HJOG An Obstetrics and Gynecology International Journal

Case Report

HJOG 2023, 22 (2), 83-87 | DOI: 10.33574/HJOG.0528

Primary malignant melanoma of the vagina: A case report and a mini review

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Abstract

Primary vaginal melanoma is a rare and aggressive entity affecting the vaginal wall without any involvement of the uterine cervix or the vulva. It usually occurs in elderly women. We hereby present an 87-year-old woman who presented with recurrent vaginal bleeding. Vaginal examination revealed a 3cm hyperpigmented lesion on the anterior vaginal wall. The lesion was biopsied and the results of the histopathological examination were compatible with primary malignant vaginal melanoma. The diagnosis of vaginal melanoma is usually established by histology and immunochemistry. The therapeutic management includes surgical and nonsurgical modalities. Although surgery combined with adjuvant radiotherapy or chemotherapy are acceptable therapeutic approaches, further studies are needed in order to assess the optimal management of women with primary vaginal melanoma.

Key words: Melanoma, Malignant, Rrimary vaginal melanoma, Diagnosis, Treatment

Introduction

Mucosal melanomas are malignant primary tumors arising from melanocytes located in the mucosal membranes of the respiratory tract, gastrointestinal tract, and genitourinary tract.[1] Mucosal melanomas represent 1% of melanoma cases.[2] Malignant melanoma of the female genital tract has rarely been reported. The vagina and the vulva are the most common affected sites of the female genital tract.[3] Vaginal melanomas account for fewer than 3% of all vaginal carcinomas and constitute 0.3% of all malignant melanomas.[4] We hereby present a rare case of a woman with primary malignant melanoma of the vagina and also discuss the associated cases reported so far.

Case report

An 87-year-old woman presented to the gynecological outpatient department with a history of occasional vaginal bleeding for the past two weeks. According to her gynecological history, a total ab-

dominal hysterectomy with adnexal preservation was performed 45 years ago due to symptomatic uterine fibroids. The patient had no routine follow up visits to hey gynecologist since then. She also had a medical history of well-controlled arterial hypertension.

On vaginal examination, a 3 cm hyperpigmented lesion was detected on the anterior vaginal wall which bled easily during palpation (Figure 1).

A transvaginal ultrasound revealed no other pathology. A cytologic sample and a biopsy were taken from the lesion and send for examination. The cytology smear showed clusters of tumor cells with most cells showing rominent macronucleoli. Scattered bi and multinucleated tumor cells and presence of intracytoplasmic melanin pigments were also noted (Figure 2).

Histopathological examination revealed pleomorphic malignant cells with hyperchromatic nuclei, intranuclear inclusions, abundant eosinophilic cytoplasm and a high mitotic figure rate. The results were compatible with primary malignant melanoma of the vagina while positive immunohistochemical staining for CKAE1/AE3, HMB4, S-100, Melan-A, CK5/6, p63 confirmed the diagnosis.

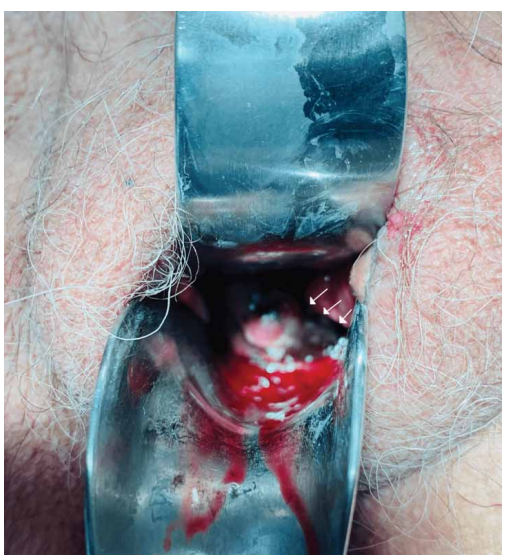

Figure 1. Speculum examination showing the pigmented friable lesion(white arrows) in the anterior vaginal wall.

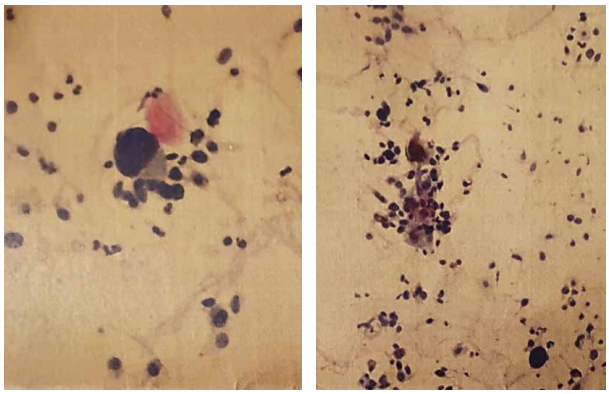

Figure 2. Pap smears showing clusters of malignant cells with melanin pigments in some cells (Pap x400).

A Computerized Tomography (CT) of the brain and abdomen scan was performed on the patient did not demonstrate any signs of local spread, lymphadenopathy or distant metastasis.

