Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Case Report

A Diagnostic Conundrum: Amelanotic Vulvar Malignant Melanoma in a Postmenopausal Patient

Vaishali Bhankhodia[1], Gyanendra Singh[1], Tarang Patel[1], *Parth Goswami[1].

[1]Department of Pathology, AIIMS Rajkot, India

Abstract

Amelanotic vulvar malignant melanoma is an exceedingly rare and aggressive malignancy, accounting for only 2% of vulvar melanomas and presenting unique diagnostic challenges due to its lack of pigmentation. This report discusses the case of a 57-year-old postmenopausal woman who presented with a 2x2 cm greyish-white growth on the labia majora, accompanied by itching and burning for three months. Clinical examinations and routine investigations were inconclusive, necessitating a biopsy for definitive diagnosis. Histopathological analysis revealed nests of atypical cells exhibiting high-grade features, including a high nuclear-to-cytoplasmic ratio, vesicular chromatin, prominent eosinophilic nucleoli, and mitotic activity. The absence of melanin pigment complicated the diagnosis, requiring immunohistochemical confirmation with markers such as S100, Melan-A, and HMB45. Differential diagnoses, including poorly differentiated squamous cell carcinoma, neuroendocrine tumor, and adenocarcinoma, were meticulously excluded through morphological and immunohistochemical evaluation. This case underscores the critical importance of histopathological examination and immunohistochemistry in accurately diagnosing vulvar lesions, particularly in amelanotic variants, where clinical presentation can mimic other malignancies. Given the high metastatic potential and poor prognosis of vulvar melanoma, early recognition, accurate diagnosis, and prompt surgical intervention, including wide local excision and lymphatic dissection, are essential. This case highlights the need for heightened clinical suspicion and a multidisciplinary approach in managing rare vulvar malignancies to optimize patient outcomes.

Keywords: Amelanotic; Vulvar; Malignant Melanoma, Postmenopausal Patient.

***Correspondence:** Dr. Parth Goswami. [1]Department of Pathology, AIIMS Rajkot, India. **E-mail:** goswamiparth42@gmail.com

How to cite: Bhankhodia V, Singh G, Patel T, Goswami P. Diagnostic Conundrum: Amelanotic Vulvar Malignant Melanoma in a Postmenopausal Patient. Niger Med J 2025; 66 (4):1667-1671.https://doi.org/10.71480/nmj.v66i4.777.

Quick Response Code:

Introduction

Melanocytes are situated in the stratum Basale of the epithelium and derive from the neural crest. Melanin-containing melanocytes are also present at mucosal locations devoid of apparent melanin pigmentation. Malignant melanoma is a neoplasm of melanocytes. Melanoma is an exceedingly aggressive neoplasm characterized by a high metastatic propensity. Primary malignant melanomas (MMs) of the female vaginal tract are infrequent, accounting for 3% to 7% of all mucosal melanomas.[1] Vulvar malignant melanoma is an exceedingly rare tumor, constituting 1% of all melanomas in women and 5% of all vulvar malignancies. Amelanotic melanomas constitute merely 2% of all vulvar malignant melanomas. [2] Vulvar melanoma can arise from preexisting junctional or compound nevi, as well as de novo from melanocytes located in the basal layer of squamous epithelium. [3]

The pathophysiology of vulvar melanoma is inadequately comprehended, with some asserting that it is indirectly associated with continuous sun exposure. Ultraviolet lights induce modifications in the cell-mediated immune response and contribute to vulvar cancer. Vulvar melanoma predominantly affects postmenopausal women, although a limited number of occurrences in children have also been documented. The vulva, specifically the labia majora, labia minora, and clitoris, is a common location for melanoma. Early identification of lesions is challenging due to nonspecific signs and symptoms, and vulvar lesions are not readily observable during routine examinations. Vulvar malignant melanoma is linked to a worse outcome. The documented five-year survival rates are below 60% [4].

Due to the overlapping clinical symptoms and diverse physical appearance of lesions, histological evaluation of vulvar lesions remains essential for diagnostic confirmation.

Case Report

A 57-year-old postmenopausal female presented to the gynaecology outpatient clinic with complaints of a growth in the vulvar region, accompanied by itching and burning for three months. The growth was approximately 2x2 cm, exhibited an irregular outline, was greyish white in colour, and had a hard consistency on the inner side of the Labia Majora. She had neither a familial history nor a personal history of cancer. She had no additional medical history. Her blood tests and urine analyses were within normal limits.

