

Primary Malignant Melanoma of the Vagina: A Case Report

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Abstract

Case Report

Vaginal melanoma is an exceedingly rare entity, accounting for 2.6–2.8% of all primary malignant tumors of the vagina and 0.4–0.8% of all malignant melanomas in the female, vaginal melanoma is rare and there are less than 250 cases in the literature, biologically aggressive neoplasms. This tumor usually occurs in the 6th and 7th decades of life and the most common presenting symptoms are similar to other tumors and include abnormal discharge, vaginal bleeding, pruritus, and the presence of a polypoid mass. The prognosis currently tends to be very poor. Currently, there are no official recommended therapeutic treatments for primary vaginal melanomas. A case of primary malignant melanoma located in the vagina was encountered. An excisional biopsy of the lesion was reported as malignant melanoma. Patient having a computed tomography showing pulmonary cerebral metastases with a pelvic floor invasion patient died 10 days later.

Keywords: Melanoma, Vagina, incidence, radical surgery.

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INTRODUCTION

Vaginal melanoma is an exceedingly rare entity, accounting for 2.6–2.8% of all primary malignant tumors of the vagina and 0.4–0.8% of all malignant melanomas in the female [1]. This tumor usually occurs in the 6th and 7th decades of life. The most common symptoms of this disease are vaginal bleeding, palpable masses, and discharge. Although the disease is often limited to the vagina upon the first diagnosis, it frequently recurs and spreads rapidly, involving the local nodes (iliac and inguinal nodes), the lungs, the brain, the liver, and the bones. The prognosis currently tends to be very poor. Currently, there are no official recommended therapeutic treatments for primary vaginal melanomas. Surgery seems to play the most important role in treatment, providing local control of the tumor in a better way than that shown by radiotherapy.

CASE REPORT

A case of primary malignant melanoma located in the vagina was encountered; 20 years after menopause, 75-year-old patient was complaining of vaginal discharge and vaginal bleeding in spotting, appeared for the first time 2 years ago. The medical history was unremarkable. There was no malignancy in family history. During the examination, a nodular lesion was felt in the posterior wall near the cervix a second lesion present in the posterior part of the vagina at the

distal one-third. The largest diameter of the lesion was 1.5 to 2 cm and it bleeds easily on contact (fig 1). The general physical examination was negative. An excisional biopsy of the lesion was reported as malignant melanoma and the entire biopsy material contained these malignant cells. Under the microscope, the squamous epithelium was ulcerated and infiltrated by the neoplastic cells. The nodular tumor growth pattern was both pseudoglandular and solid. Patient having a Computed tomography showing pulmonary cerebral metastases with a pelvic floor invasion patient died 10 days later.

DISCUSSION

Primary mucosal melanomas are rare, biologically aggressive neoplasms. The distribution of head and neck, female genital tract, anal/rectal, and urinary tract sites is 55.4%, 18.0%, 23.8%, and 2.8%, respectively. Primary mucosal melanomas of the female genital tract account for 18% of all mucosal melanomas and 3% of melanomas diagnosed in women. Vulvar melanomas, which are the second most common vulvar malignancy, greatly outnumber vaginal melanomas. Primary cervical and uterine melanomas are much more rare [2]. Vaginal melanoma is rare and there are less than 250 cases in the literature [3] accounting for 2.6–2.8% of all primary malignant tumors of the vagina and 0.4–0.8% of all malignant melanomas in the female [1].

Malignant melanoma is a tumor of the melanocytes of the skin and mucosal membranes. Melanocytes are embryologically derived from neural crest cells and can be found in the basal portion of the vaginal epidermis in 3% of healthy women. Some of these melanocytes are located aberrantly in the vaginal mucosa and these are the sites that vaginal melanoma is thought to arise [4]. The etiopathogenesis of mucosal melanomas is not yet fully elucidated. As neuroectodermal derivatives, melanocytes are known to migrate to the skin, retina, uveal tract, and other ectodermally derived mucosa. Melanocytes migrate much less frequently to endodermally derived mucosa although their function is not fully understood; the presence of melanocytes in the mucous membranes is well established [5]. Melanocytes have also been documented in the deep stroma of the nasal cavity (including the nasal septum and middle and lower turbinates), respiratory mucosa, mucous glands, esophagus, small bowel, and urogenital tract [6]. Because mucosal melanomas are frequently found at mucocutaneous junctions, they were once believed to arise only as extensions of melanocytic hyperplasia from adjacent skin. Indeed, some mucosal melanomas do evolve in this manner. However, there are now several cases describing primary melanocytic junctional activity solely within the mucosal epithelium [7].

