

A RARE CASE OF PRIMARY VAGINAL MALIGNANT MELANOMA-CASE REPORT

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Key Clinical Message:

Rare, aggressive primary vaginal melanoma presents late with bleeding and palpable masses. Histology and immunohistochemistry confirm the diagnosis. Nivolumab and Ipilimumab offer hope in advanced stages. Early diagnosis is critical for better outcomes.

ABSTRACT

Only a few examples of vaginal melanoma have been documented in the literature, making it an unusual change. Patients frequently present with vaginal bleeding, discharge, or a lump that may be felt. Postmenopausal Caucasian women between the ages of 60 and 80 are most commonly affected. The prognosis for vaginal melanomas is worse because the diagnosis is made when the condition is further advanced. This case involves a 54-year-old woman who visited the clinic complaining of foetid transvaginal haemorrhage. The diagnosis of aggressive melanoma with AJCC stage IV was made based on the biopsy results. The patient declined drastic surgery due to her advanced age and the severity of her cancer, so postoperative radiation and conservative surgery were used instead. Nivolumab and ipilimumab immunotherapy was subsequently used.

KEYWORDS: Foetid Transvaginal Haemorrhage, Immunotherapy, Postmenopausal Women, Vaginal Melanoma,

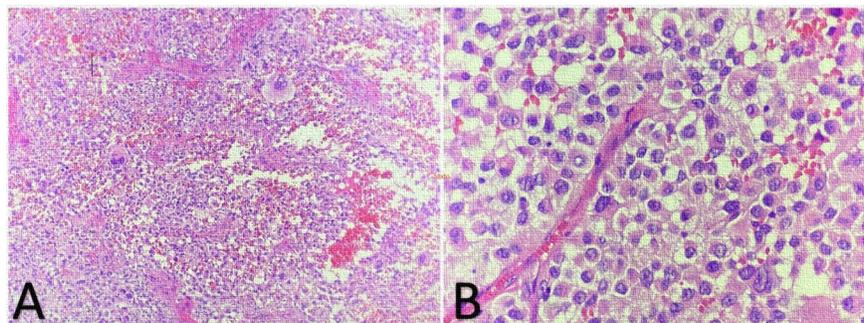
INTRODUCTION

It is believed that melanocytic cells found in the skin and mucosal membranes are where malignant melanoma cells develop. Primary malignant melanoma of the vagina is a rare tumour that has a short survival period and a significant risk of recurrence. even though the first mention of it was in 1887 [1]. Few than 250–300 cases have been documented in the literature, or just 0.46 cases per million women annually [2]. Malignant melanoma makes up 3-5% of all vulvar malignancies and 10% of all female genital tract melanomas and for 0.3–0.8% of all malignant melanomas [2]. Primary malignant melanoma of the vagina typically affects postmenopausal women aged 60 to 80 (average age is 68) [3,4]. Vaginal discharge, vaginal bleeding, the development of widespread, irregular, occasionally mottled macular hyperpigmentation, or a palpable mass, are the most typical symptoms of this tumour. Despite treatment, 5-year survival rates for melanoma of the vagina have been reported to be less than 30% due to the disease's markedly greater aggressiveness compared to its cutaneous counterparts [6]. The case of vaginal melanoma is described in the current article, along with a review of the available treatments.

CASE PRESENTATION

A 54-year-old female patient who visited the oncology unit with myalgia, arthralgia, and fatigue, as well as a palpable mass and pain in the genital area with foetid transvaginal bleeding that had progressed over two weeks, reported the following medical history: history of gynaecology and obstetrics, menarche at 11 years of age, the start of an active sexual life at 20 years of age, two sexual A prolapse of the vaginal vault with an ulcerated tumour measuring roughly 10 centimetres, extending from the proximal third to the distal third, hyperpigmented, friable, and with transvaginal haemorrhage, was discovered during the gynaecological examination . When the lesion was biopsied, it revealed abnormalities in the epithelial cells that were suggestive of melanoma [Figure 1], melanoma with lymphovascular invasion, with vertical growth and superficial dissemination, with mucosal ulceration present, with four mitoses per mm², and surgical limit

of excision of the vulva in focal contact with the limit. CKAE1/AE3 (+/+), vimentin (+/+++), CD45 (-) and chromogranin (-), PS-100 ++/+++ (40%), and HMB45 ++/+++ (40%), were all focally positive according to the immunohistochemistry report. A thoracoabdominal tomography revealed lung metastases, a tumour mass in the uterine topography, and multifocal liver disease with metastasis. With acceptable tolerance, treatment began with a conservative surgical resection, followed by post-operative radiation and biological therapy using nivolumab and ipilimumab.



10X image showing epithelioid neoplasm with rhabdoid characteristics, with significant nuclear pleomorphism.

40X image showing the characteristics of the cytoplasm, hyperchromasia and nuclear pleomorphism.

Figure 1. Vaginal melanoma: histopathological pictures.

DISCUSSION

Melanoma is a highly metastatic, highly aggressive tumour of melanocytes that most frequently develops in the skin but can also occur in the eyes and mucous membranes to a much lower level. One percent of all melanomas are mucosal, and 18 percent of them develop in the vulvovaginal areas. Even more infrequently, between the ages of 60 and 80, just 0.46 instances per million women are diagnosed with vaginal melanoma each year [2]. As in our instance, vaginal melanomas are typically located in the lower portion of the anterior vaginal wall. There are no clear identifiable causes of vaginal melanomas, and the literature does not show any appreciable variations among racial or ethnic groups [1]. The cellular microenvironment and interactions between any of these have been implicated in proposed mechanisms of its pathogenesis and etiological variables, however these hypotheses are at best [6].

