VULVAR MALIGNANT MELANOMA – CASE REPORT

MALIGNI MELANOM VULVE – PRIKAZ SLUČAJA

Marko STOJIĆ[1, 2], Miloš PANTELIĆ[1, 2], Jovan UGARKOVIĆ[1, 2], Gabriel-Stefan NAĐ[1, 3] and Aleksandra ILIĆ[1, 4]

ORCID NUMBER
Marko Stojić – 0000-0002-6986-4742
Miloš Pantelić – 0000-0003-2539-730X
Jovan Ugarković – 0009-0005-2927-128X
Gabriel-Stefan Nađ – 0000-0002-9938-431X
Aleksandra Ilić – 0000-0003-1657-3914

University of Novi Sad, Faculty of Medicine Novi Sad[1]
University Clinical Center of Vojvodina, Clinic of Obstetrics and Gynecology, Novi Sad[2]
Oncology Institute of Vojvodina, Sremska Kamenica[3]
University Clinical Center of Vojvodina, Department of Pathology and Histology, Novi Sad[4]

Case report
Prikaz slučaja
UDK 618.16-006.81-08
https://doi.org/10.2298/MPNS2412338S

Abstract

Introduction. Vulvar carcinoma is a rare gynecological malignancy, accounting for 0.6 percent of all female cancers. **Case Report.** A-76-year-old woman presented with a tumorous lesion in the lower third of the left labia majora and minora, measuring approximately 25 mm. A multifocal biopsy was conducted, and pelvic magnetic resonance imaging revealed slight enlargement of a left inguinal solid lymph node. The patient underwent a left hemivulvectomy with inguinofemoral lymphadenectomy. Histopathological analysis confirmed a malignant lentiginous tumor, and inguinofemoral lymphadenectomy revealed metastatic malignant melanoma. Despite a negative histopathological finding of the contralateral side during the initial biopsy, the patient returned within three months with a 9-mm mucosal nodular type melanoma on the lower third of the right labia majora. A wide excision of the vulva was subsequently performed. Following consultation with a multidisciplinary tumor board, adjuvant immunotherapy with Pembrolizumab (200 mg per cycle, 9 cycles) was initiated. **Conclusion.** Vulvar malignant melanoma is rare, aggressive, and unpredictable tumor that predominantly affects women in later life. It is associated with a high recurrence rate and a poor overall prognosis.

Key words: Vulvar Neoplasms; Melanoma; Neoplasm Metastasis; Magnetic Resonance Imaging; Gynecologic Surgical Procedures; Chemotherapy, Adjuvant

Sažetak

Uvod. Karcinom vulve je retko ginekološko oboljenje sa učestalošću od 0,6 procenata svih karcinoma kod žena. **Prikaz slučaja.** Sedamdesetšestogodišnja žena je upućena zbog tumorske promene lokalizovane u donjoj trećini velikih i malih usana, sa leve strane, promera oko 25 mm. Urađena je multifokalna biopsija. Magnetnom rezonancijom karlice uočeno je blago uvećanje ingvinalnog limfnog čvora sa leve strane. Načinjena je levostrana hemivulvektomija sa ingvinofemoralnom limfadenektomijom. Patohistološki nalaz potvrđuje prisustvo malignog lentiginoznog tumora. Ingvinofemoralnom limfadenektomijom dokazano je prisustvo metastatskog malignog melanoma. I pored urednog patohistološkog nalaza kontralateralne strane vulve, dobijenog multifokalnom biopsijom, za manje od tri meseca, pacijentkinja se ponovo javlja sa de novo tumorskom promenom nodularnog tipa melanoma promera oko 9 mm, lokalizovanom u donjoj trećini velike usne sa desne strane. Urađena je široka lokalna ekscizija vulve. Onkološka komisija je indikovala adjuvantnu imunoterapiju pembrolizumabom, 200 mg po seriji, devet serija. **Zaključak.** Maligni melanom vulve je redak, nepredvidiv i agresivan tumor koji se najčešće javlja kod žena starijeg životnog doba sa visokom stopom recidiva i ukupno lošom prognozom.

