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Case Report

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

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Abstract: Primary malignant melanoma of the vagina (PMMV) is an extreme variant of melanoma, however the incidence of this disease ranks second in the female genital tract and accounts for <3% of all vaginal malignancies. The treatment outcomes and prognosis of PMMV are very poor. This study presents the diagnosis and treatment of a patient with PMMV. A 73-year-old postmenopausal Chinese woman visited our hospital due to "abnormal vaginal bleeding for 20 days" was enrolled in this study. Gynecologial examination showed dark blue cauliflower tubercle in the lower 1/3 segment of posterior and left vaginal wall. Biopsy indicated malignant melanoma of the vagina. The patient was then hospitalized in our hospital and laboratory examination confirmed the diagnosis. She received temozolomide oral chemotherapy and half a month later underwent wide local excision. After surgery, she continued temozolomide oral chemotherapy. Unfortunately, both vaginal ultrasound and CT showed a space-occupying lesion in uterus. Endometrial biopsy showed tumor metastasis. The patient refused any additional surgical interventions but only received chemotherapy. After finishing the third chemotherapy cycle, the patient was discharged and died due to cachexia. PMMV is an extremely aggressive tumor with poor prognosis and gynecologists should pay close attention to suspicious lesions associated with abnormal vaginal bleeding or mass.

Keywords: Primary malignant melanoma, vagina, case report

Introduction

Primary malignant melanoma of the vagina (PMMV) is an extremely aggressive tumor, accounting for 0.3-0.8% of malignant melanoma. Most patients are postmenopausal women, with the average onset age of 57 years [1]. Patient with VPMM usually have symptoms such as abnormal vaginal bleeding, vaginal discharge, and palpable mass [2]. The annual incidence of PMMV is reported to be 0.026/100000 all over the world and there is no significant difference in incidence among races [3, 4]. Additionally, socioeconomic factors such as education level, income, and poverty do not affect the incidence rate [5].

PMMV is a malignant tumor originating from the basal layer of melanocytes, however, the etiology is still unclear. Studies have shown that PMMV is associated with KIT gene mutations [6]. In addition, PMMV depends on the variation of the microenvironment rather than the effect of ultraviolet light [5]. In this study, we present as case a patient with PMMV so as to extend the clinical spectrum of this disease.

Case report

A 73-year-old postmenopausal Chinese woman (gravida 10, para 9) visited our hospital due to "abnormal vaginal bleeding for 20 days". Her age of natural menopause was 53 years old. She had a history of hypertension for more than 20 years. In addition, the woman had undergone appendectomy and bypass surgery. No medical history of cancer was found in first-degree relatives. Gynecology outpatient clinics showed a dark blue cauliflower tubercle in the lower 1/3 segment of posterior and left vaginal wall, and the tumor was purple blue and sessile (**Figure 1A**). The rest of the pelvic examination

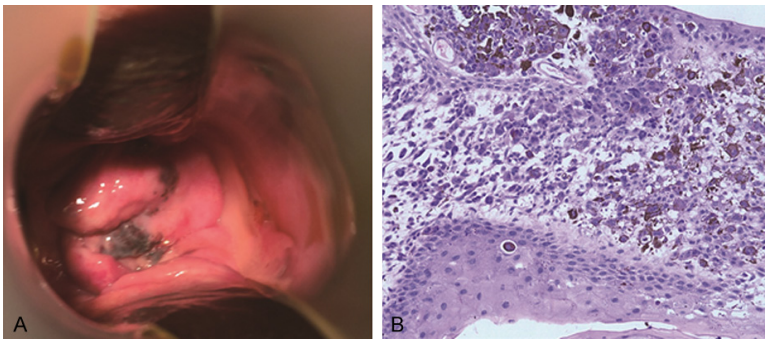

Figure 1. Results of gynecologic examination and pathological examination. Dark blue cauliflower tubercle in the lower 1/3 segment of posterior and left vaginal wall (A). Histopathology showed infiltration heterosexual cell nests at the basal layer and basal layer of epidermis (B. HE staining, ×100).

