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Primary Malignant Melanoma Of Vagina: A Case Report

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Abstract

Malignant melanoma of the vagina is a rare and aggressive malignancy of poor prognosis that mostly affects elderly women in their 6th and 7th decade of life. We present a case report of 58 year female who presented with complaints of vaginal discharge from 4 months. Patient was thoroughly worked up and diagnosed as a case of locally advanced primary malignant melanoma of vagina. Patient being inoperable was treated with radiotherapy following which there was no evidence of disease locally but later she developed distant subcutaneous metastasis and was considered for palliative chemotherapy.

Keywords: Malignant Melanoma, Primary Malignant Melanoma of Vagina

Introduction

Melanoma, also known as malignant melanoma, is a type of cancer that develops from the pigment-containing cells known as melanocytes which arise from the neural crest and migrate to the epidermis, uvea, meninges, and ectodermal mucosa. The tumor develops as a result of metaplasia or misplacement of mesodermal and epithelial tissue. The mucosal melanoma is a rare cancer and account for approximately 1% of all melanomas [1] and is clearly distinct from its cutaneous counterpart in biology, clinical course, and prognosis. Genital mucosa lacks melanocyte which makes melanoma a rare entity in vagina, vulva and cervix [2]. Generally, it arises from aberrant melanocytes present in the vaginal mucosa [3].

Primary malignant melanoma of vagina is a rare and very aggressive tumor that accounts for 0.3–0.8% of all malignant melanomas, 2–5% of female genital tract melanomas, and less than 3% of all vaginal malignancies [4,5]. Globally 500 cases have been reported in the literature [4,5]. The age of onset of vaginal melanoma that has been reported in the literature ranges from 38-90 years, where most of the patients were diagnosed between the ages of 60 and 80 years. Patients commonly present with complaints of vaginal bleeding, vaginal discharge or a palpable mass [1].

Although a variety of treatment options are available, no standard treatment protocol has been established. The treatment options for vaginal melanomas include local excision with wide margins, radical surgery, chemotherapy, and immunotherapy. Radiotherapy is used as adjuvant therapy, as data suggest that radiotherapy does not bring overall benefit as sole therapy [6]. Patient preference and quality-of-life should be considered as critical factors in determining initial management since patients with vaginal melanoma ultimately develop distant metastases regardless of the primary treatment approach. Despite aggressive treatment approach in a multidisciplinary team, the prognosis of vaginal melanoma is poor, and the 5-year overall survival rate is 0-25% [7].

Case report

A fifty-eight year old, non-smoker, non-alcoholic, vegetarian, multipara, post-menopausal female presented to us with complaints of vaginal discharge

and urinary incontinence from last 4 months. General examination was not significant, and patient was ECOG-2 (eastern cooperative oncology group). Local examination revealed an ulceroproliferative growth along entire length of anterior wall of vagina till introitus. Bilateral inguinal lymphadenopathy was present. Histopathological evaluation of the biopsy taken from the growth showed features compatible with malignant melanoma. **[figure 1]** Immunohistochemistry showed Vimentin, HMB-45 and Melan-A positive tumor cells. **[figure 2]** PET scan was advised but was not affordable. MRI of abdomen and pelvis showed vaginal growth reaching superiorly upto cervix and inferiorly upto vaginal orifice with loss of fat planes with distal third of urethra along with bilateral inguinal lymphadenopathy. **[figure 3]** No other investigations were remarkable. Patient was advised for surgery but was declared inoperable because of locally advanced disease. Patient was taken up for radical EBRT (external beam radiotherapy) 50 Gy over 5 weeks in 25 fractions (5 days in a week) to pelvis addressing both local disease and inguinal lymphadenopathy and was advised boost with brachytherapy which was refused by the patient and salvage EBRT 16 Gy/8# was given to pelvis. Both local disease and inguinal lymph nodes showed complete response, but after six months of follow-up, she presented with shortness of breath and multiple painful subcutaneous nodules over lower thorax which were tender hard and fixed. **[figure 4]** FNAC from those nodules were positive for melanoma. X-ray chest revealed multiple round opacities over both lung zones. Patient was planned for palliative chemotherapy with inj. Paclitaxel and inj. Carboplatin three weekly cycles and after 6 cycles patient showed good symptomatic relief and given 2 more cycles after which metastatic nodules were resolved and chest x-ray also showed resolution.