Ključne reči: tumori vulve; melanom; metastaza; magnetna rezonanca; ginekološke operativne procedure; adjuvantna hemoterapija

Introduction

Vulvar carcinoma is a rare gynecological malignancy, accounting for approximately 0.6% of all female cancers [1–3]. Despite its rarity, the vulva represents the most common site for melanoma within the female genital tract, even though vulvar melanomas (VM) constitute a small fraction of both vulvar cancers and melanomas overall [4, 5]. VM is the second most common type of vulvar carcinoma after squamous cell carcinoma [6, 7]. While predominantly affecting white postmenopausal women, cases have been documented in younger individuals, with a median diagnostic age of 68 years [5]. Due to its rarity, treatment protocols for VM are largely extrapolated from those established for cutaneous melanomas. This report presents a case of malignant vulvar melanoma and discusses the associated management strategy.

Case Report

A 76-year-old multiparous woman with a history of hypertension presented with a tumorous vulvar lesion, which she had noticed for approximately one year. There was no family history of malignancy. Ethical approval for this study was obtained on September 19, 2024, under protocol number 00-336 from the Ethics Committee of the University of Novi Sad, Faculty of Medicine Novi Sad, Serbia.

✉ Corresponding author: Marko Stojić, E-mail: marko.stojic@mf.uns.ac.rs

Abbreviations

VM	– vulvar melanoma
MRI	– magnetic resonance imaging
MDT	– multidisciplinary meeting
HPF	– high power field
VMM	– vulvar malignant melanoma
AJCC	– The American Joint Committee on Cancer
FIGO	– The International Federation of Gynecology and Obstetrics
GOG	– The Gynecologic Oncology Group

On clinical examination, the vulva displayed a tumorous lesion with an uneven surface and irregular shape, characterized by exophytic growth in the lower third of the left labia majora and minora. The lesion measured approximately 25 mm and showed hyperpigmentation in certain areas **(Figure 1).** The vaginal vault and walls were smooth, with no evidence of pigmentation.