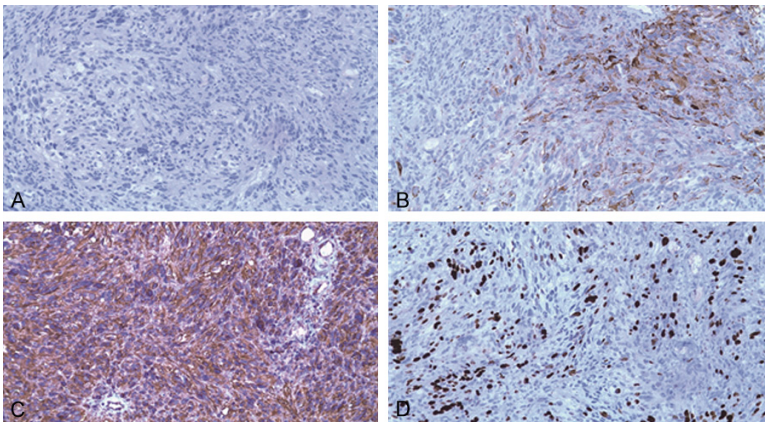

Figure 2. Immunohistochemical stains for the tumor tissue. CK (-) (A. ×200), HMB45 (+) (B. ×200), vimentin (+) (C. ×200), Ki-67 (+) (D. ×200).

was normal and bilateral inguinal lymph nodes were not palpable. Biopsy illustrated malignant melanoma of the vagina: HMB45 partially positive, S-100 negative, and about 30% of Ki-67 positive. She was initially diagnosed as PMMV based on the result of biopsy.

The patient was then hospitalized in our hospital and laboratory examination was as follows: CEA, 3.2 ng/ml; CA125, 14 U/ml; CA19-9, 21 U/ml; and SCC, 0.7 ng/ml. No abnormality was found by transvaginal ultrasonography. She received temozolomide oral chemotherapy (200 mg per day for five days) and half a month later underwent wide local excision. Histopathology demonstrated infiltration heterosexual cell nests at the basal layer and basal layer of epidermis, indicating malignant melanoma of vagina (**Figure 1B**). As illustrated in **Figure 2**, Immunohistochemical examination showed: CK (-), vimentin (+), most of HMB-45 (+), part of Melan-A (+), part of S-100 (+), Ki-67 >30% (+). After operation, she continuedtemozolomideoralchemotherapy (daily 200 mg for five days, interval three weeks repeat). A small amount of vaginal bleeding occurred during the second course of chemotherapy and both vaginal ultrasound and CT showed a space-occupying lesion in uterus (49*40*47 cm), with uterine cavity effusion (**Figure 3**). Tumor metastasis was then suspected and endometrial biopsy was performed. The tumor marker CEA was 164.82 ng/ml and no other abnormity was revealed. The patient refused any additional surgical interventions but only received chemotherapy with the original scheme. She was discharged after the third chemotherapy cycle and follow up show that the patient had vaginal bleeding, secondary anemia, and finally died of cachexia one month after discharge.

Discussion

PMMV primarily occurs in the lower 1/3 segment of the anterior wall of vagina and multiple lesions can also be found in vagina [7]. Malignant melanoma often presents with dark blue or dark grey, and only 10-23% is amelanotic [8]. Few malignant melanomas lack pigmentation, and malignant melanoma without pigmentation is similar to vaginal epithelial tumors [9]. Our patient had a dark blue cauliflower tubercle in the lower 1/3 segment of posterior and left vaginal wall. The most common symptoms in patients with PMMV are vaginal bleeding, vaginal discharge, vaginal mass, and pain. Contact bleeding of the tubercle and ulcerative lesions are typical clinical manifestations in most patients. Our patient was a 73 year old menopausal woman. The main clinical symptom was postmenopausal vaginal bleeding, which was consistent with the reported PMMV cases. It is worth noting that non pig-