A biopsy was obtained from the vulval growth under local anaesthesia and sent to the laboratory for histological analysis. There were two pieces of greyish-white tissue, one measuring 2x1x1 cm and the other 1.5x1x1 cm. The Histopathology Laboratory treated the tissue sample and then produced a paraffin block. The section was sectioned with a microtome, and a microscopic slide was prepared using Hematoxylin and Eosin staining. Histopathological investigation revealed cellular nests, organized in groups separated by thin fibrous septa. Individual cells exhibit characteristics of high-grade atypia, including a high nuclear-to-cytoplasmic ratio, vesicular chromatin, large eosinophilic nucleoli, and mild cytoplasm, accompanied by necrosis and mitotic activity. Pigment was absent. The diagnosis has been established. (Figure 1 and 2) Poorly differentiated malignancy-amelanotic malignant melanoma verified by immunohistochemistry. Immunohistochemistry demonstrated positivity for S100, MelanA, and HMB45.

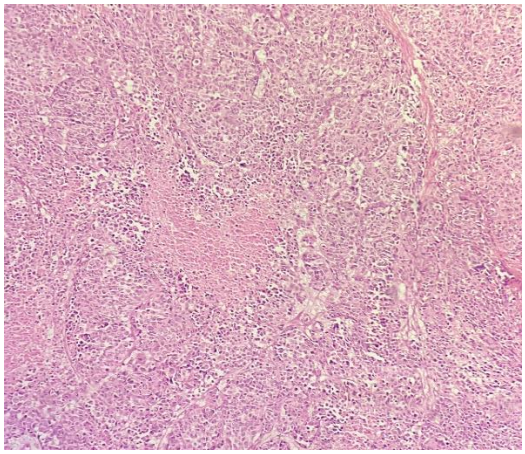

Figure 1: Photomicrograph of Vulval melanoma (10x, H&E stain)

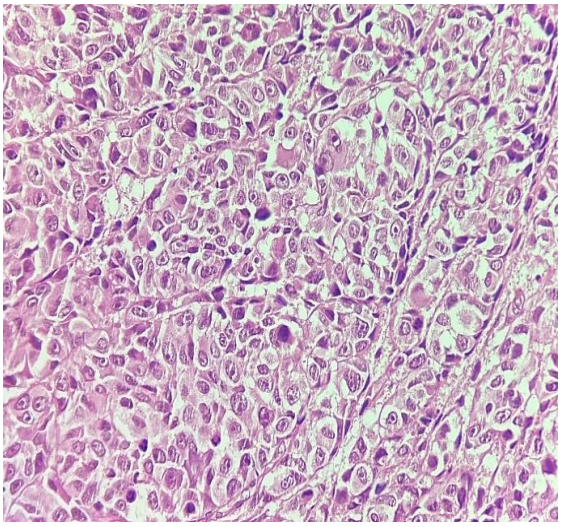

Figure 2: Photomicrograph of Vulval melanoma (40x, H&E stain)

Discussion

Incidence of Vulval melanoma is very rare with poor prognosis. Vulval melanoma known to affect mainly postmenopausal women between the ages of 60 and 80 [5,6] which is in concordance with our case report. Clinically, Vulval Malignancy may remain oligosymptomatic or asymptomatic flat or raised pigmented or non-pigmented lesions during early disease stages [7], sign and symptoms like bleeding, ulceration, itching, pain are seen in advanced stage. Clinical diagnosis is difficult due to vague clinical manifestation. So, histopathological examination is necessary for definitive diagnosis. The "ABCDE" rule may aid as a simple guide for a first assessment of pigmented lesions: "A" stands for asymmetry, and most melanomas are asymmetrical; "B" stands for border as melanomas typically exhibit an irregular border, while nevi typically have a smoother border. "C" stands for colour. While benign moles are often unicolor brown, multiple colours including different shades of brown, black, blue, white, or red are typically a sign for malignancy. "D" stands for diameter and lesions greater than 6 mm should raise awareness. "E" stands for elevation or evolving and any change of shape, size, structure, colour, or symptoms is a potential indicator for malignancy [8].

There are three histological subtypes of melanoma like superficial spreading melanoma, nodular melanoma and acral lentiginous melanoma. but it does not have any prognostic significance. Vulval Melanoma is ranked second after vulval Squamous cell carcinoma accounting for 90% of vulval malignancy. It is easy to diagnose vulval melanoma if the melanin is seen grossly and microscopically. But a Lack of the melanin pigment, as seen in the case of amelanotic melanoma, creates diagnostic confusion as carcinoma. Amelanocytic vulvar carcinoma also shows histopathological diagnostic challenges due to the lack of pigmentation. Close differentials like Poorly differentiated Squamous cell carcinoma, Neuroendocrine tumor, poorly differentiated adenocarcinoma and Paget's disease are considered and definitive diagnosis must be done after ruled out other diagnosis histologically. In some cases, immunohistochemistry is required for definitive diagnosis.