After a detailed discussion with the patient regarding the treatment options, she and her family opted for a more conservative management; hence radiotherapy was recommended. The patient received external pelvic radiotherapy and six months after the diagnosis a telephone follow-up took place. We were informed that patient was asymptomatic and there was no evidence of recurrence or metastasis.

Discussion

Primary malignant vaginal melanoma is a rare and aggressive entity, detected in the vaginal wall without involvement of the cervix or the vulva. Vaginal melanoma is originated from melanocytes occurring in the basal membrane of the vaginal epithelium.[5]

Primary vaginal melanoma is often diagnosed in elderly women during the 6th or 7th decade of their life, usually at an advanced stage (50% lymph node infiltration and 20% distant metastasis) and is characterized by early recurrence and a poor prognosis

(5-year overall survival rate between 5%-25%).[6-7]

Similar to our case, the most common location of vaginal melanomas is the anterior vaginal wall. Frequently reported symptoms include abnormal vaginal bleeding, palpable mass, pain, discharge from the vagina and less commonly dysuria or ulceration.[4,8] Vaginal melanomas may appear as nodular or polypoid with black, blue or brown appearance. However, amelanotic tumors have been also reported.[4,9] The mass detected in our patient was a 3 cm nodular friable dark blue tumor affecting the anterior vaginal wall.

Diagnosing malignant melanoma by cytological evaluation is difficult, since melanoma is a great mimicker and can present with a variety of cytological features.[10] Thus, the diagnosis of vaginal melanoma is usually established by histology and immunohistochemistry.[3] Histologically, the cells of a mucosal melanoma may be epithelioid, spindle-shaped or both types.[9] Positive immunohistochemical staining of protein S-100, melan A, human melanoma black 45 (HMB-45) and vimentin (3, 18, 19) confirm the diagnosis of primary melanoma, while negative testing for chromogranin, cytokeratin, estrogen and progesterone receptors assists in the differential diagnosis from other vaginal tumors.[11] In our case, immunohistochemistry with double staining verified the histological features of melanoma, since melanocytic markers of protein S-100, melan A, HMB-45 combined with epithelial makers AE1/AE3, CK5/6 and p63 were performed.

Pretreatment staging procedures include thoracic-abdominal-pelvic computerized tomography (CT), positron-emission tomography – CT scan and X-ray, although of relatively limited value.[12] However, magnetic resonance imaging can differentiate melanoma from other vaginal tumors due to specific signal patterns of melanin; in particular high signal on T1-weighted images and low signal on T2-weighted images.[13]

Molecular characteristics of primary vaginal melanoma may include mutations in B-Raf proto-oncogene, serine/threonine kinase (BRAF), N-rat sarcoma virus proto-oncogene (NRAS), and mast/stem cell growth factor receptor CD117 (c-KIT) genes.[14] Hence, genetic testing should be offered during initial diagnosis in order to exclude mutations in c-KIT, BRAF and NRAS.[15] In patients with vaginal melanoma and mutation in the above-mentioned genes, targeted therapy against these mutations can also be beneficial.[14]

The aggressiveness of the vaginal melanoma is due to rapid local spread or relapse, lymph node infiltration, distant metastasis and excessive bleeding.[3] Vascular and lymphatic supply of the vaginal epithelium is extensive and therefore facilitates the invasion of surrounding tissues and distant spread.[16] Lungs, liver, bones, and brain are the most common sites of metastasis.[3] A comparative study by Seifried et al. concluded that cutaneous melanoma staging system by the American Joint Committee on Cancer (7th edition) can be also utilized for vaginal melanomas, but there is no consensus to date regarding the optimal staging method.[17] Tumor size (<3cm) is considered the only prognostic factor in cases of primary vaginal melanoma.[18]

Therapeutic management of vaginal melanoma includes surgical and nonsurgical modalities. Surgical modalities vary from conservative (wide local excision) to radical (vaginectomy or pelvic exenteration).[9] Surgery combined with adjuvant radiotherapy, adjuvant immunotherapy with interferon alpha-2b, or adjuvant chemotherapy are considered acceptable combined therapeutic approaches.[19] The treatment option decided by our patient and her family was that of radiotherapy alone. Chemotherapy with dacarbazine (dimethyl-triazeno imidazole-carboxamide; DTIC) as monotherapy or in combination with surgery, radiotherapy or immunotherapy is considered a viable option in relapsed patients.[19] Monoclonal

antibody-targeted therapy has been also used for vaginal melanoma extending survival and decreasing the possibility of a recurrence.[15]

Conclusion

Primary melanoma of the vagina is a rare but aggressive malignancy with a poor prognosis. Raising the index of suspicion in elderly patients with pigmented friable vaginal lesions may assists timely diagnosis. There is no consensus yet regarding the optimal management of women with primary vaginal melanoma, therefore further randomized clinical trials are needed in order to compare the outcomes of different therapeutic approaches.

Competing interests

The authors declare no competing interest.