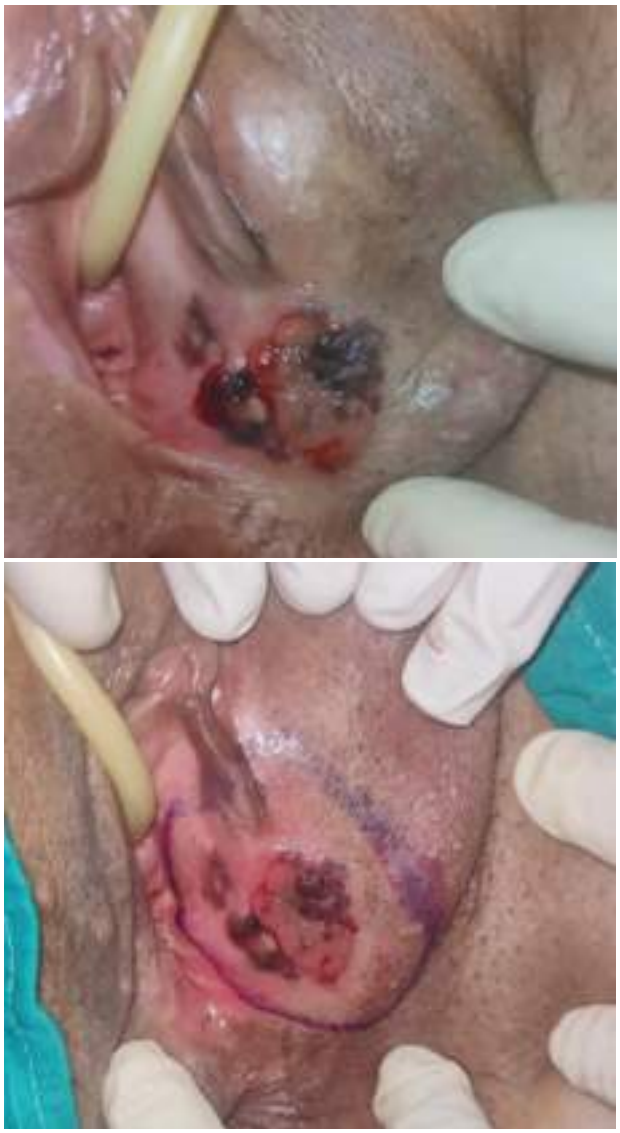

Figure 1. Macroscopic view of the initial vulvar tumor

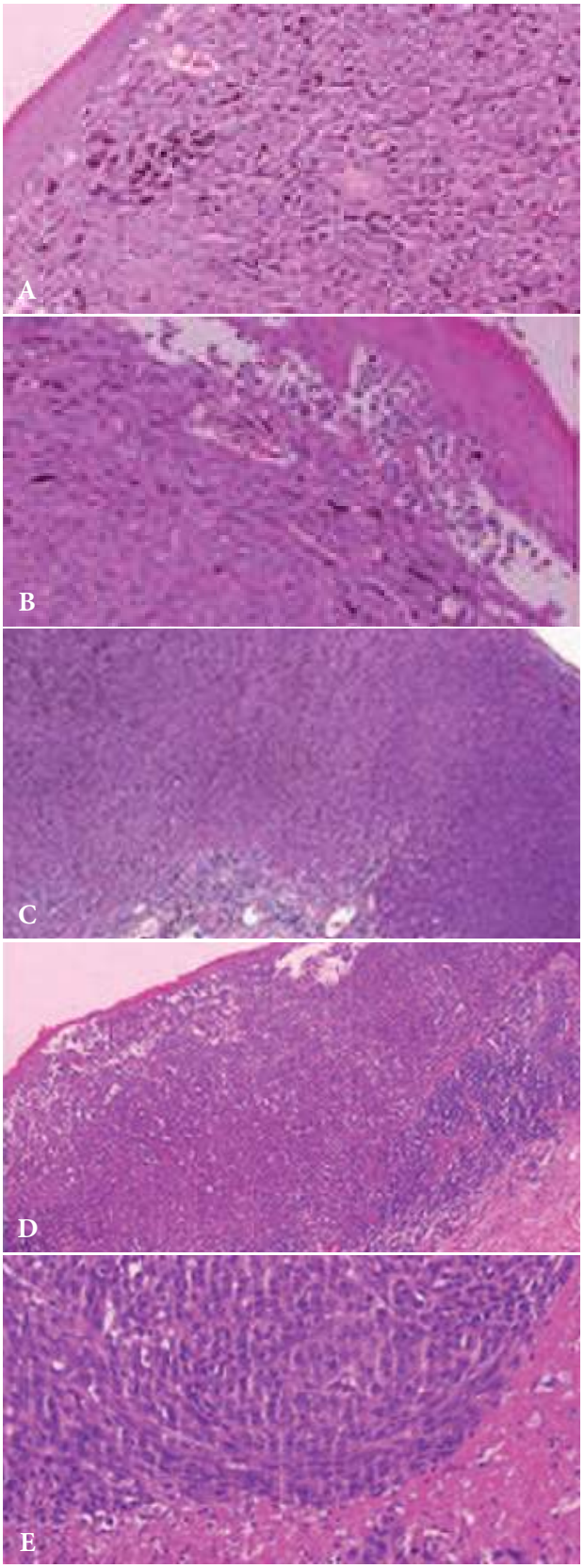

Figure 2. A), B) vulvar malignant melanoma after biopsy, HE, 10x **C), D)** vulvar malignant melanoma (mucosal lentiginous melanoma) after resection, HE, 5x **E)** Vulvar malignant melanoma after resection, HE, 20x.

