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Vaginal Malignant Melanoma: Case Report and Review of the Literature

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Abstract **Case Report**

The authors report a case of primary malignant melanoma of the vagina in a patient 60 years old, revealed by with autopalpation of a vaginal mass 18 months after radical surgery for right lobular carcinoma under adjuvant hormone therapy. Gynaecological examination revealed a vegetative pigmented tumour in the lower third of the posterior wall of the vagina measuring 2 × 2 cm with no cervical involvement, biopsied as a malignant melanoma. A search for metastases was negative, leading to the conclusion of malignant melanoma. a primary malignant melanoma of the vagina classified as FIGO stage II. The patient underwent a local excision of the vaginal melanoma with detachment of the recto vaginal cul de sac by prior laparoscopy. Adjuvant External radiotherapy was delivered at a dose of 46 Gy at pelvic level, with a complement by vaginal cutherapie at the dose of 11 gy in 2 fraction.

Keywords: Vaginal melanoma, Primary malignant melanoma, Postmenopausal women, FIGO stage II, Local excision and radiotherapy.

INTRODUCTION

Malignant melanoma is a common and aggressive malignancy of the skin. Malignant melanoma is also known to occur in the mucous membrane lining of respiratory tract, gastrointestinal tract, and genitourinary tracts.

The incidence of mucosal melanomas is low, accounting for 1% of all melanomas. Primary malignant melanoma of the female genital tract accounts for approximately 3% to 7% of all malignant melanomas, and 0.3% to 0.8% of all melanomas in women. It affects postmenopausal women ages 60 to 80 years. The present study describes a case of vaginal melanoma and a discussion of the treatment options.

CASE REPORT

Mrs B. is 60 years old, followed for a lobular carcinoma of the breast operated by radical surgery 18 months ago, the patient is on anti-aromatase. She presented with whitish leucorrhoea associated with spontaneous metrorrhagia of low with autopalpation of a vaginal mass vaginal mass. These symptoms had been evolving for seven months, without pelvic pelvic pain and no urinary or digestive disorders.

Clinical examination revealed a patient in good general condition with a WHO performance status of 0. gynecological examination revealed an indurated black lesion about 2 cm long on the posterior wall of the vagina without palpable inguinal adenopathy.

A biopsy was performed in the gynecology department, and the anatomopathological study revealed a vaginal tumor with an immunomorphological profile compatible with melanoma A pelvic MRI was performed finding a well-limited mass in the posterior wall of the vagina, measuring 22 mm x 19 mm x 11 mm, coming into contact with the anterior wall of the lower rectum with no detectable locoregional invasion, no pelvic or lumbo-aortic adenopathy was found.

An extension work-up including a complete skin examination, and pet scan was performed finding 18 mm hypermetabolic tissue nodule in the posterior wall of the vagina, close to the anterior wall of the anorectal junction and no suspicious hypermetabolic focus in local or distant lymph nodes.

Collegiate surgery was performed, with the first part being laparoscopic for recto-vaginal detachment to remove the posterior part of the vagina, and the second part gynecological with local vaginal removal of the melanoma.

Histological examination revealed a tumor 27 mm in diameter x 11 mm thick, with aspects of a MELANOMA. No convincing emboli were seen. The lateral borders pass into healthy tissue. The deep border is also healthy, but with a margin that is focally millimetric at 0.9 mm, with no immunohistochemical overexpression of BRAF.

In view of the inadequate margin of deep excision, we carried out adjuvant radiotherapy. The patient underwent adjuvant intensity-modulated pelvic radiotherapy at a dose of 45 Gy) with a fractional spread of 1.8Gy per session, five sessions per week. Radiotherapy was delivered in 25 sessions. a complement by vaginal cutherapie was done at the dose of 11 gy in 2 fraction.

