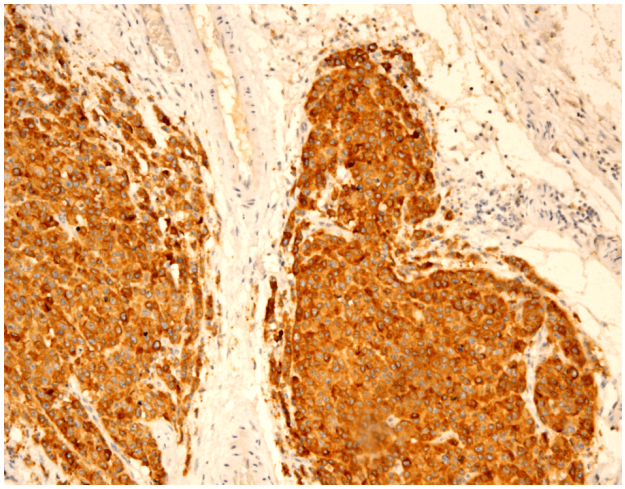

Figure 10 – ***Mart-1 (Melan A) immunostaining (A103 clone, Cell Marque) demonstrates the nodular growth pattern of the tumor, ×200.***

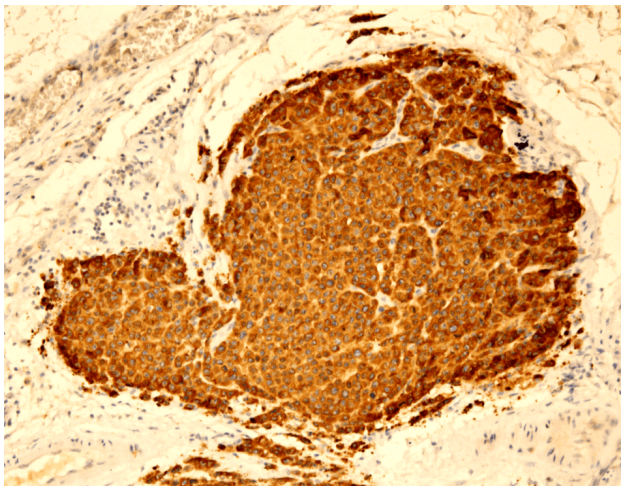

Figure 11 – ***HMB-45 immunostaining (HMB-45 clone, Cell Marque). Deep invasion area and nodular growth pattern of the tumor, ×200.***

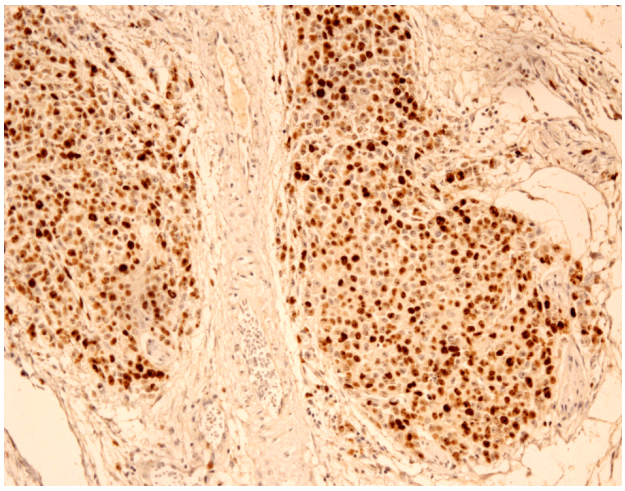

Figure 12 – ***Ki67 immunostaining (SP6 clone, Cell Marque). Deep invasion area with a 70% nuclear index, ×200.***

Discussion

Vulvar malignant melanomas are extremely rare neoplasms, representing less than 3% of all cancers in women, 9% of all external genital tract malignancies and 9% of all primary vulvar malignancies [9, 10].

In general terms and confirmed in statistical terms, melanoma is one of the most aggressive forms of human cancer, although it represents only 4% of all skin cancers, it accounts for 80% of skin cancer deaths and it is placed second after adult leukemia in terms of potential productive life-years loss [11, 12].

Vulvar malignant melanomas must be distinguished from Paget's disease, squamous cell carcinomas, atypical vulvar nevomelanocytic nevi or other junctional or congenital nevi, as well as from other malignant tumors such as soft tissue tumors or large cell lymphomas [2, 13].