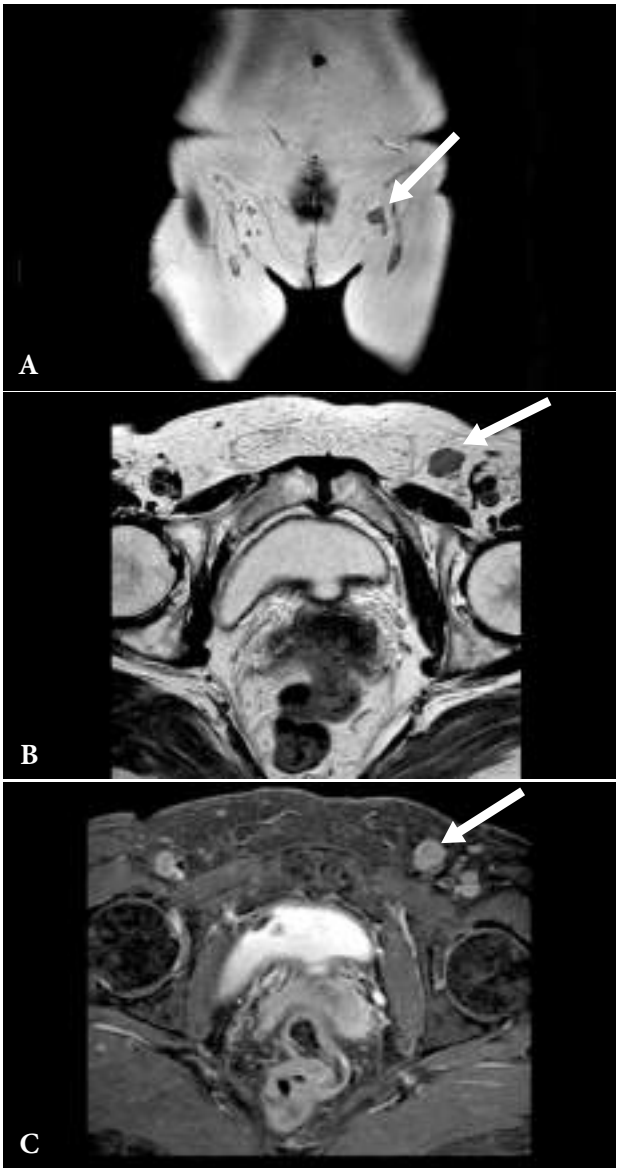

Figure 3. Pelvic MRI showing a suspicious, pathologically altered left inguinal lymph node (marked with arrow) in: A) T2W coronal plane, B) T2W axial plane and C) T2 SPAIR axial plane.

Multifocal biopsy revealed malignant cells infiltrating the left-sided vulvar tissue. These cells were arranged in solid sheets and clusters within the epidermis, dermis, and papillary dermis **(Figure 2).** The tumor consisted of epithelioid to spindled cells, with scattered intracytoplasmic melanin pigment and tumor-infiltrating lymphocytes. No lymphovascular or perineural invasion was observed. Biopsies from the contralateral vulvar side were negative for malignancy.

Pelvic magnetic resonance imaging (MRI) identified a mild enlarged, potentially pathologically altered left inguinal solid lymph node **(Figure 3).**

After a multidisciplinary (MDT) discussion and preoperative planning, the patient underwent a left hemivulvectomy and inguinofemoral lymphadenectomy. Suspicious superficial and deep left inguinal nodes were included in the resection and submitted for histopathological analysis.