Our patient's clinical symptoms included myalgias, arthralgias, weariness, a palpable mass in the genital area, pain, and 2 weeks' worth of foetid transvaginal haemorrhage. According to the bibliography, genital bleeding (80%) and a palpable mass (15%), genital secretions (25%), and local pain (10%) are among the symptoms of vaginal melanoma [1,3]. Vulvar and vaginal melanomas have beginnings that are typically missed by routine examination, with the anatomical location of the lesion being the primary factor in the late diagnosis and poor prognosis of these lesions. [4], Any discoloured growth in the vagina with complaints of vaginal bleeding should be believed to be melanoma since the growth is typically blue-black or blackish with plaques or ulceration [3].

Most patients have advanced disease when they are first diagnosed [1]. Vaginal melanomas are diagnosed using a combination of histological analysis and visual inspection. When the protein S-100, Melan A, and HMB-45 markers are positive, the diagnosis is confirmed by pathological investigation using IHC of the biopsy sample [1]. Histologically, there are three main forms of vaginal melanomas: epithelioid (which accounts for 55% of cases), spindled, and mixed [2]. The big, spherical cells of the epithelioid type have a lot of eosinophilic cytoplasm. They have peppered moth nuclei, which are vesicular nuclei with coarse,

uneven chromatin and peripheral condensation. The most typical locations for this cell type in melanomas are nodular and superficial spreading. The pigment is distributed erratically, there is dermal fibrosis, and the inflammatory infiltrate is varied (brisk, non-brisk, or nonexistent) in the stromal compartment [4]. In order to identify the tumor's Breslow depth, the quantity of mitoses, the kind of ulceration, the presence of microsatellites, and the look of the tumour margins, a thorough pathological investigation should also be carried out [1], as described in the case of our patient.

Prognostic variables and treatment regimens for vaginal melanoma are not well characterised because there are not enough patients to conduct randomised clinical studies.

The American Joint Committee on Cancer's tumour, node, and metastases and the International Federation of Obstetrics and Gynaecology systems are currently used to stage primary vaginal melanoma, but the evidence from various studies suggests that the AJCC stage, tumour size, and lymph node status are the main prognostic factors. Poorer outcomes were linked to AJCC stage III, tumour size 3 cm, and lymph node involvement. In general, MM has a 10-to-20% 5-year overall survival rate compared to 93% for CM.

Additionally, the vaginal melanoma 5-year survival rate is less than 15% [5]. In appropriate circumstances, surgery is the go-to treatment because it's linked to a higher overall survival rate. Quality of life and patient preferences are crucial in determining the extent of surgery, as is the case with our patient, who refused extensive surgery. However, the radicality of the surgery had no discernible impact on outcomes. Routine groyne or pelvic lymphadenectomy is not advised for individuals without signs of clinical or radiological involvement due to the low rate of regional lymph node metastases; instead, prognosis is the key consideration [5]. In the absence of lymph node metastases, local excision of recurrence results in a 50% 5-year disease-free survival rate [1]. If surgical resection is not possible, lymphatic invasion, regional extension, or as a palliative measure, radiotherapy may be utilised as a neoadjuvant treatment [4]. Immune checkpoint inhibitors or targeted therapy are the preferred first-line treatments for metastatic or incurable vaginal melanoma in the context of driver mutations. Nivolumab and ipilimumab combination therapy or anti-PD1 monotherapy with pembrolizumab or nivolumab are the recommended starting regimens for advanced stages (stage III-IV), respectively. This was the treatment of choice for our patient [2,4]. Agents including dacarbazine, interleukin-2, and interferon alpha-2b have showed promise in extending survival [2].

According to evidence, cytotoxic therapy mostly employs dacarbazine, temozolomide, cisplatin, and paclitaxel as neoadjuvant or palliative care [2,4]. It is worthwhile to investigate topical imiquimod as an adjuvant treatment further [6]. Adjuvant chemotherapy (dacarbazine) or the combination of targeted therapy (ipilimumab) and radiotherapy have also been mentioned in the literature, with promising outcomes, in addition to surgical excision.

CONCLUSION

The least common gynaecological neoplasia, primary vaginal melanoma has an aggressive evolution and a bad prognosis since it has a marked tendency to produce metastases. For these reasons, it is typically detected at an advanced stage. It is advised to perform a biopsy and an immunohistochemistry study of any lesions suspected of being cancerous when a hyperpigmented tumour is found during a gynaecological examination as this is suggestive of vaginal melanoma. Being so unusual, there are no standardised recommendations for the therapy. The current main therapy strategy appears to be surgery followed by postoperative radiation. In the instance of our patient, no tumour regression or metastasis was seen despite cautious surgical resection, postoperative radiotherapy, and 5 rounds of immunotherapy, however the patient was still alive after 2 years after diagnosis. It takes a multidisciplinary effort involving gynaecologists, pathologists, dermatologists, and surgeons to have a standardised diagnostic and therapeutic approach to this pathology as early diagnosis is currently the only way to modify the prognosis of this neoplasm.

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