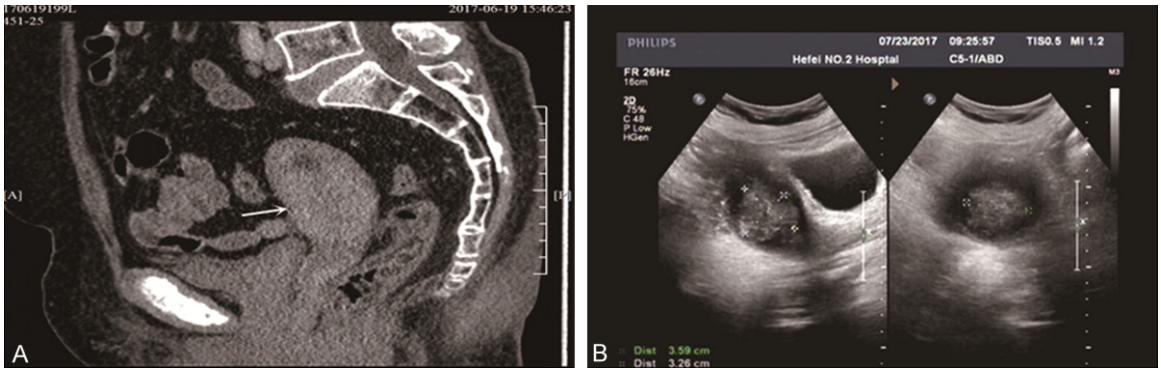

Figure 3. CT (A) and vaginal ultrasound (B) showed an area of accumulation in uterus (size 49*40*47 cm) with uterine cavity effusion.

mented PMMV is often misdiagnosed and the treatment is often delayed, therefore, gynecologists should pay close attention to suspicious lesions associated with abnormal vaginal bleeding or mass. Histological examination is the basis for the diagnosis of PMMV. Immunohistochemical staining for melanin granule, HBM-45, and S-100 protein can assist the diagnosis [10]. Imaging techniques, such as X-ray, CT, PET-CT, and ultrasound can also be used in the diagnosis. Sentinel lymph node biopsy can be used to determine whether there is metastasis [8]. Early diagnosis of this patient was due to careful gynecological examination, vaginal lesions together with timely biopsy, and pathology. After admission, auxiliary examination and physical examination showed no metastasis of pelvic organs and lymph nodes, additionally, the tumor markers were normal, therefore early lesions were considered.

Although there are many treatments for PMMV, the most suitable and effective treatment protocols and criteria are still unclear [1]. Surgery is the first choice for treatment of primary malignant melanoma in the female reproductive system as it can significantly prolong the survival time [11, 12]. The choice of surgical procedures is still controversial. Recent reports have shown that wide local excision of the lesion can achieve a survival rate similar to radical surgery [2]. Huang et al. argue that radical surgery does not prolong survival significantly, however, local recurrence and infiltration have been reported to be associated with conservative surgery [1, 13]. In conclusion, patients with early PMMV should avoid radical surgery as far as possible, and patients with advanced stage can be treated with radical surgery. Considering the patient's age, previous cardiac surgery, and no standard treatment for PMMV, radical surgery might lead to serious complications and may not necessarily improve the prognosis of elderly patients. Here systemic oral temozolomide chemotherapy was used and vaginal malignant melanoma lesions had a wide local excision. The general condition of the patient was initially satisfactory, however, recurrence and metastasis occurred quickly and unfortunately the patient died. Notwithstanding we identified the disease as early as possible, and adopted the treatment plan for the patient's own characteristics, the patient still did not get good prognosis, indicating that PMMV is a disease with high malignancy and poor prognosis.

Although malignant melanoma is not sensitive to radiotherapy and chemotherapy, recent small sample study shows that appropriate adjuvant therapy can prolong the progression-free survival of patients after extended resection of local lesions [2]. Radiotherapy can be used to reduce the lesion before surgery and adjuvant treatment of pelvic metastases could not completely remove the lesion by surgery [12]. Radiotherapy combined with chemotherapy and immunotherapy has been proven to be an effective postoperative adjuvant therapy, but could not be used as an independent treatment [12]. AJCC (American Joint Committee on Cancer) recommends immunotherapy for II-IV stage VPMM patients, including IFN-alpha, anti GM2 antibody, and IL-2 [14]. Targeted therapy has rapidly become into a new therapeutic approach and monoclonal antibodies for the treatment of PMMV can prolong survival and reduce recurrence [15]. Therefore, as a new adjuvant therapy, molecular targeted therapy

can improve the prognosis of advanced primary malignant melanoma of vagina. For our patient, wide local excision was performed and was well tolerated with no adverse reactions or complications. Despite the rapid recurrence, metastasis, and death after operation, as radical surgery has the large trauma and risk and could not significantly prolong the survival rate, surgical treatment was suitable for this patient. Surgery combined with molecular targeted therapy might improve the progress, and it needs to be proved by further study.

Disclosure of conflict of interest

None.

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