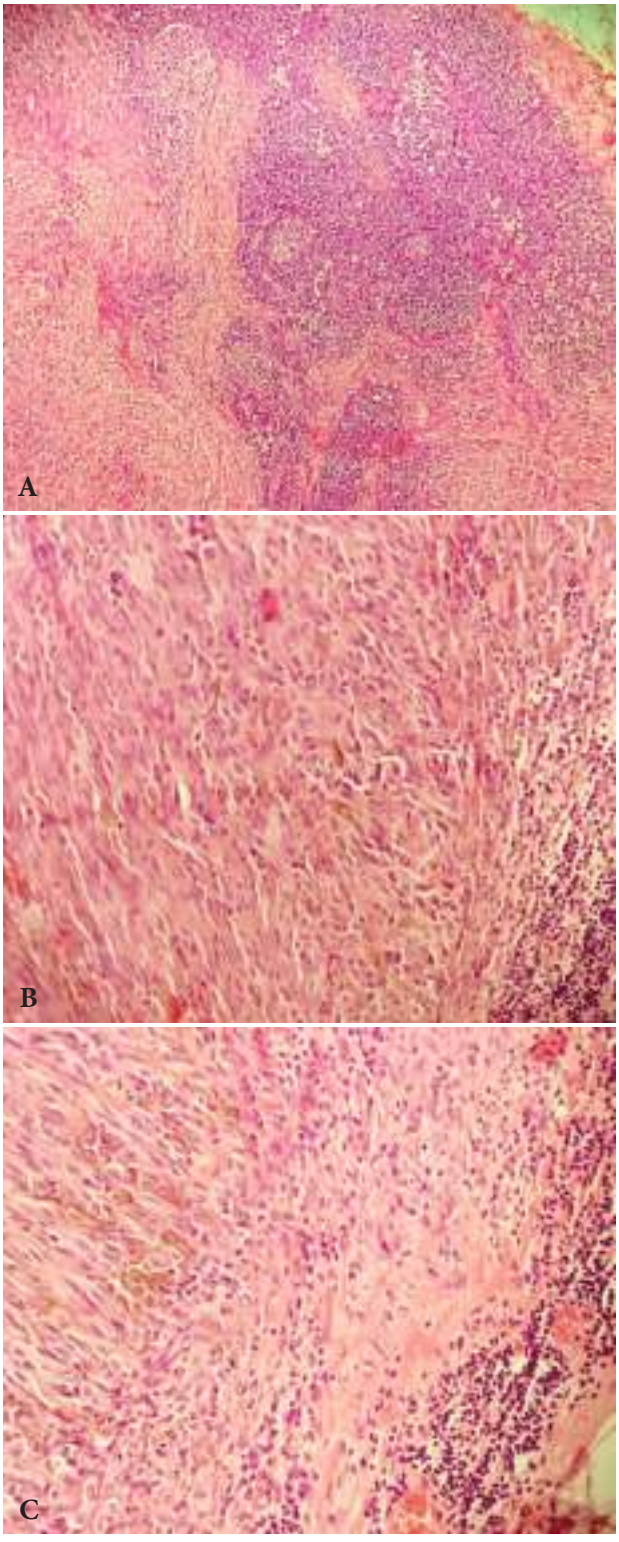

Figure 4. Melanoma metastases in the lymph node, **A)** HE, 5x, **B)** 20x, **C)** 20x

Histopathology revealed a malignant lentiginous tumor extending into the papillary and reticular dermis (Clark Level IV) with epidermal ulceration **(Figure 2).** The tumor exhibited a mitotic index of 13/10 high-power field (HPF) and a Breslow thickness of 1.5 mm. Brisk tumor-infiltrating lymphocytes were noted, but there was no evidence of perineural or lymphovascular invasion. The closest resection margin measured 10 mm. Inguinofemoral lymphadenectomy confirmed metastatic malignant melanoma in 3 of 6 lymph nodes **(Figure 4).** Immunohistochemical analysis showed HMB45+, Melan A+, AE1/AE3-, p40-. The final diagnosis was mucosal lentiginous melanoma, pT2b N2b M0, Stage IIIB.

Within three months of the initial surgery, the patient returned with a 9-mm tumor-like in the lower third of the right labia majora, despite the earlier contralateral biopsy findings being negative. MRI of the pelvis showed no pathological changed in the right inguinofemoral region; thus, lymphadenectomy was not performed. A wide local excision of the vulva was conducted. Histopathological analysis revealed Clark's Level IV involvement, with tumor extension into the reticular dermis **(Figure 5).** The tumor demonstrated a Breslow thickness of 2.5 mm with ulceration but no inguinal lymph node involvement. The mitotic index was 11/10 HPF, and the closest resection margin measured 12 mm. The diagnosis was mucosal nodular melanoma.

