A Case Series of Rare Vaginal Malignant Melanoma

Soemanadi*, Widyorini Lestari Hutami Hanafi, Veinardi Madjid
Division of Gynecology Oncology, Dharmais Cancer Hospital - National Cancer Center, Jakarta, Indonesia

ARTICLE INFO
Received: 03 August 2023
Reviewed: 14 August 2023
Accepted: 01 September 2023

Keywords:
malignant melanoma, oncology, vaginal melanoma

*Corresponding author:
Soemanadi
Division of Gynecology Oncology, Dharmais Cancer Hospital - National Cancer Center, Jakarta, Indonesia
soemanadi08@gmail.com

ABSTRACT
Introduction: Vaginal melanoma is a rare malignancy. Sadly, melanoma is a very aggressive tumor with a 5-year survival rate of 5%–25%. There is no publication about the incidence of vaginal malignant melanoma in Indonesia. Due to the lack of cases in Indonesia, this study aims to report the challenges and explore the risk factor, treatment, and prognosis of Vaginal Malignant Melanoma.

Case Presentation: This case series report 2 patient with vaginal malignant melanoma who were diagnosed at Dharmais Cancer Center Hospital.

Conclusions: Diagnosis and optimal treatment plans can be established through rapid and precise recognition of Malignant Melanoma to achieve better outcomes.

INTRODUCTION
Primary vaginal malignant melanoma is a rare melanoma that accounts for < 3% of all vaginal malignancies [1–3]. The percentage of malignant melanoma among them is only around 5% [2]. Mucosal melanomas are rare, making up just 1% of all melanomas [1]. Forty percent of all mucosal melanomas are amelanotic compared to < 10% cutaneous amelanotic melanomas. The female genital tract is a rare site of malignant melanoma, and accounts for < 10% of all female genital tract melanomas [3]. The vulva and vagina are the most common sites for malignant melanoma in the female genital tract. The frequency of vaginal melanoma is just 0.46 cases per one million women per year, and there have only been 250 cases described in the literature to date. Vaginal melanoma makes up only 2.4% to 2.8% of all genital tract melanomas in women and 0.3% to 0.8% of all malignant melanomas in women[1–3]. Vaginal melanomas account for fewer than 3% of all melanomas. Vaginal melanoma is extremely rare, with the first case reported in 1887, and a low number of cases worldwide [4].

Vaginal melanoma belongs to a subtype of mucosal melanoma. Typically, mucosal melanoma is aggressive [1,5]. High incidence of recurrence, spread to regional lymph nodes, and distant metastasis is responsible for poor prognosis of Primary vaginal malignant melanoma (PVMM). PVMM has a poor prognosis with a 5-year survival rate of only 5%–25%. PVMM has a worse prognosis than other non-genital melanomas or other vaginal malignant neoplasms. The most common presenting symptoms for vaginal malignant melanoma are vaginal bleeding (60%–100%), vagina discharge, vaginal masses, pain, or discharge are other reported symptoms. 10% of patients will not have any symptoms [1,3].

Vaginal and vulvar melanomas have origins that are typically overlooked by frequent inspection, with the anatomical position of the lesion being the primary cause for its delayed diagnosis and poor prognosis [6]. Contrary to cutaneous melanoma, which is most frequently distributed on photo-exposed areas (face, trunk, lower limbs), it is possible to diagnose it from its early stages [7]. They are pigmented lesions that can vary in size (often over 7 mm), have a macular, papular, or nodular look, are commonly asymmetrical, and have an uneven appearance in terms of pigmentation [6]. In the additional examination, similar to histopathology, the epidermis’ impairment, melanocytes’ pagetoid spread, or melanocytes arranged in nests are examples of the characteristic microscopic aspects [6]. Immunohistochemical staining positive for vimentin, protein S-100, Melan A, and HMB-45 should also be used to confirm the diagnosis [3].

