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### RESEARCH ARTICLE

#### PRIMARY VAGINAL MELANOMA: ABOUT TWO CASES TREATED BY RADIOTHERAPY

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#### Abstract

Vaginal melanomas are extremely rare gynaecological malignancy and very aggressive tumor. There is no standardized treatment owing to the extreme rarity of the disease. The prognosis of vaginal primary melanoma is very poor despite treatment modality, because most of the cases are diagnosed at advanced stage. This paper details the clinical course of 2 patients with primary vaginal melanoma treated by definitive radiation therapy, this report includes also a summary of available treatments of this uncommon disease, with focus on the role of radiotherapy.

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#### Introduction:-

Gynaecological melanomas are rare and outcomes are poor compared to cutaneous melanomas [1]. Vaginal melanomas are even rare gynaecological malignancy with an incidence of 3 per 10 million women per year [2]. It accounts for only 3 0.3%–0.8% of all melanomas in females [3]. There is no standardized treatment owing to the extreme rarity of the disease. Surgery, when feasible, is often recommended as the standard of treatment for, and is the most frequently used primary therapy described in the literature [4-5]. In one large review of 805 cases of vaginal melanoma, only 5% of patients were treated with radiotherapy alone [4]. The prognosis of primary vaginal malignant melanoma (PVMM) is poor and 5-year survival is only 5%–25%. [6]. This paper describes the treatment of 2 cases of vaginal melanoma with primary definitive radiation therapy

#### Observations:-

##### Case N°1

A 68-year-old woman, her medical history included hypertension and diabetes, presented with genital bleeding since 7 months, without pelvic pain, rectal or urinary symptoms. On gynecologic examination there was a pigmented, ulcerated lesion 4 cm, bulging in the lower third of anterior vaginal wall. There were no palpable inguinal lymph nodes, the rest of pelvic examination was normal, and the body skin examination was normal. A biopsy was performed. Histopathology and immunohistochemistry confirmed the diagnosis of melanoma. A pelvic magnetic resonance imaging (MRI) showed a 45x40x30mm tumor of the anterior vaginal wall not crossing the boundaries of the vaginal wall with 2 suspicious inguinal adenopathies (Figure 1). A chest and abdominal CT scan were normal. The melanoma was staged as T4N2M0 using the American Joint Committee on Cancer Melanoma Tumor-Node-Metastasis Staging System (8th Edition) and could not be treated surgically. The patient has undergone normofractionated external beam radiotherapy at the dose of 46 Gy in one daily fractions of 2Gy, delivered to the total vagina, uterine cervix, primitive iliac lymph node, internal and external iliac lymph node, and inguinal lymph node.

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After completion of 46Gy external radiotherapy, Gynecological examination found a good clinical response with 1.5cm nodule in the lower third of anterior vaginal wall pelvic. The surgery was again discussed. Pelvic MRI was performed and showed regression of the vaginal tissue process of the lower third of the vagina measuring 13x06mm in diameter versus 45x40x30mm (Figure 2). Surgery was deemed feasible but the patient refused the radical surgery and was lost to follow-up before reconsulting again 10 months later for a suprapubic skin nodule of 1cm diameter. Chest and abdominal CT scan showed vaginal tissue process measuring 30x29mm, associated with nodular lesions in the vulva and ipsilateral pubic wall without distant metastases. The patient was referred to medical oncology department for management.

### Case N°2

An 80-year-old woman, whose medical history included breast cancer at age 76, presented with genital bleeding for 2 months, without pelvic pain or rectal or urinary symptoms. Gynecologic examination revealed a bluish pigmented lesion at the vaginal fundus. Examination of the skin of the body showed four skin lesions, two on the scalp, one on the cheek, and one on the forehead, all of which were resected with clear histologic margins and whose anatomopathologic result was in favor of a basal cell carcinoma.

The patient underwent wide local excision of the vaginal melanoma. The diagnosis of nodular melanoma was confirmed, the tumor size was 10 mm and the Breslow thickness was 4 mm. The histological margin was clear. The thoracoabdomino-pelvic CT scan was normal. The patient was a candidate for adjuvant radiotherapy. Clinical examination before radiotherapy revealed several bluish lesions in the upper third of the vagina for which surgical revision was not possible. The patient has undergone hypofractionated external beam radiotherapy at the dose of 20Gy in 4 fractions of 5Gy plus high-dose-rate brachytherapy at the dose of 28Gy in 4 fractions of 7Gy prescribed at 5 mm from cylinder surface in contact of the tumor lesions. 3 months after irradiation, the patient consulted for a deterioration of her general condition, the thoraco-abdomino-pelvic scanner showed secondary pulmonary, hepatic, adrenal and bone localizations. The evaluation of local control could not be performed.

### Discussion:-

Primary vaginal melanoma (PVM) is an extremely rare tumor of the female genital tract, it accounts for only 3% of all melanomas of female genital tract [3]. 0.3%–0.8% of all melanomas in females,<sup>[1]</sup> with an incidence of only 0.46 cases per one million women per year, [6].

Malignant melanoma can arise anywhere in vagina; however, anterior wall of the lower one-third part is the most common site. [7].

The most common symptoms and signs in patients with VPMM are vaginal bleeding (80%), vaginal discharge (25%), palpable vaginal mass (15%), and pain (10%) [8,9,10,11].