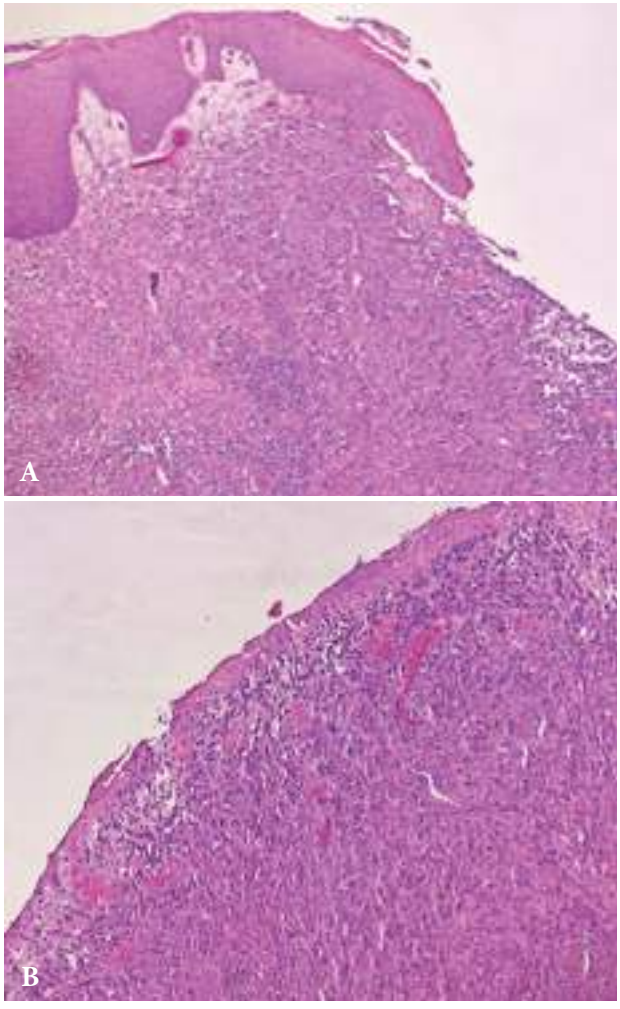

Figure 5. Vulvar malignant melanoma (mucosal nodular melanoma) after resection: **A)** HE, 5x, **B)** HE, 10x.

Further diagnostic examination, including MRI of the endocranium, computerized tomography (CT) of the chest, abdomen, and pelvis, and ultrasound of the neck, axilla, and inguinal regions, revealed no pathological lymph nodes. Testing for the BRAF V600 gene mutation was negative.

Based on the findings, the multidisciplinary tumor board indicated adjuvant immunotherapy with Pembrolizumab (200 mg per cycle, 9 cycles).

Discussion

Melanomas are malignancies originating from melanocytes, with over 90% arising in the skin. The pathophysiology of vulvar melanoma (VM) remains poorly understood; however, it is thought to develop de novo on the vulva, as chronic sun exposure and UV radiation damage are not associated with VM [8]. Chronic dermatoses, such as lichen sclerosus, have been suggested as potential risk factors [9].

The incidence of vulvar malignant melanoma (VMM) compared to cutaneous melanoma is approximately 1:17, and is associated with a high recurrence rate [3, 10]. Vulvar melanoma typically presents in older women, as highlighted in our case [5, 8].

Vulvar melanoma carries a significantly worse prognosis than cutaneous melanoma, with a five-year survival rate of less than 50% [11]. Research indicates that lymph node status and mitotic count play critical roles in determining outcomes [12]. Nagarajan et al. reported that a high mitotic index, as observed in our case, is associated with substantially poorer outcomes compared to a low mitotic index [13].

Although vulvar cancer can manifest with symptoms such as a vulvar lump, discomfort, bleeding, and itching, early-stage vulvar malignancies may present as asymptomatic or oligosymptomatic flat or raised pigmented lesions. A carefully planned biopsy remains the gold standard for diagnosis [3, 5, 7, 12, 14]. In addition to describing the anatomical location, we documented the lesion's position using the clock–face method, noting its distance from the midline and vaginal introitus, as recommended [10].