The diagnosis of Poorly differentiated SCC was ruled out, as in SCC histology showing irregular strands and cords of atypical squamous cells within the stroma with Keratin Pearl formation. Prominent eosinophilic nucleoli are not seen in SCC. In distinguishing amelanotic melanoma (AM) from squamous cell carcinoma (SCC), histopathological features and immunohistochemistry play a critical role due to overlapping morphological characteristics. While AM lacks pigmentation and may mimic poorly differentiated SCC, the presence of melanocytic markers such as S100, Melan-A, and SOX10 confirm its diagnosis. Conversely, SCC demonstrates keratinocyte differentiation, invasion of stroma by malignant squamous cells with keratin pearls and is positive for epithelial markers like pan-cytokeratin.[9]

The second differential diagnosis is neuroendocrine tumor, in which the cells exhibit uniform, small to intermediate-sized cells with round nuclei, finely stippled chromatin, and scant cytoplasm, often arranged in nests or trabeculae. In contrast, amelanotic melanoma shows atypical, pleomorphic cells with prominent nucleoli, variable cytoplasm, and occasional multinucleation, often lacking melanin pigment. NETs are characterized by neuroendocrine differentiation on histology, while melanomas demonstrate features suggestive of melanocytic origin.[10]

In Adenocarcinoma, Tumor cells are arranged in glandular pattern with features of anaplasia and Eosinophilic prominent nucleoli are not seen in adenocarcinoma, so diagnosis of adenocarcinoma was also rule out.[11]

It is very important to make definitive diagnosis malignant melanoma as patient with very small vulval lesion can have high chances of recurrence and widespread metastasis. So even small vulval lesions are excised widely and lymphatic dissection also done.

Conclusion

This case highlights the diagnostic and clinical challenges of amelanotic vulvar malignant melanoma, a rare and aggressive malignancy with poor prognosis. The absence of melanin pigment complicates differentiation from other poorly differentiated malignancies, necessitating histopathology and immunohistochemistry for definitive diagnosis. Early recognition and prompt surgical intervention, including wide local excision and lymph node dissection, are vital due to the high risk of recurrence and metastasis, even in small lesions. This case underscores the critical need for vigilance and comprehensive evaluation of vulvar lesions to improve patient outcomes.

References

1. Piura B. Management of primary melanoma of the female urogenital tract. Lancet Oncol 2008; 9:973–81.
2. 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; 21:285–95.
3. Flavia B, Silvia C, Elena L, Amelanotic vulvar melanoma: case report and review of the literature, Romanian Journal of Morphology and Embryology 2008, 49(2):219–228.
4. Hou J, Baptiste C, Hombalegowda R, Tergas A, Feldman R, Jones NL, et al. Vulvar and vaginal melanoma: A unique subclass of mucosal melanoma based on a comprehensive molecular analysis of 51 cases compared with 2253 cases of nongynecologic melanoma. Cancer. 2017 Apr 15;123(8):1333-1344. doi: 10.1002/cncr.30473.
5. Huang Q, Huang H, Wan T, Deng T, Liu J. Clinical outcome of 31 patients with primary malignant melanoma of the vagina. J Gynecol Oncol. 2013 Oct;24(4):330-5. doi: 10.3802/jgo.2013.24.4.330.
6. Mihajlovic M, Vlajkovic S, Jovanovic P, Stefanovic V. Primary mucosal melanomas: a comprehensive review. Int J Clin Exp Pathol. 2012;5(8):739-53.
7. Verschraegen CF, Benjapibal M, Supakarapongkul W, Levy LB, Ross M, Atkinson EN, et al. Vulvar melanoma at the M. D. Anderson Cancer Center: 25 years later. Int J Gynecol Cancer. 2001; 11:359–64.
8. Liu W, Hill D, Gibbs AF, Tempany M, Howe C, Borland R, et al. What features do patients notice that help to distinguish between benign pigmented lesions and melanomas? The ABCD(E) rule versus the seven-point checklist. Melanoma Res. 2005; 15:549–54.
9. Rakislova N, Carreras-Dieguez N, Manzotti C, Saúde O, Del Pino M, Chulo L et al. Differential etiopathogenic features of vulvar squamous cell carcinomas in sub-Saharan Africa and Europe. Int J Cancer. 2023 Feb 1;152(3):496-503. doi: 10.1002/ijc.34314.
10. Al-Janabi S, Kasius JC, Jaspars EH, Snijders MLH. Primary Cutaneous Neuroendocrine Tumor of the Vulva: A Case Report. Int J Gynecol Pathol. 2023 May 1;42(3):278-281. doi: 10.1097/PGP.0000000000000919.
11. Kojima N, Yoshida H, Uehara T, Ushigusa T, Asami Y, Shiraishi K, Kato T. Primary Clear Cell Adenocarcinoma of the Vulva: A Case Study With Mutation Analysis and Literature Review. Int J Surg Pathol. 2019 Oct;27(7):792-797. doi: 10.1177/1066896919848823.