Until now, there has been no clear consensus regarding treatment. An early, accurate diagnosis and prompt investigation are essential in reaching appropriate
treatment decisions. There are both surgical and noninvasive therapy options [7]. Studies have shown that surgery is still the best treatment for vaginal melanoma and that these patients had considerably longer OS [8]. When radical surgery (ranging from vaginectomy to pelvic exenteration) is compared with conservative surgery, there is no significant difference in the clinical outcome [6]. Therefore, the main treatment for vaginal melanoma is local excision with an appropriate surgical margin (1 or 2 cm depending on Breslow thickness). More aggressive treatment should be wisely explored if local excision is not possible or if it is impossible to assess the extent of the tumor. Radical surgery can be used alone or with adjuvant radiation in cases with close or positive margins. Surgery may be combined with radiotherapy or chemotherapy in selected cases [7].

Numerous adjuvant chemotherapy regimens have tried to lower the recurrence incidence in high-risk melanoma, but none of the drugs, including dacarbazine used alone or in combination, showed promise in randomized clinical trials. Interferon alpha, which has become the standard of therapy for patients with resected node-positive cutaneous melanoma, has recently been associated with the most favorable outcomes [7].

Studies investigating vaginal melanoma 5-year survival rates have revealed rates ranging from 13% to 32.3%. The main prognostic factors for vaginal melanoma include the AJCC stage, lymph node status, tumor size, and primary treatment. Particularly, lymph node involvement was associated with a worse prognosis. In another study, patients with negative lymph nodes exhibited a significantly higher median OS than those with positive lymph nodes (30 months versus 7.8 months). Patients in AJCC stage 0-II had significantly better 5-year OS than patients in stage III. In contrast to patients with larger tumors, those with tumors smaller than 3 cm demonstrated a median OS of 41 months as opposed to 12 months [9]. This study aims to describe two vaginal melanoma cases and discussed the therapy options.

CASE PRESENTATION

In our tertiary facility, Dharmais Cancer Center Hospital, Jakarta, we retrospectively describe two cases of vaginal malignant melanoma. These two cases were the patients who have completed workup including imaging modality.

First Case

In January 2021, a 62-year-old woman with stage IVB vaginal cancer came to the gynecological outpatient clinic with her chief complaint having vaginal bleeding. The patient also reported having abdominal pain. There was no whitish, pruritus, or body weight decrement. The patient received a diagnosis of vaginal cancer in December 2019 but chose alternative therapy instead of getting treatment for the next two years. The patient appeared alert, with a normal heart rate of 85 beats per minute, high blood pressure of 130/90 mmHg, breathing rate of 18 breaths per minute, and temperature of 36°C. There was an unremarkable finding on general examination.

A gynecology examination showed a dark red mass on the left anterior vaginal wall adjacent to the cervical, with a diameter of 5 cm, easy to bleed. There were no palpable lymph nodes. Multislice spiral computer tomography (MSCT) Scan abdomen pelvis revealed a vaginal mass, 6.7 x 4.6 cm left para-iliac lymphadenopathy, 1.4 x 4 cm right para-iliac lymphadenopathy, 2.7 cm and 2.3 cm left or right inguinal, and right hydronephrosis were detected by.

Figure 1.
(A) Initial Chest X-ray in February showed only cardiomegaly;
(B) Chest X-ray in September, showed cardiomegaly and nodules lesion in the right lower lung.
We kept the vagina cancer as a clinical diagnosis and performed a biopsy. Based on the cytology and biopsy report, malignant melanoma of the vaginal was established. A dermatoloveneroelogist had consulted about the patient’s condition. This patient planned to receive immunotherapy.

Following the procedure, the patient had 3-cycle BCG immunotherapy (3 x 106 dosage), starting in April 2021 and ending in June 2021. The patient’s condition in June, she complained of irregular, painful urination, cramping in the lower abdomen or groin, and smelly whitening vaginal discharge. Therapy is determined to be ineffective for the condition. As a result, the patient received a regimen of Fluconazole 50 mg, Mefenamic Acid 500 mg, Fucidine cream, and Cefixime 200 m

Two months later, the patient was brought to the emergency department, Dharmais Cancer Hospital, due to an unconscious condition. Her relatives report that she had abdominal pain, weakness, fatigue, problems with eating and drinking, urinary incontinence, and a 3-day history of diarrhea. In July 2021, She tested positive on the nasopharyngeal swab test for severe acute respiratory syndrome coronavirus. A rontgen thorax showed a nodule lesion in the right lower lung (Figure 1). After comparing the results eight months ago, we suspected the patient had a metastatic lesion. We stabilized the patient’s emergency condition. The patient is alert and chooses to discharge.

