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Primary Vaginal Malignant Melanoma, Rare Form of Malignant Melanoma - A Case Report

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Abstract

Malignant Melanoma is a tumor of melanin producing cells called melanocytes. Vulvovaginal melanomas represent a unique subset of malignant melanoma, with reported incidence of 0.026/100 000 women per year. We present a case of 68 years post-menopausal lady who presented with mass per vagina. On examination there was 4*3 cms bluish-black colored polypoid growth arising from antero-lateral wall of vagina on right side in the lower third, and bleed on touch. Excisional biopsy was done under anesthesia. Histopathological findings showed large pleomorphic high-grade epithelioid melanocytic cells, confirming malignant melanoma. The malignant cells showed diffuse staining for S-100, HMB-45, Melan-A and focal weak positivity for SOX-10. Vulvovaginal melanomas are aggressive tumors with poor prognosis. They pose significant diagnostic and therapeutic challenges, underscoring the importance of early detection and intervention. Increased awareness and understanding of vulvovaginal melanomas can lead to earlier diagnosis and better management strategies, ultimately improving the survival rates.

Introduction:

Maliganant Melanoma is a tumor of melanin producing cells called melanocytes. Vulvovaginal melanomas represent a unique subset of malignant melanoma, accounting for approximately 5% of malignancies within the vulva and vagina (1).Vaginal malignant melanoma (type of mucosal melanoma) accounts for 3% of all melanomas of female genital tract (2). The Estimated incidence of vaginal melanoma is 0.026/100 000 women per year (3). Unlike cutaneous melanomas, which are often associated with ultraviolet radiation exposure, vulvovaginal melanomas do not share this correlation, presenting a distinct clinical challenge (4). Though clinically suspicion of malignant melanoma can be made, final diagnosis is by histopathology and immuno histochemistry. These are very aggressive tumor with poor prognosis. Surgery is main-stay of treatment. Newer treatment modalities like adjuvant check point inhibitors, have shown promising results in advanced stages of disease.

Case report:

A 68 yrs old lady , Para 8 presented with mass per vagina. She attained menopause 10 years back. On vaginal examination, there was 4*3 cms bluish-black coloured polypoid growth arising from antero-

lateral wall of vagina on right side in the lower third, and bleeds on touch, on per speculum examination cervix looked healthy. On bimanual pelvic examination, uterus was atrophic, and fornices were free. Excisional biopsy was performed under anaesthesia and patient discharged on the same day. Histopathological findings revealed ulcerated nodular lesion showing sheets of large pleomorphic high-grade epitheloid melanocytic cells (figure-1, figure-2), some with prominent nucleoli and cytoplasmic melanin pigment. There was lentigenous growth of atypical melanocytes (figure-3) in the adjacent basal epithelial layer with focal melanoma in situ component. There was no evidence of lymphovascular invasion or angiotropism or peripheral infiltration or neurotropism. The malignant cell showed diffuse staining for S-100, HMB-45, Melan-A and focal weak positivity for SOX-10. Cells were negative for pan cytokeratin. Contrast CT done after the histopathology report, showed no intra-throracic or intra-abdominal metastasis. Patient was referred to onchology unit for further managment.

Discussion:

Melanoma is a tumor of melanin producing cells called melanocytes, notorious for their ability to spread quickly. These are usually common in skin, but the incidence of mucosal melanoma is low, accounting for 1% of all melanomas. Vaginal malignant melanoma (type of mucosal melanoma) accounts for 3% of all melanomas of female genital tract (2) with estimated incidence of vaginal melanoma is 0.026/100 000 women per year (3).

Malignant melanoma can arise anywhere in vagina however, anterior wall of the lower one-third part is the most common site (5). In our patient also tumor was seen in lower third in antero-lateral wall of vagina which is the most common site. Presence of pigmentation, location of the tumor, polypoid nature and bleeding on touch are features highly suspiscious of maliganat melanoma. The most common symptoms with VMM are vaginal bleeding (80%), vaginal discharge (25%), palpable vaginal mass (15%) and pain (10%) (6). Our patient presented with mass per vagina which is one of the common presenting features of the tumor.

The diagnosis of VMM includes pathological analysis and IHC of the biopsy sample, and genetic testing. Histologically, Vulvovaginal melanomas display epithelioid or spindled morphology with marked pleomorphism and variable melanin pigmentation. Lentiginous growth pattern may be observed where, atypical melanocytes populate the basal layer, leading to nests or confluent growth. Immunohistochemically, vulvovaginal melanoma cells typically react to melanocytic markers, facilitating accurate diagnosis (7). 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(8). Our patient was positive for S-100, HMB-45, Melan-A and focal weak positive for SOX-10. For patients considered for targeted therapies, diagnostic molecular pathology, including BRAF and KIT mutation testing, can yield critical insights (9).

