MAR Oncology & Hematology (2023) 3:10

Case Report

Malignant Melanoma of Vagina—A Rare Case Report and Review of Literature

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Received: 12 September 2023

Published: 30 September 2023

Introduction

Gynecologic melanomas have a poor prognosis and a high mortality rate because they don't have any early or distinctive signs and symptoms. Primary gynecologic melanomas have been more common recently.[1] Less than 0.2% of all melanomas are primary vaginal melanoma, an exceptionally rare gynaecological malignancy.[2] 5-year survival rates are reported at less than 30% despite treatment. The first primary malignant vaginal melanoma case was documented in 1887, and as of the present, there have been 500 cases worldwide, according to the literature. No staging system has been demonstrated to be a useful predictor of prognosis in vaginal melanoma. The American Joint Committee on Cancer staging system in vaginal melanoma proposed a standardization system in which they distinguished stages I, II, and III corresponding to clinically localized disease, regional lymph node involvement, and distant metastases, respectively.[3]

Malignant melanomas (MM), mainly derived from the basal layer of melanocytes, occur in the eyes, skin, and mucosal membranes (e.g., respiratory, gastrointestinal, and genitourinary mucosa). Several molecular mechanisms or signalling pathways may be involved in the carcinogenesis of cutaneous and mucosal melanocytes.[4] In 3% of healthy women, basal portions of the vaginal epidermis contain melanocytes, which develop embryologically from neural crest cells. The areas where vaginal melanoma is hypothesized to develop are those where some of these melanocytes are found abnormally in the vaginal mucosa.[5]

This neoplasm usually occurs between the sixth and the seventh decade.[6] The tumour can be amelanotic or present as a dark node or spindle-shaped lesion, and the size of the lesion indicates the prognosis. The tumour is primarily found in the distal one- third (58%) of the vagina and mostly on the anterior wall (45%).

Usually presents as inconstant pigmented plaques, ulcerated or polypoid masses in the anterior wall of the vagina.[7] It is important to note that cervical melanoma typically involves the vagina, so when symptoms are observed it is necessary to determine whether it is a primary vaginal malignant melanoma or not. The most common symptom of vaginal melanoma is bleeding, which can manifest as irregular vaginal bleeding or increased vaginal discharge.[8] Other symptoms include vaginal wall mass, increased discharge, and dyspareunia. As treatment options, there are some standard modalities used individually or in combination, such as conservative wide local excision, radical surgical extirpation, irradiation and chemotherapy. Importantly, it is difficult to stage and treat this condition because there aren't many cases of it, either in clinical practice or in the literature. In this report, we describe a primary vaginal melanoma that we found in a 78- year-old postmenopausal woman.

Case Presentation

A 78year old female, known hypertensive and diabetic presented to us in gynae oncology OPD with complaints of postmenopausal bleeding along with mass per vagina for 1 month. On pelvic examination, a hyperpigmented polypoidal mass of size approximately 2x2cm with irregular margins was seen arising from the anterior and right lateral vaginal wall reaching up to the introitus. (Image1) The vulva, urethra and rest of the perineal area appeared normal. There was no palpable node at physical examination.

On evaluation, the MRI pelvis showed an irregular lobulated lesion measuring approximately 1.3 x 2.4 x 2.0 cm in the lower vagina probably arising from its right lateral and posterior wall. The lesion involved the entire thickness of the vaginal wall? mitotic lesion. No adnexal mass, free fluid or lymphadenopathy was seen in the pelvis. The urinary bladder does not show any focal abnormal wall thickening.

PET-CT scan showed FDG avid heterogeneously enhancing soft tissue density lesion of size 2.2 x 1.7 cm x 2.2 cm at the right lateral wall of the vagina filling the right vaginal fornices and reaching up to the level of vaginal introitus (likely mitotic). The lesion was infiltrating >50% of the right vaginal wall and reaching up to the serosal wall, however, there were no signs of local spread, lymphadenopathy or distant metastases.

After the tumour board meeting patient was planned for a vaginal biopsy which revealed positive for malignant cells likely malignant melanoma. Taking into consideration the imaging results and general condition of the patient the decision for radical surgery for complete resection of the tumour was taken. A total abdominal hysterectomy with bilateral pelvic lymph node dissection with total vaginectomy was done. (Image 2)

Intra-op and post-op period was uneventful and the patient was discharged at post-op day 10 of surgery with a bladder catheter in situ that was removed in subsequent visits. The patient is currently on a follow-up and is planned for adjuvant radiotherapy based on the final histopathological report which revealed malignant melanoma of the vagina (positive for S100, HMB 45, Vim and negative for CK), with no LVSI or PNI. The depth of infiltration was 1cm and the margins were free of tumor. Out of the total of 26 resected pelvic lymph nodes, one right pelvic lymph node was found positive for metastatic deposit.