The mass can manifest as nodular, polypoid, or mushroom umbrella. An ulcer is often formed on the mass's surface, mostly blue-black or gray-black, and 10% to 23% of the masses are non-pigmented [12]. Vaginal malignant melanoma can be diagnosed by immunohistochemistry, S-100, HMB-45, and melanoma-associated antigen recognized by T cells (MART-1)—the latter 2 are most commonly used because of their specificity. [12].

To date, there is no consensus regarding the optimal management of women with PVM [2,13,14]. Specifically, it is unclear if treatment strategies should follow current practice regarding female genital tract cancer or should be extrapolated from established strategies used for cutaneous melanomas [15,16].

According to literature review, surgery is recommended as the preferred primary treatment for vulvovaginal melanomas. Surgical modalities range from wide local excision to vaginectomy with or without vulvectomy. Wide excision may be wide radical excision or wide local excision where <2 cm circumferential margin is obtained because of difficult anatomic location of tumor. [17]. Studies have found that the recurrence rate and survival are similar in patients who have undergone of radical surgery and local excision [18]. No survival benefit was demonstrated with prophylactic lymphadenectomy [19]. Nakagawa et al. recommended the sentinel lymph node technic to avoid unnecessary lymphadenectomy [20]

Radiotherapy can be applied as primary treatment for patients who are unable or unwilling to have surgery [7,21,22,23]. It can be applied preoperative as adjuvant treatment to reduce tumor size and enable a more

conservative surgery [7,21,22,23]. Also it can be applied postoperatively as adjuvant treatment for patients with incomplete tumor resection or with pelvic metastases [7,21,22,23]. Melanoma is not a radioresistant disease [24], but giving its low  $\alpha/\beta$  that is explained by great capacity to repair radiation-induced DNA lesions; high doses per fraction are mandatory to achieve local control [25]. Many authors had reported that radiotherapy, when given in high individual fractions (4Gy) to the pelvis, is well tolerated and can result in partial or complete responses of vaginal melanoma [26]. Petru et al. reported that radiotherapy could be an option in patients having vaginal melanoma of size less than 3 cm [22]. The radiation fields, doses, fractions and target volumes should be chosen according to tumor size and location, type of surgery and lymph node status [27].

Due to the highly immunogenic nature of MM, immunotherapy is an effective treatment strategy for primary VMM [28]. Studies have shown that RT and anti-angiogenic therapy combined with immunotherapy can enhance the immune efficacy in melanoma [29,30].

Although a number of adjuvant chemotherapy regimens have been tested in the effort to reduce recurrence rate in high-risk melanoma, none of the agents, such as dacarbazine, used either alone or in combination proved beneficial in randomized clinical trials.

The prognosis of vaginal melanoma is very poor, regardless the treatment modality, because most cases are diagnosed at a late stage [31]. Survival rate of patients with primary malignant vaginal melanoma is 0–25%, irrespective of the type of treatment followed [32].

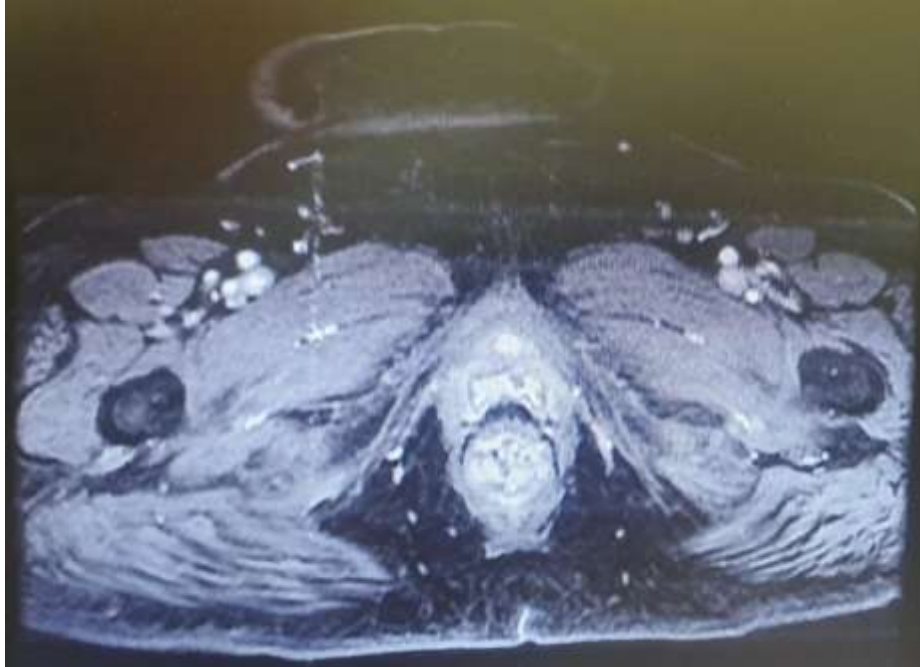
### Conclusion:-

There are currently no practice guidelines for primary malignant melanomas located in the genital mucosa due to the rarity of this location. surgery is recommended as the preferred primary treatment for vulvovaginal melanomas

Radiation therapy is recommended as a consideration for adjunctive therapy after surgery and for advanced or recurrent disease that is not amenable to surgical resection



**Figure 1:-** Pelvic T1-weighted MRI in axial plan after Gadolinium injection showing 45x40x30mm tumor of the anterior vaginal wall. (Before radiotherapy).



**Figure 2:-** Pelvic T1-weighted MRI in axial plan after Gadolinium injection showing 13x06mm tumor of the anterior vaginal wall. (After radiotherapy).

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