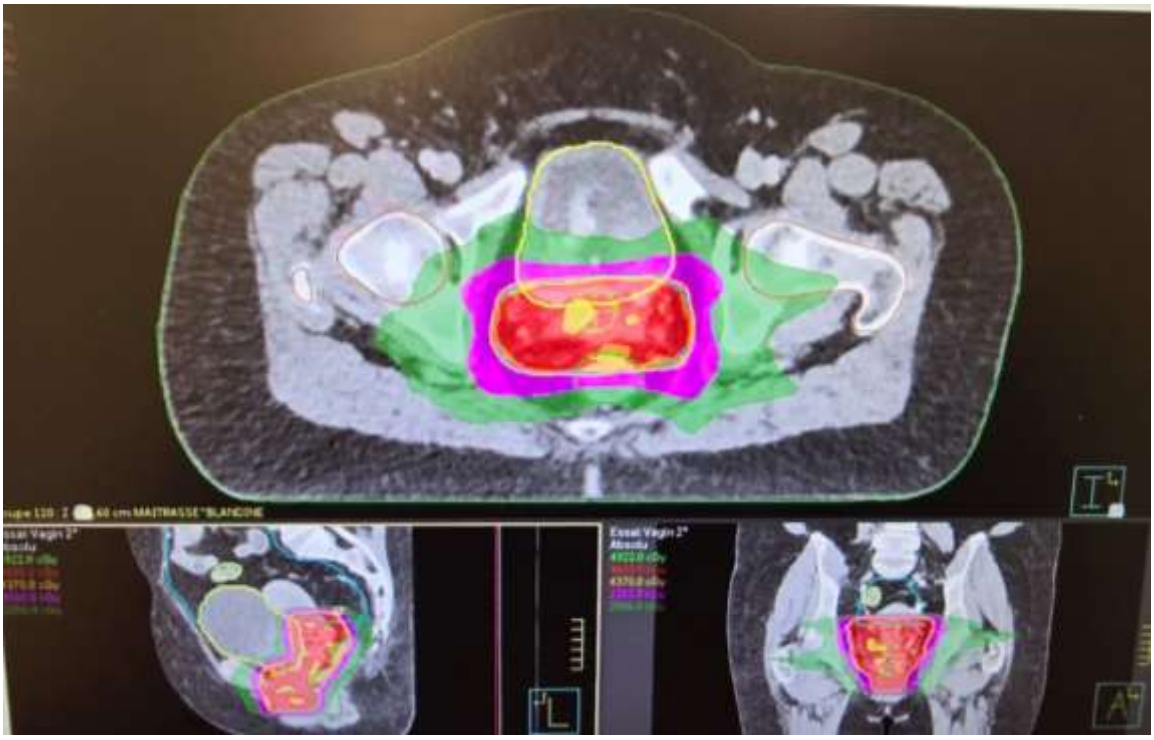

Figure 1: Illustration of delineation for adjuvant prophylactic radiotherapy

Radiation therapy was tolerated fairly well, a grade I vaginal radiomucositis and an anitus of the same grade were recorded. The patient is in complete remission after six months of follow-up.

DISCUSSION

Primary vaginal cancer is rare, affecting fewer than 1,000 patients a year in France, with a third dying [1]. Melanoma is a highly aggressive tumour of melanocytes originating most commonly in the skin and to a much lesser extent in other areas like the eyes and mucosal membranes. Mucous membranes account for less than 2% of melanomas [2], of which 1.6% are genital melanomas, with the vulva (70%), vagina (21%) and cervix (9%) in order of frequency. Malignant melanoma can arise anywhere in vagina; however, anterior wall of the lower one-third part is the most common site [3], unlike our case.

It more commonly affects women in the post-menopausal period between 60 and 70 years of age, but sometimes it might also be observed in younger patients. In general, the female gender appears to be a risk factor for MM, as they are twice as common in women compared to men. In contrast, cutaneous melanoma distribution is similar between both genders. Furthermore, activating mutations in SF3B1 and KIT, deletion of CDKN2A, PTEN, or SPRED1, and amplification of CDK4, TERT, KIT, MDM2, or CCND1 are among the genetic changes linked to MM. BRAF and NRAS mutations are less common in MM than in CM [4]. Targeted therapy is made possible by the identification of driver mutations by MM gene sequencing.

There are no obvious causes for vaginal melanomas because they are so uncommon. It is believed that viral infections, irritating chemicals, and chronic inflammatory diseases are contributing factors [4, 5]. Melanomas can be visually recognized as pigmented lesions, while nonpigmented lesions resemble vaginal epithelial tumors [6]. The differential diagnosis includes blue nevus, sarcoma, lymphoma, poorly differentiated squamous cell carcinoma, and metastases from other locations [7]. Every histological variation is observed, with epithelioid being the most prevalent. Other variations include spindled and mixed [6].