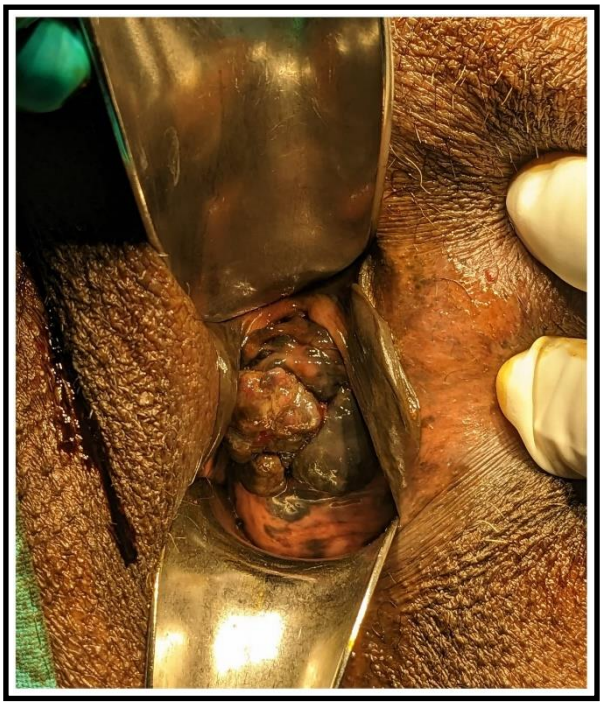

Image 01

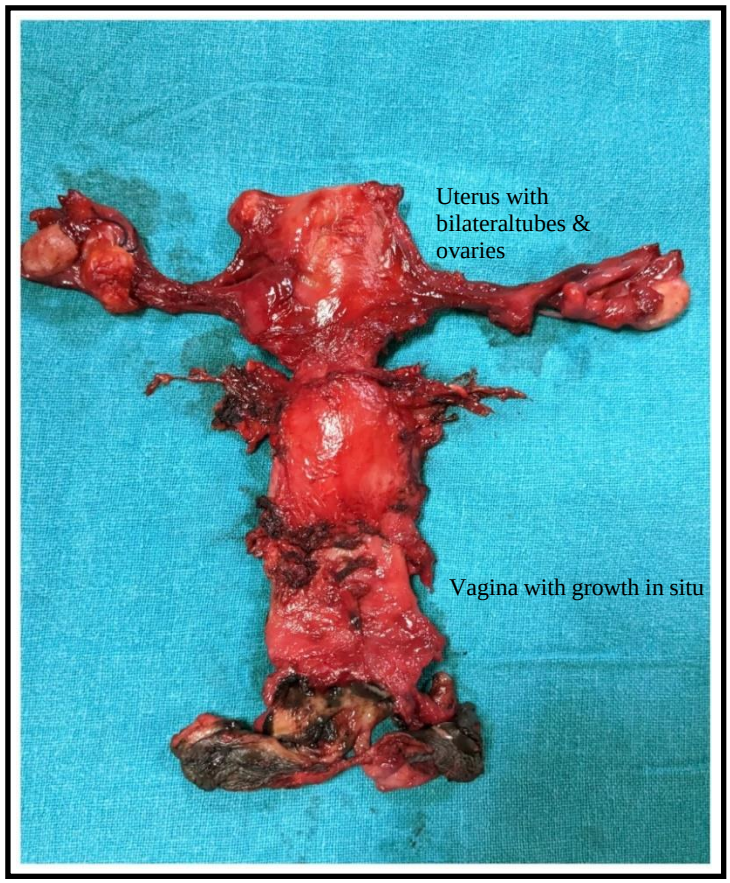

Image 02

Discussion

A review by Leitao et al. found 37 cases of malignant vaginal melanoma during a 29- year period. Similar findings were found in 43 instances in a 17-year investigation by the Gynecologic Oncology Group.**[**9**]** Primary malignant vaginal melanoma is expected to occur in 0.026 per 100,000 and 0.46 per one million women annually, respectively.**[**10**]** The rarity of primary vaginal melanoma prevents accurate characterization of the condition, and as a result, there is still substantial uncertainty regarding our knowledge of and clinical strategy for treating this illness. This is especially true for treatment selection and staging.**[**11**]**

Its aetiology and etiological factors have been proposed to involve interactions be- tween or among genetics, the environment, and even the cellular microenvironment. The pathophysiology and aetiology of primary

malignant vaginal melanoma are unknown at this time. Other varieties of melanomas also fall under this enigma. The ideas also suggest that melanomas with BRAF mutations may spread throughout the body, implicating this gene in causing nevi, or irregularities of the skin, but not enough to result in melanoma. However, primary malignant vaginal melanoma is a mucosal melanoma, and KIT gene alterations rather than BRAF mutations, which are more frequently observed in cutaneous melanomas, are related to mucosal melanomas.**[**12**]**