Authors' contributions

KZ, E-AE and KB wrote the first draft. OK and AD critically reviewed and amended the draft. All authors read and approved the final version of the manuscript.

References

1. Goldemberg DC, Thuler LCS, de Melo AC. An Update on Mucosal Melanoma: Future Directions. Acta Dermatovenerol Croat. 2019;27(1):11-15.
2. Ballester Sánchez R, de Unamuno Bustos B, Navarro Mira M, Botella Estrada R. Mucosal melanoma: an update. Actas Dermosifiliogr. 2015;106(2):96-103. doi:10.1016/j.ad.2014.04.012
3. Puri S, Asotra S. Primary vaginal malignant melanoma: A rare entity with review of literature. J Cancer Res Ther. 2019;15(6):1392-1394. doi:10.4103/jcrt.JCRT_893_15
4. Kalampokas E, Kalampokas T, Damaskos C. Primary Vaginal Melanoma, A Rare and Aggressive Entity. A Case Report and Review of the Literature. In Vivo. 2017;31(1):133-139. doi:10.21873/invivo.11036
5. Gupta D, Malpica A, Deavers MT, Silva EG. Vaginal melanoma: a clinicopathologic and immunohistochemical study of 26 cases. Am J Surg Pathol. 2002;26(11):1450-1457. doi:10.1097/00000478-200211000-00007
6. Kühn F, Dieterich M, Klar E, Gerber B, Prinz C. Primary Malignant Vaginal Melanoma - Case Report and Review of the Literature. Geburtshilfe Frauenheilkd. 2012;72(8):740-743. doi:10.1055/s-0032-1315006
7. Hu DN, Yu GP, McCormick SA. Population-based incidence of vulvar and vaginal melanoma in various races and ethnic groups with comparisons to other site-specific melanomas. Melanoma Res. 2010;20(2):153-158. doi:10.1097/CMR.0b013e32833684e8
8. Tacastacas JD, Bray J, Cohen YK, et al. Update on primary mucosal melanoma. J Am Acad Dermatol. 2014;71(2):366-375. doi:10.1016/j.jaad.2014.03.031
9. Androutsopoulos G, Terzakis E, Ioannidou G, Tsamandas A, Decavalas G. Vaginal primary malignant melanoma: a rare and aggressive tumor. Case Rep Obstet Gynecol. 2013;2013:137908. doi:10.1155/2013/137908
10. Zin AAM, Nafis NSM. Primary Vaginal Melanoma – Cytohistological Correlates and Literature Reviews. Gynecol Obstet (Sunnyvale) 2015;5:312. doi:10.4172/2161-0932.1000312
11. Chen L, Xiong Y, Wang H, Liang L, Shang H, Yan X. Malignant melanoma of the vagina: A case report and review of the literature. Oncol Lett. 2014;8(4):1585-1588. doi:10.3892/ol.2014.2357
12. Patrick RJ, Fenske NA, Messina JL. Primary mucosal melanoma. J Am Acad Dermatol. 2007;56(5):828-834. doi:10.1016/j.jaad.2006.06.017
13. Lee JH, Yun J, Seo JW, Bae GE, Lee JW, Kim SW.

Primary malignant melanoma of cervix and vagina. Obstet Gynecol Sci. 2016;59(5):415-420. doi:10.5468/ogs.2016.59.5.415

14. Rouzbahman M, Kamel-Reid S, Al Habeeb A, et al. Malignant Melanoma of Vulva and Vagina: A Histomorphological Review and Mutation Analysis--A Single-Center Study. J Low Genit Tract Dis. 2015;19(4):350-353. doi:10.1097/LGT.0000000000000142
15. Leitao MM Jr, Cheng X, Hamilton AL, et al. Gynecologic Cancer InterGroup (GCIG) consensus review for vulvovaginal melanomas. Int J Gynecol Cancer. 2014;24(9 Suppl 3):S117-S122. doi:10.1097/IGC.0000000000000198
16. Androutsopoulos G, Adonakis G, Ravazoula P, Kourounis G. Primary malignant melanoma of the vagina: a case report. Eur J Gynaecol Oncol. 2005;26(6):661-662.
17. Seifried S, Haydu LE, Quinn MJ, Scolyer RA, Stretch JR, Thompson JF. Melanoma of the vulva and vagina: principles of staging and their relevance to management based on a clinicopathologic analysis of 85 cases. Ann Surg Oncol. 2015;22(6):1959-1966. doi:10.1245/s10434-014-4215-3
18. Kühn F, Dieterich M, Klar E, Gerber B, Prinz C. Primary Malignant Vaginal Melanoma - Case Report and Review of the Literature. Geburtshilfe Frauenheilkd. 2012;72(8):740-743. doi:10.1055/s-0032-1315006
19. Rapi V, Dogan A, Schultheis B, Hartmann F, Rezniczek GA, Tempfer CB. Melanoma of the Vagina: Case Report and Systematic Review of the Literature. Anticancer Res. 2017;37(12):6911-6920. doi:10.21873/anticanres.12155

Received 05-05-23
Revised 09-05-23
Accepted 18-05-23