Histologically, primary lesions are characterized by nested and single growth of atypical melanocytes in the surrounding mucosa. Similar to the methods used for cutaneous melanoma, immunohistochemical stains, such as S-100, HMB-45, MelanA, and Mart-1, can aid in the diagnosis of these tumors. Other histopathologic features of mucosal melanomas include frequent angioinvasion and multicentricity [8, 9]. These findings are important factors in the aggressive behavior, early metastatic spread, and local control failure characteristic of mucosal melanoma [10].

These findings of multiple HPV DNA and integrated HPV 16 in skin associated with vulvar malignant melanoma indicate that HPV may play a role in the development of vulvar malignant melanoma. The role of HPV could be either direct through infection of melanocytes or indirect as a cofactor with free radicals in chronic fibroinflammatory vulvar disorders such as lichen sclerosus [33]. Familial disposition has been suggested as a risk factor for ocular melanoma [34, 35]. In an review by Wechter *et al.* [33] 15% of patients with vulvar melanoma reported a family history of cutaneous melanoma. Although melanomas are more common among whites compared with blacks in the United States, the differences are less pronounced for mucosal melanoma than for cutaneous and ocular melanomas. For mucosal melanoma, the rate among whites is 2 times higher than among blacks, whereas the rates of cutaneous and ocular melanoma are 5–20 times higher [30, 37, 38-40].

This tumor usually occurs in the 6th and 7th decades of life and the most common presenting symptoms are similar to other tumors and include abnormal discharge, vaginal bleeding, pruritus, and the presence of a polypoid mass. Most of these lesions are black or gray-black in color, whereas only 6% are amelanotic [11, 12]. Exemplifying the aggressiveness of mucosal melanomas of the female genital tract. The authors stressed the importance of including the genitalia in routine total body skin examinations [29]. Because of the typical delay in diagnosis, the vast majority of mucosal melanomas present to clinicians as large, polypoid tumors with nodal involvement. Because of this advanced presentation, Breslow depth alone is of little use in the staging of the majority of primary mucosal melanomas. With this in mind, most authors advocate continued use of the clinical staging system developed for cutaneous melanoma, where stage I is clinically localized disease, stage II is regional lymph node disease, and stage III is disseminated disease [7, 8, 30, 31].

The tumor is primarily found in the distal one-third (58%) of the vagina and mostly on the anterior wall (45%). A low occurrence of this type of tumor makes the assessment of various treatment options difficult. The aim should have been to completely resect the tumor with tumor-free surgical margins and evaluate the related lymph nodes for tumor involvement in primary treatment. Miner *et al.* reported improved outcomes with surgical removal of macroscopic disease whenever possible there are several treatment options but none of them is proved to be standard approach. 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 [4]. The spectrum of surgical therapy ranges from conservative surgery such as wide excision of the lesion or total vaginectomy to radical extirpation with en bloc removal of involved pelvic organs [12]. Many authors think that even in the most minimally invasive and small lesions of vagina, radical surgical resection must be performed. Otherwise, the local recurrence is claimed to be as high as 80% Chung and Ariel, with separate series of 19 and 48 patients, respectively, defend the opinion that the appropriate management of this disease requires radical extirpation of the vagina supplemented by dissection of the regional lymphatics [4]. Geisler *et al.* advised primary pelvic exenteration for vaginal melanoma over 3 mm of invasion and showed that 50% 5-year survival rate might be obtained if the pelvic nodes were free of metastases [14]. Skawronek and Rozsak also defended aggressive surgical therapy [15]. Raber *et al.* claimed that radical surgery seemingly achieved the best results [16]. Chakalova *et al.* performed anterior and posterior exenteration in the woman with a relapse of the melanocarcinoma [17]. The role of elective lymph node dissection remains controversial. Instead, sentinel lymph node mapping gained popularity recently. In this

conservative approach, the determination of the 'sentinel node'. Abramova *et al.* defended sentinel lymph node biopsy being an accurate low-morbidity procedure in vulvar and vaginal melanoma stating that prophylactic lymphadenectomy had not been shown to improve survival in melanoma patients. In a case report Nakagawa *et al.* suggested sentinel node mapping could be a routine procedure in malignant melanoma arising from the vagina and vulva due to its ease with minimal trauma [18,19]. Gonzalez-Bosquet *et al.* claimed that radical local excision of the lesion with homolateral inguinofemoral lymphadenectomy was the most accepted treatment for patients with vulvar malignant melanoma but the available data are not adequate for this procedure in vaginal melanoma [20].