Visual inspection and histological analysis are combined to make an accurate diagnosis of primary vaginal melanoma. Although changes in the appearance of lesions can lead to misdiagnosis, physical examination alone frequently provides a reasonable degree of suspicion for a vaginal melanoma. For instance, primary melanomas of the vagina are typically detected in the bottom third segment of the anterior vaginal wall, are typically pigmented, bleed freely on touch, and have a polypoid look as was the situation with our patient. However, some case reports indicate that the tumour can also develop in the upper third.**[**13,14**]** Gökaslan et al. reported malignant vaginal melanoma cases presenting lesions on the posterior wall near the vaginal entrance **[**15**]**, while Shah et al. reported the presence of pigmented tumours in the middle and lower thirds of the vagina.**[**16**]**

Despite the fact that the tumour is frequently discovered as a pigmented mass, amelanotic tumours have also been reported in individuals, which frequently results in misdiagnosis and delayed treatment.**[**17**]** As a result, a histological assessment should be done in addition to the clinical evaluation. The histological results in our patient are essentially in line with the characteristics of primary vaginal melanoma that have been documented in the literature. Positive immunohistochemical staining of protein S-100, melan A, human melanoma black 45 (HMB-45), and vimentin are used to identify primary melanoma.**[**18**]** In our case, IHC markers that were positive for S100, HMB 45, and Vim and negative for CK helped to support the histological findings.

The International Federation of Gynecology and Obstetrics (FIGO) guidelines for vaginal cancers were historically used to stage vaginal melanomas as gynaecological cancer; however, evidence in the literature appears to favour the American Joint.

Committee on Cancer (AJCC-TNM) system as a more accurate predictor of prognosis. The AJCC-TNM system also showed a stage-dependent variation in the results. Three stages make up the overall staging system: Stage I, clinically localized disease with no involvement of regional lymph nodes; Stage II, lymph node involvement in the region; and Stage III, distant metastatic disease.

Given that studies have shown that patients who underwent surgery had considerably longer OS, surgery is still the chosen course of treatment for vaginal melanoma. **[**19,20**]** The WLE approach is a common surgical technique for treating tumours in their early stages. Along with pelvic irradiation, WLE is conducted with a safety margin of 1 cm for tumours with a Breslow depth of 2 mm or less and 2 cm for tumours with a Bres- low depth of more than 2 mm. Advanced primary malignant vaginal melanoma is aggressively treated with radical surgery, lymphadenectomy, adjuvant chemotherapy, or radiotherapy.**[**21**]** Reports show that radical surgery can include total hysterectomy, vaginectomy and vulvectomy depending on the location of the tumour (proximal, middle or distal to the vagina).**[**22**]** We performed radical surgery for complete resection of the tumour, and total abdominal hysterectomy with bilateral pelvic lymph node dissection with total vaginectomy.

Radical surgery is an effective alternative either alone or in combination with adjuvant radiotherapy when there are near or positive margins.**[**23**]** The use of SLNB in the treatment of vaginal melanoma is not supported by the data currently available.**[**24**]** Due to the low prevalence of regional lymph node metastases, many studies do not advise individuals without clinical or radiologic evidence of a positive lymph node to have groin and/or pelvic lymphadenectomy. However, in individuals with clinically positive lymph nodes, excision of the groin and/or pelvic lymph nodes can enhance regional control and lower the chance of recurrence.**[**25**]** To minimize the size of the tumour and enable WLE, radiation can be administered as a neoadjuvant prior to surgery. For patients with high-risk criteria including a tumour size higher than 3 cm, positive or unclear surgical margins, and positive groin and/or pelvic lymph nodes, it can also be utilized as a postoperative adjuvant therapy.**[**26**]** Due to the rarity of vaginal melanoma, the function of chemotherapy or biotherapy is un- known.

Conclusion

This review of current literature shows that primary malignant vaginal melanoma is a rare but aggressive melanoma that affects women in their 6th and 7th decade of life. Compared to cutaneous melanomas and other gynaecological malignancies, vaginal melanomas have a worse prognosis. The revised AJCC 2017 staging system is presently used to identify vulvar melanoma, whereas the FIGO 2018 staging system is advised for cervical melanoma. However, there is no staging system available for vaginal mucosal melanoma. For early-stage vaginal melanoma, full excision of the original tumour is the recommended course of action.

If positive lymph nodes are suspected symptomatically or radiologically (e.g., via ultra- sonography, CT, MRI, or PET), groin lymphadenectomy should be taken into consideration. For patients with advanced tumours, as adjuvant therapy for positive margins or histologically positive lymph nodes, or both, radiotherapy may be helpful. More research must be done on female lower genital tract melanomas since they might differ from other melanoma subtypes. New prognostic and predictive indicators must also be found in order to provide better therapy recommendations. Finally, the key to boosting the number of long-term survival will be the development of individualized treatment programs for individuals who do not respond to routine therapy.

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