Differential diagnosis of VMM is often complex due to the overlapping clinical and pathological features of benign and malignant lesions [12, 15].

While advancements in dermoscopy have significantly improved the early diagnosis of cutaneous melanomas, its utility in vulvar melanoma diagnosis requires further validation.

For biopsy-confirmed vulvar melanomas, the American Joint Committee on Cancer (AJCC) staging system is preferred over the International Federation of Gynecology and Obstetrics (FIGO) system, which is used for vulvar squamous cell carcinoma. The Gynecologic Oncology Group (GOG)-73 study demonstrated that AJCC staging provides a more accurate survival prediction, a finding supported by recent population-based analyses [5, 12].

The AJCC 8th edition on melanoma staging and classification uses the Breslow thickness to determine the depth of invasion, providing a critical parameter for tumor staging under the traditional tumor-node-metastasis framework [16]. Although no universally accepted staging system exists for VM, the GOG recommends using the AJCC guidelines rather than FIGO [10].

Histological assessment of melanoma tumors with macroscopic data, and additional clinical diagnostic standards remain essential. While many histological subgroups may be clinically less significant, lentiginous and nodular melanomas – identified in this case – are the most common subtypes and warrant specific attention [17, 18].

Given the advanced stages at presentation, preoperative imaging is critical for surgical planning and delineating disease extent [10, 19]. In this case, pelvic MRI facilitated a comprehensive evaluation of the tumor.

The absence of standardized therapeutic guidelines for VM, coupled with its frequent presentation at metastatic or locally advanced stages, remains a significant challenge. As a result, treatment approaches often mirror those for cutaneous melanoma [18].

Surgical excision remains the cornerstone for vulvar melanoma management [10, 12, 18, 19]. Wide local excision with adequate safety margins is preferred, as radical excision has not demonstrated a significant therapeutic advantage [18, 20, 21].

Consistent with the National Comprehensive Cancer Network and European Society of Medical Oncology guidelines, our surgical margins for the lentiginous tumor with a Breslow thickness of 1.5 mm ranged from 1 to 2 cm. However, for the nodular melanoma with a Breslow thickness of 2.5 mm, we opted for narrower margins to preserve the functional integrity of midline structures, including the anus, urethra, and clitoris [1, 22, 23].

Conclusion

Vulvar melanoma is a rare and aggressive malignancy with a high recurrence rate and poor overall prognosis. It predominantly affects women in latter decades of life. Biopsy remains the gold standard for accurate diagnosis given the overlapping features of benign and malignant tumors. Prognosis is largely determined by lymph node involvement and mitotic count. Surgical excision remains the primary treatment, offering effective local disease control and improving quality of life by minimizing morbidity.

References

1. Pantelić M, Baturan B, Stojić M, Mladenović Segedi Lj, Panjković M, Krsman A. Vulvar cancer in young woman-case report. Eur J Gynaecol Oncol. 2024;45(5):193-6.

2. Pantelić M, Đurđević S, Nikolić D, Maksimović M. Surgical treatment of invasive vulvar cancer. Med Pregl. 2012;65(3-4):97-101.

3. ul Ain Q, Rao B. A rare case report: malignant vulvar melanoma. Indian J Gynecol Oncol. 2020;18:23.

4. Sánchez-Prieto M, Fargas F, Tresserra F, González-Cao M, Baulies S, Fábregas R. Surgical management of vulvar melanoma: a case series. Case Rep Oncol. 2021;14(2):1144-51.

5. Wohlmuth C, Wohlmuth-Wieser I, May T, Vicus D, Gien LT, Laframboise S. Malignant melanoma of the vulva and vagina: a US population-based study of 1863 patients. Am J Clin Dermatol. 2020;21(2):285-95.

6. Olawaiye AB, Cuello MA, Rogers LJ. Cancer of the vulva: 2021 update. Int J Gynecol Obstet. 2021;155 (Suppl 1):7-18.

7. Khaba MC, Lekala ML, Mosehle SD. Malignant nodular melanoma of the vulva: a rare and aggressive tumour of the female genital tract (case report). Pan Afr Med J. 2021;38:115.