Currently, there are no specific UICC staging criteria for melanomas in the female genital system. It is recommended that the staging system for cutaneous melanomas be applied to vulvovaginal melanomas to guide prognosis and treatment strategies (10). The prognostic factors and treatment protocols are not clearly defined as there are not many cases and hence, lack of randomaised control trials. Surgery is the treatment of choice, ranging from less-extensive to radical surgery. Less-extensive surgery like local excision and radiotherapy, can be offered to patients with satisfactory loco-regional control, with advantage of less morbidity and disfigurement. Routine SLN biopsy is not recommended for patients with thin melanomas that are T1a (nonulcerated lesions < 0.8 mm in Breslow thickness), it may be

considered for thin melanomas that are T1b (0.8 to 1.0 mm Breslow thickness or < 0.8 mm Breslow thickness with ulceration) and is recommended for patients with intermediate-thickness melanomas (T2 or T3; Breslow thickness of > 1.0 to 4.0 mm)(11). Adjuvant check-point inhibitors for high-risk melanoma have improved the survival rates. Pembrolizumab and nivolumab, are adjuvant check-point inhibitors now available as effective agents, along with the combination of dabrafenib and trametinib as an additional option for *BRAF*-mutant melanoma (12). Role of chemotherapy for women with urogenital-tract melanoma has not been established, and biotherapy methods presented to date have been anecdotal (13). In our patient, we went with local excision, as we were not sure of the diagnosis. Patient has been referred to onchology centre for follow ups after establishing the diagnosis.

Overall survival of these tumors is reported to be below 20%. Poorer prognosis is mainly due to late diagnosis related to poor visibility, early local recurrence, anatomical proximity to the vulvovaginal plexus, tumour biology, high likelihood of distant metastases and amelanotic tumours resulting in later diagnosis (14). Only LN status was significantly associated with survival outcomes in VMM. Two-year survival of cutaneous MM improved over the years, but vulvovaginal MM survival has been constant (13). Most of the outcomes are based on studies for vulvovaginal MM and not specifically for VMM. Also due to rarity of the disease, mostly retrospective studies have been performed and not prospective studies. Hence, more prospective studies are needed to understand the prognosis of VMM specifically and response to newer treatment modalities.

Conclusion:

Vulvovaginal melanomas pose significant diagnostic and therapeutic challenges, signifying the importance of early detection and intervention. Surgery is the treatment of choice, ranging from less-extensive surgery to radical surgery. Overall 5-year survival is below 20% with treatment. Adjuvant check-point inhibitors for high-risk melanoma and advanced disease have shown to improve the survival rate. Most of the outcomes are based on studies for vulvovaginal MM and not specifically for VMM, also most of these are retrospective studies and not prospective studies. Continued research is essential to elucidate the effectiveness of various treatment modalities, including immunotherapy, to improve patient outcomes in this rare and aggressive malignancy. Increased awareness and understanding of vulvovaginal melanomas can lead to earlier diagnosis and better management strategies, ultimately improving the survival rates.

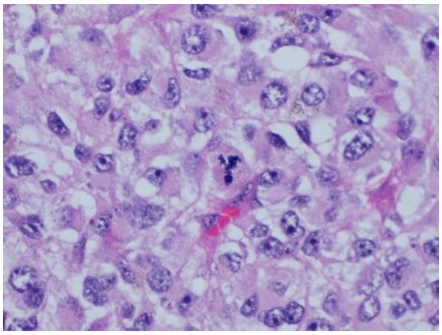

Figure-1: Sheets of pleomorphic epithelioid tumor cells displaying eosinophilic cytoplasm , prominent nucleoli and an abnormal tripolar mitotic figure (400X)

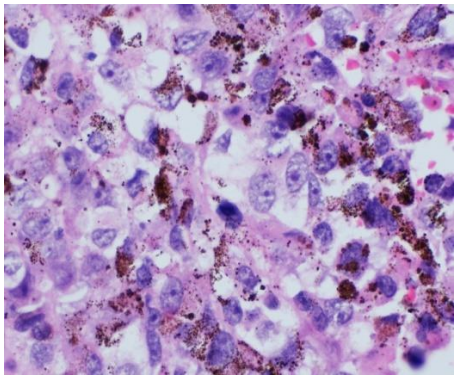

Figure-2: Tumor cells with variably dense melanin pigmentation (400X)

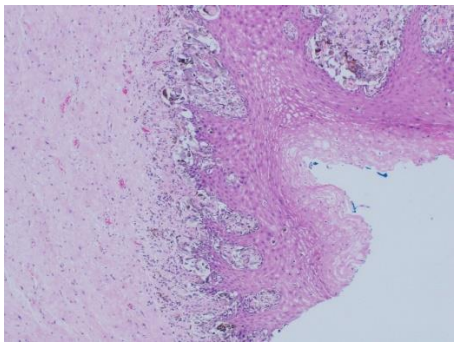

Figure-3: Lentiginous nests of tumor cells within overlying and adjacent vaginal epithelium (40X)

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