**Second Case**

In October 2022, a 68-year-old woman went to the urology outpatient clinic with urethral bleeding. A genital exam revealed a mass and blood at the urethral meatus. In September 2022, the patient was diagnosed with malignant melanoma urethra, confirmed by biopsy at another hospital. The general examination of the patient is good overall, and all vital indicators are within normal ranges. Following urethroscopy and cystoscopy procedures in October 2022, a mass in the urethra was found. The tissue was transferred to the pathology lab along with vaginal tissue for additional testing.

Microscopically, the vagina tissue showed a stratified squamous epithelium. Tumor cells that form nests in subepithelial connective tissue are pleomorphic nucleated and hyperchromatic, their daughter nuclei are primarily unstable, and their transparent cytoplasm contains some brownish pigment. Mitosis causes lymphocytes and plasma cells to bulk up in the stroma, which does not cause a tumor embolism in the artery. Then, urethra tissue shows a layer of squamous epithelial tissue that has partially become a tumor mass similar to a tumor in the vagina. Immunohistochemical staining results were positive for S100, MelanA, and HMB45 in the immunoreaction same as malignant melanoma in the vagina and urethra. Then, the patient was diagnosed with Malignant Melanoma of the urethral and vagina.

Gynecologist was consulted due to positive immunohistochemistry around the vagina tissue. On the general examination, there were no remarkable findings. In November 2022, a gynecological examination showed no masses in the anterior vagina or vulva, but a residual was visible on the catheter. The cervical portio surface was smooth, the vulva looked normal, and there were no shown anomalies in that area. One month later, a gynecological examination showed a vulva with multiple hyperpigmented thin plaques, densely lenticular. Speculum examination revealed the melanoma had advanced to the cervix from the urethra, vagina, and vulva.

This patient had advanced melanoma, according to the gynecological examination. On December 20, 2022, a pelvic MRI revealed a 0,7 cm diameter left para-iliac lymphadenopathy with no pathogenic intensity. The Rontgen thorax and abdomen MSCT (Multislice Computerized Tomography) scans revealed no apparent abnormalities. The multidisciplinary team (MDT) in oncology at Dharmais Hospital decided to provide radiotherapy based on the findings. The patient is currently receiving radiotherapy and regular monitoring.

In these two cases, both patients are undergoing follow-up care. In the first case, the patient was advised to seek emergency care if any life-threatening condition. Second case, the patient received radiotherapy and had been under monitoring.

**DISCUSSION**

A rare gynecological tumor of the female genital tract, vaginal malignant melanoma has become the main focus of this case series. Vaginal malignant melanoma account for 0.3% of all melanoma in women. It predominantly occurs in postmenopausal women. The survival rate for vaginal malignant melanoma is lower than that of cutaneous melanoma at all stages. The poor prognosis cannot only be attributed to a later diagnosis in more advanced stages of the disease because those diagnosed with vaginal malignant melanoma already had metastatic disease, and survival was consistently worse across all disease stages compared with vulva malignant melanoma. Vaginal malignant melanomas are commonly pigmented but occasionally may be devoid of pigment or contain both pigmented and non-pigmented lesions in a zosteriform pattern. Particularly in amelanotic melanomas devoid of melanin pigment, it may be challenging to distinguish a polypoid carcinoma from a melanoma [10].

Advanced melanoma of the vagina may misdiagnose due to a lack of awareness of the potential diagnosis. We compare both cases, which is noteworthy. The first case had vaginal bleeding, and the second case had urethral bleeding. The gynecological examinations are also different, with the first case having a vaginal mass and the second case having no mass either the vulva
CONCLUSIONS

Since vaginal melanoma is a rare form of cancer, it is urged in this situation that routine gynecological exams should pay close attention to any concerning pigmented lesions. It is necessary to perform a biopsy, immunohistochemical staining, and a pelvic node assessment. Vaginal melanoma has a poor prognosis, but an early diagnosis and application of the effective combination modality therapy with MDT choice may improve that.

DECLARATIONS

Competing of Interest
The authors declare no competing interest in this study.

Acknowledgment
The authors would like to give their gratitude to Dharmais Hospital for providing the opportunity to conduct this research.

REFERENCES