Discussion

Primary malignant melanoma of vagina is a very rare and aggressive tumor. The precise histogenesis of primary malignant melanoma of vagina is relatively unknown and it is thought to originate from aberrant melanocytes located in vaginal epithelium [8,9]. These melanocytes can be found in the basal layer of vaginal epithelium in 3% of healthy women [10]. Active junctional changes are thought to be the initial stage of development in malignant mucosal melanomas [11]. The first case of primary malignant melanoma of vaginal was reported in 1887 and modern literature has noted about 500 cases, globally [12].

Although primary malignant melanoma of vagina might arise anywhere, it is primarily found in the lower one third (34%) and mostly on the anterior wall (38%) of the vagina [5, 13]. It may be single or multiple, pigmented or nonpigmented, polypoid or ulcerated [8]. In our patient, the ulcerated pigmented tumor is located in whole of the anterior vaginal wall.

Patients with primary malignant melanoma of vagina most commonly presents with vaginal bleeding (80%), vaginal discharge (25%), palpable vaginal mass (15%), and pain (10%) [8,13]. The main symptom of our patient was vaginal discharge. The most common histologic cell type seen in primary malignant melanoma of vagina is epithelioid (55%), other histologic cell types are spindled (17%) and mixed (28%) [8]. The molecular biology of these melanomas also differs from cutaneous melanomas, with BRAF being rarely seen (seen in almost 70% cases of cutaneous melanomas) [14]. There is also a possible implication of hormonal influence and HPV in melanomas [15,16]. Whenever the pathological appearance is conspicuous, immunohistochemistry (IHC) helps in confirming the diagnosis. Melanomas stain positive for S-100, HMB-45 and Melan-A [17].

Several treatment options are administered, but none of them are a standard approach. The surgical resection is considered the first choice with survival benefits [18]. The spectrum of surgical treatment ranges from conservative surgery such as wide local excision with sentinel lymph node dissection (SLND) or elective lymph node dissection (ELND), total vaginectomy or radical extirpation with en bloc removal of the involved pelvic organs. However, research has continued to demonstrate that actually there is no difference in survival between patients who have radical surgical procedures and those who have more conservative surgical procedures. The role of ELND remains controversial. Instead, SLND provides important prognostic and staging data with minimal morbidity has recently gained popularity. Buchanan et al. reported tumor diameter <:3 cm carries better prognosis [19]. Patients who are unable or unwilling to have surgery can be given radiotherapy as primary treatment [5].

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Radiotherapy can also be used in preoperative setting to reduce tumor size and enable a more conservative surgery [5]. Also it can be used postoperatively as adjuvant treatment for patients with incomplete tumor resection or with pelvic metastases [5]. Our patient was declared inoperable by surgeon and was given external beam radiotherapy as primary treatment.

Adjuvant systemic therapy is indicated in high-risk cases. The cytotoxic agents including dacarbazine, temozolomide and platinum compounds, nitrosourea and taxanes either as a single agent or combination has been tried with limited or no success. The response rate is 11%–22% and the median overall survival of 5.6–11 months [20]. Role of monoclonal antibodies (MABs): Ipilimumab (Food and Drug Administration approved) is a Cytoxic T–Lymphocytic-associated protein - 4 has demonstrated remarkable promise in patients with unresectable/metastatic melanoma. Nivolumab is a monoclonal antibody to programmed cell death receptor – 1 protein (PD-1). It blocks the interaction between PD-1 and its legends PDL-1 and PDL-2. It is indicated for unresectable / metastatic melanoma. If both drugs ipilimumab and nivolumab given together, the 2 years' overall survival is 64%, however, drug-related adverse reactions also increased. In this patient, Temozolomide was selected in view of her advanced age, less toxicities, better efficacy, and ease of oral administration at home.

This tumor is very aggressive, and most of the patients are diagnosed at advanced stage [4]. This might be due to delayed diagnosis and the rich vascular and lymphatic network of the vaginal mucosa [13]. Those factors contribute to early tumor spread and development of metastases.

Despite of variety of treatment modalites, 5-year survival ranges from 8.4% to 17.5% [4,9,13]. Tumor size (<3 cm) is the most important prognostic factor, whereas tumor thickness is only a weak predictor of survival [15]. Many patients have local recurrences in the pelvis and distant metastases in the lungs, liver, bones, and brain [8,13]. Most of the patients with distant metastasis also have a concomitant local recurrence in the pelvis [13]. Our patient had tumor size >3 cm, and this is a dismal prognostic factor. After 7 months of initial diagnosis, she has no evidence of local recurrence but has developed distant subcutaneous metastasis.