The surgical treatment for the vulvar melanoma was in our case radical vulvectomy and bilateral superficial and deep inguino-femoral lymphadenectomy, as well as pelvic lymphadenectomy, taking into account the extensive sizes of the tumor and its thickness of more than 7 mm.

Tumor thickness is inversely related to absolute survival as well as total length of survival. Patients with vulvar malignant melanoma with a thickness of more than 7 mm have a global survival rate of 22% [2, 14, 15].

It is estimated that, overall, approximately a third of the patients with vulvar melanoma survive for five years. The prognosis is even worse as the age is older and the tumor is more advanced at the time of diagnosis [16].

The surgical management also included total abdominal hysterectomy with bilateral adnexectomy, representing the optimal therapeutic conduct for the diagnosis of uterine leiomyoma and areas of internal adenomyosis, at the same time also performing bilateral pelvic lymphadenectomy, taking into account the extent of the vulvar tumor [17].

Irvin *et al.* consider that the patients diagnosed with vulvar malignant melanoma have an average survival rate of 61 months. According to the same author, the five-year survival rate is 60%, and the 10-year survival rate is 50% [18].

Most studies on vulvar malignant melanoma show that, in general, it has an unfavorable prognosis, relatively unpredictable, tending to recur locally on the one hand, and on the other hand there being the possibility of metastases remotely by hematogenous dissemination [1, 19, 20].

Even though there are many studies, some on large groups of patients with vulvar melanoma, there are currently no prospective data from randomized clinical studies that would assess the ideal excision in the case of this lesion [1].

The *American Joint Committee on Cancer* (AJCC) extensively revised the TNM staging system for cutaneous melanoma [16].

Starting from this system, in correlation with the Clark level and Breslow Index, meaning the tumor less than 2 mm and positive necrotic areas, the patient can fall as staging pT3bN0Mx.

Melanomas are typically immunoreactive for melanoma-specific antigen (HMB-45), Melan-A (Mart-1) and S100 [2].

The relevance of immunohistochemistry could be highlighted in terms of differential diagnosis. As described in our paper, immunohistochemical analysis indicated positivity for these antibodies.

Squamous cell carcinomas are immunoreactive for keratin or carcinoembryonic antigen (CEA) and they are negative for the S100 antigen or HMB-45 [2, 7, 13].

Wilkinson & Hassanein mention the fact that soft tissue tumors are typically not reactive for melanoma-specific antigens and in some cases, metastatic melanoma may be immunoreactive for CEA and negative for HMB-45 [2].

For the case presented in this paper, we believe that the surgical treatment through radical vulvectomy and bilateral superficial and deep inguino-femoral lymphadenectomy, and bilateral pelvic lymphadenectomy is supported by Clark IV, with tumor involvement in the subcutaneous fat and a Breslow Index >2 mm.

The accurate correct and prompt diagnosis is essential in the case of vulvar malignant melanoma, being unani-

mously recognized that they are characterized by an unfavorable prognosis. Surgical treatment is the central element of therapeutic management. The sizes of the tumor, the thickness and invasion degree, as well as the number of mitosis and involvement of lymph nodes are essential factors influencing the survival [21–23].

Although there are many comparative studies and numerous surgical techniques adapted depending on the surgeons' experience and various centers with tradition in oncological surgery, there is virtually no evidence of significant improvement of the survival rates in recent decades [24, 25].

The patient's age at the time of diagnosis, micro-staging and lymph invasion are important for determining the prognosis. In a multivariable analysis, younger age, localized disease, and negative lymph nodes were independent prognostic factors for improved survival [26, 27].

In the case of the vulvar malignant melanoma, surgical treatment is the central element of the therapeutic management and we consider it is very important for the initial surgery to be optimally chosen, so the patient is not predisposed or not to influence the time until the appearance of recurrences, in case of a sub-optimal surgical management.

Conclusions

The accurate and prompt diagnosis is essential in the case of the vulvar malignant melanoma. Generally, it has an unfavorable relatively unpredictable prognosis, tending to recur and form metastases. Surgical treatment is the central element of the therapeutic management. The initial surgical intervention must be optimally chosen so the appearance of recurrences is not influenced. The sizes of the tumor, the thickness and invasion degree, as well as the number of mitosis and involvement of lymph nodes, the patient's age at the time of diagnosis and micro-staging are essential factors influencing the survival.

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper. All authors read and approved the final manuscript.

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