As the vagina is characterized by a very rich lymphatic network, and given the high risk of hematogenous extension of melanoma, the diagnosis is often made at an advanced stage; in our case, the tumor was limited to the vaginal wall, and no secondary localization was detected. The common sites of recurrence of vaginal melanoma are vagina, vulva, and groin [8]. Most common presenting symptom is vaginal bleeding. Other less common presenting symptoms are vaginal discharge, vaginal mass, and pain [9]. The common sites of distant metastasis are the lungs, liver, bones, and brain [6].

IHC can be helpful in difficult cases to confirm that the neoplasm is of melanocytic origin. Widely used markers include protein S-100, melanoma antigen recognized by T-cells-1 (MART-1) or Melan-A, melanoma-specific antigen (HMB-45), microphthalmia transcription factor (MITF), and vimentin [10].

The main prognostic indicators, according to the evidence from several research, are lymph node status, tumor size, and AJCC stage. Tissue size ≥3 cm, lymph node involvement, and AJCC stage ≥III were linked to poorer results [5].

There are a number of therapeutic options, but no established standard. Surgery seems to play the most important role in therapeutic management. However, the optimal surgical technique has yet to be defined. Because to the tumor's challenging anatomic position, broad excision can be either wide radical excision or wide local excision with a circular margin of less than 2 cm [11]. According to studies, people who have had both local excision and radical surgery have comparable survival and recurrence rates [12]. For individuals without clinical or radiographic evidence of involvement, regular groin or pelvic lymphadenectomy is not advised due to the low rate of regional lymph node metastases. In order to enable surgical resection, radiotherapy can be utilized as a neoadjuvant treatment to shrink the tumor. Radiotherapy may be regarded as adjuvant therapy for patients with positive or ambiguous surgical margins, tumor size ≥3 cm, or regional lymph node involvement [5]. While several adjuvant chemotherapy regimens have been explored to lower the recurrence rate in high-risk melanoma, randomized clinical trials have shown no benefit from any of the drugs, including dacarbazine, when taken alone or in combination.

During conservative treatment of vaginal melanoma, pelvic radiotherapy and/or postoperative brachytherapy may be performed, particularly if resection margins are less than 1 cm or not healthy [13]. If there are risk factors (presence of capsular rupture, high number of affected lymph nodes), postoperative radiotherapy of lymph nodes is often considered [14, 15]. Although a variety of radiotherapy methods and treatment plans are described, EBRT administered with intensity-modulated radiation or 3D conformal irradiation. Stereotactic radiation was described in five patients with doses ranging from 24 Gy to 30 Gy in three to five fractions, whereas conventional doses ranged from 45 Gy to 70 Gy utilizing regimens of 2 Gy per fraction.

Based on the radiobiological features of VM, stereotactic body radiation therapy (SBRT) has also been used more frequently in recent years. This is due to the fact that SBRT may have an impact on increased immunogenicity in addition to being a therapeutic option that can overcome melanoma's inherent radio-resistance [16]. Based on aforementioned interactions and synergy, as well as the efficacy in the patient reported in the present case, a trimodal approach combining RT with anti-angiogenic therapy and immunotherapy is a promising treatment strategy [17].

Immunocheckpoint inhibitors or targeted therapy in the presence of driver mutations are the preferred first-line treatments for metastatic or incurable vaginal melanoma. Initial regimens are advised to be either anti-PD1 monotherapy with pembrolizumab or nivolumab or combination therapy with nivolumab and ipilimumab [18–20]. It has been demonstrated that tyrosine-kinase inhibitors such as larotrectinib for patients with NTRK gene fusion and imatinib and nilotinib are helpful in cases with genetic C-KIT abnormalities [21–23]. Regardless of the treatment method, vaginal melanoma has a very bad prognosis because most instances are discovered too late [24]. Conventional chemotherapies such as dacarbazine, fotemustine orcisplatin can be used with poor results.

The 5-year survival rate for PVMM, an uncommon and aggressive malignancy, is between 5% and 25% [11]. The danger of distant metastases and local recurrence is the reason for the poor prognosis. Surgery and postoperative radiation therapy are the most widely used treatments for malignant melanoma of the vagina.

CONCLUSION

Primary VM is an aggressive and rare malignancy that is usually diagnosed at an advanced stage, has a high rate of recurrence and metastasis, and has no consistent guidelines in terms of treatment. With surgery, radiation, and immunotherapy being the three primary approaches now available, the best course of treatment for vaginal melanoma is still up for debate. Naturally, as surgery is still the most often chosen course of treatment, patients who are not suitable for invasive methods may be candidates for radiotherapy.

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