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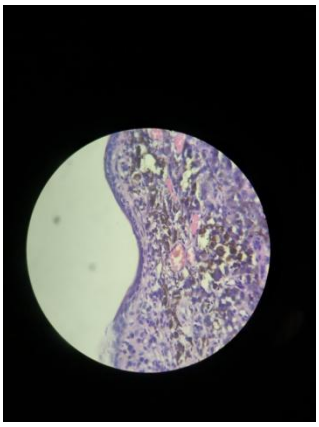

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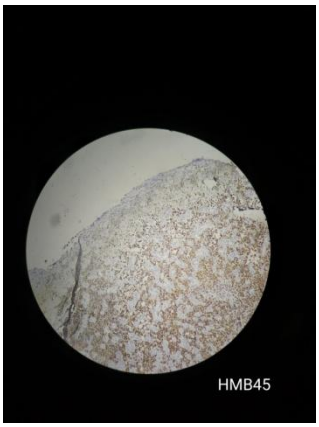

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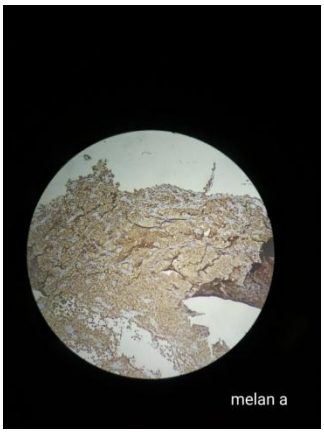

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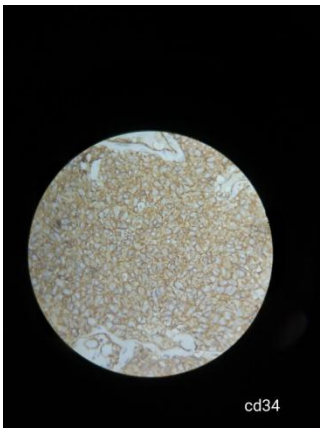

Figure 2c

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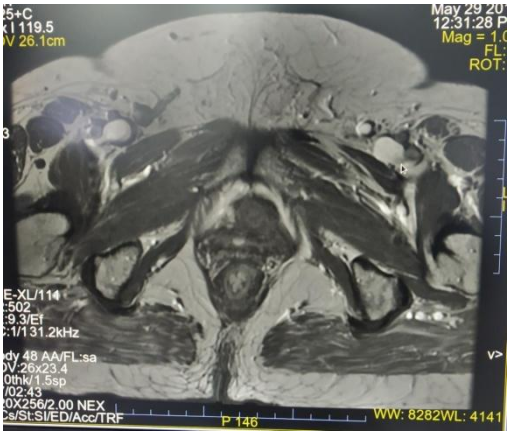

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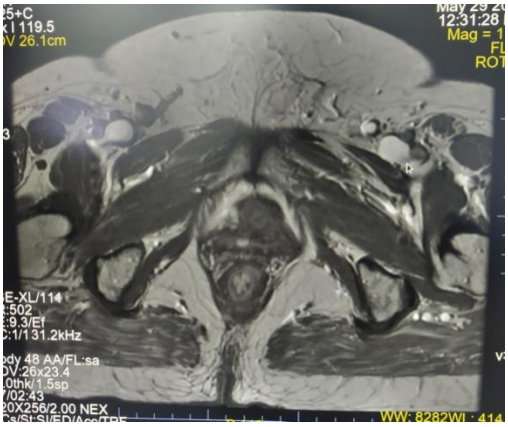

Figure 3b

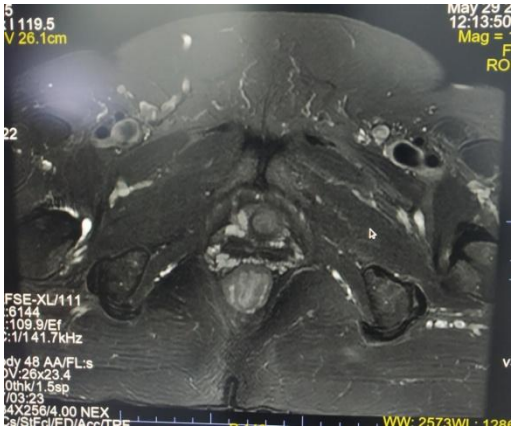

Figure 3c

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