Numerous authors have referred to malignant melanoma, of any site, as a radio resistant tumor [21] in the 1970s, however, new interest developed in the use of radiotherapy in the treatment of malignant melanoma. Higher rates of partial and complete regression of cutaneous melanomas were noted with the use of high-dose individual fractions of greater than or equal to 400 cGy per fraction compared to conventional dose treatments of 180 cGy per fraction [4,22]. The investigations of Irvin *et al.* and other reports in literature showed that the malignant melanoma was not a "radioresistant" tumor and even large vaginal melanomas could respond to radiotherapy if given in high-dose individual fractions. According to the hypothesis of Irvine *et al.* [23] Petru *et al.* reported that radiotherapy might be of value as an alternative to surgery or an adjunct modality in patients with lesions 3 cm in diameter [28].

Unfortunately, any surgical approach has been disappointing, and there appears to be no difference in the survival of radical versus local resections [12, 24, 25]. Because distant metastases were a component in 78% of cases of recurrence, one must wonder whether adjuvant systemic therapy might be of worth in these high-risk tumors. Multiple traditional cytotoxic agents, including dacarbazine, temozolomide, and platinum compounds, both as single agents and in combination, have been evaluated in the treatment of melanoma, with limited or no success. Stellato *et al.* claimed that chemotherapy with photosensitive dacarbazine (DTIC) and interferon (IFN)-alpha was effective. It was the first agent to show a survival benefit in high-risk melanoma patients in a randomized controlled trial [23, 27]. The addition of interleukin-2 to traditional cytotoxic agents has failed to show an improvement in overall survival but has considerably increased toxicity [26]. Some authors have considered the combination of chemo- and radiotherapy as a possible valid option after surgery to improve the survival time, while others suggested the role of pelvic anticancer drug infusion to decrease the tumor size and make possible the surgery and RT, minimizing systemic toxicities [28, 32].

The nature of vaginal malignant melanoma differs from that of the skin with a more aggressive behavior showing high incidence of local recurrence and metastases. The overall prognosis is dismal. Due to the ability of the tumor to spread hematogenously, early metastases are common and regardless of primary therapy chosen [41-43]. Unfortunately, most afflicted individuals harbor micrometastatic disease and experience a course characterized by multiple local recurrences before the clinical development of distant disease. The 5-year overall survival rate for women with vaginal melanoma is only 18%. This is considerably lower than the 5-year overall survival rate for patients with melanoma of the vulva (47%) [4, 22, 44, 45]. Plains the poor prognosis of these lesions and several studies has corroborating data that link survival most closely with tumor thickness. Patients with lesions less than 2-mm thick have a significant survival advantage over those with lesions greater than 2 mm [4, 46]. Reid *et al.* found only the tumor size is of prognostic significance in vaginal melanoma. A data analysed for 115 patients showed that patients with vaginal lesions <3 cm experienced significantly better survival than those with lesions >3 cm ($p = 0.024$). A more thorough understanding of the prognostic factors involved is needed so that a comprehensive, uniform staging system can be developed. Regardless of the extent of primary surgery, positive histological margins or presence of melanoma in situ at the edge of the specimen result in a higher incidence of recurrence and poorer survival rates [4].

CONCLUSION

Malignant vaginal melanoma has a very poor prognosis. Patients treated surgically have longer survival than those treated nonsurgically. Radiotherapy after wide excision reduces local recurrence and may increase survival but not distant recurrences.

Conflicts of interest

None of the authors have any conflicts of interest to declare.



Fig-1: A lesion was felt in the posterior wall near the cervix a second lesion present in the posterior part of the vagina at the distal one-third

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