8. Boer FL, Ten Eikelder MLG, Kapiteijn EH, Creutzberg CL, Galaal K, van Poelgeest MIE. Vulvar malignant melanoma: pathogenesis, clinical behaviour and management: review of the literature. Cancer Treat Rev. 2019;73:91-103.

9. Hieta N, Kurki S, Rintala M, Söderlund J, Hietanen S, Orte K. Association of vulvar melanoma with lichen sclerosus. Acta Derm Venereol. 2019;99(3):339-40.

10. Wohlmuth C, Wohlmuth-Wieser I. Vulvar malignancies: an interdisciplinary perspective. J Dtsch Dermatol Ges. 2019;17 (12):1257-76.

11. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70(1):7-30.

12. Wohlmuth C, Wohlmuth-Wieser I. Vulvar melanoma: molecular characteristics, diagnosis, surgical management, and medical treatment. Am J Clin Dermatol. 2021;22(5):639-51.

13. Nagarajan P, Curry JL, Ning J, Piao J, Torres-Cabala CA, Aung PP, et al. Tumor thickness and mitotic rate robustly predict melanoma-specific survival in patients with primary vulvar melanoma: a retrospective review of 100 cases. Clin Cancer Res. 2017;23(8):2093-104.

14. Wölber L, Prieske K, Mendling W, Schmalfeldt B, Tietz HJ, Jaeger A. Vulvar pruritus-causes, diagnosis and therapeutic approach. Dtsch Arztebl Int. 2020;116(8):126-33.

15. Vaccari S, Barisani A, Salvini C, Pirola S, Preti EP, Pennacchioli E, et al. Thin vulvar melanoma: a challenging diagnosis: dermoscopic features of a case series. Clin Exp Dermatol. 2020; 45(2):187-93.

16. Keung EZ, Gershenwald JE. The eighth edition American Joint Committee on Cancer (AJCC) melanoma staging system: implications for melanoma treatment and care. Expert Rev Anticancer Ther. 2018;18(8):775-84.

17. Gershenwald J, et al. Melanoma of the skin. In: Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, et al, editors. AJCC cancer staging manual. 8th ed. New York: Springer; 2017. p. 563-88.

18. Dobrică EC, Vâjâitu C, Condrat CE, Crețoiu D, Popa I, Gaspar BS, et al. Vulvar and vaginal melanomas-the darker shades of gynecological cancers. Biomedicines. 2021;9(7):758.

19. Hashim M, Yayanto NH, Muda Abdullah BZ, Ramly F, Abd Rashid R, Duski DR. Vulvar malignant melanoma: a case report and review of its management. Dermatol Reports. 2022;14(4):9345.

20. Sinasac SE, Petrella TM, Rouzbahman M, Sade S, Ghazarian D, Vicus D. Melanoma of the vulva and vagina: surgical management and outcomes based on a clinicopathologic review of 68 cases. J Obstet Gynaecol Can. 2019;41(6):762-71.

21. Yuan GW, Li XG, Li N, Yao HW, Wu LY. Analysis of treatment and prognosis of 59 cases of vulvar melanoma. Zhonghua Fu Chan Ke Za Zhi. 2020;55(6):395-401.

22. NCCN. NCCN clinical practice guidelines in oncology: cutaneous melanoma. Version 4 [Internet]. 2020 [cited 2020 Dec 7]. Available from: http://medi-guide.meditool.cn/ymtpdf/ACC90A18-6CDF-9443-BF3F-E29394D495E8.pdf

23. Michielin O, van Akkooi ACJ, Ascierto PA, Dummer R, Keilholz U. Cutaneous melanoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2019; 30(12):1884-901.

Rad je primljen 25. XI 2024.
Recenziran 19. XII 2024.
Prihvaćen za štampu 26. XI 2024.
BIBLID.0025-8105:(2024):LXXVII:9-12:338-343.