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Malignant Melanoma of Vulva with Breast Tumour-Remote Metastasis or a Synchronous Carcinoma - A Case Report of an Uncommon Clinicopathological Presentation

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Abstract: ***Background: Malignant melanoma is the most common malignancy of skin which also shows involvement of other organs. Early diagnosis of malignant melanoma is extremely crucial as it carries a bad prognosis with a potential to metastasize widely. Knowledge of potential sites of metastasis would help both in diagnosis and timely intervention. Case presentation: A 72 years old lady presented with a large vulval pigmented tumour along with a left breast mass. On histopathological examination the vulval mass was diagnosed as malignant melanoma. Simultaneous FNAC from the breast mass revealed presence of malignant melanocytic cells confirming the breast lesion to be a metastatic tumour. Immunohistochemistry also confirmed the diagnosis of melanoma. The left breast mass that was primarily thought to be a synchronous neoplasm turned out to be a rare case of metastasis from vulval melanoma potentially making this case worth of reporting.***

Keywords: Malignant melanoma, Synchronous tumour, Metastasis.

1. Introduction

Malignant Melanoma is a type of skin cancer that carries a poor prognosis. The likelihood of developing this cancer in one's lifetime is approximately 2.6% (1 in 38) for Caucasians, 0.1% (1 in 1,000) for African Americans, and 0.6% (1 in 167) for Hispanics. Although there is limited data available in India, Malignant Melanoma accounts for 0.3% of all cancers and there were 3,916 reported cases in 2020 according to globocan[1].In India, superficial spreading melanoma is the commonest melanoma encountered followed by nodular melanoma[2].

A synchronous cancer is a new or second primary cancer that develops at the same time (within six months) as the first primary cancer, either in the same organ or in a different organ with the same molecular basis. Synchronous cancer is not considered metastatic relapse. Malignant melanoma can theoretically metastasize to any organ but the commonest organ of metastasis constitutes lung, liver, brain, bone and gastro intestinal system[3]. But as metastasis of malignant melanoma to breast with primary being in the vulva is extremely rare initially the breast lesion was thought to be a synchronous neoplasm that turned out to be a metastasis.

2. Case Presentation

A 72 years old lady presented in the emergency department of ESI-PGIMSR and ESIC medical college Joka, Kolkata with complaints of acute abdominal pain with vaginal bleeding. The bleeding per vagina was started 5 months back but it was the lower abdominal pain that forced her to seek an emergency medical consultation. She was the mother of six children, all delivered vaginally, and attained her menopause 20 years back with no history of radiation exposure. Patient was severely anaemic with a fixed, firm to hard palpable mass at her left breast at upper outer quadrant measuring approximately (3X3) cm.

On local examination a left sided large vulval mass covering the introitus was seen with irregular margin, variegated surface and discoloration of the overlying skin associated with foul smelling dirty discharge. The mass measured approximately (5X6) cm in size and was bleeding on touch. Superficial inguinal lymph nodes were also palpable.

The patient underwent Vulval biopsy and FNAC of breast lump concomitantly. Per operative local examination revealed a huge cauliflower like growth arising from the vulva involving left sided labia majora and minora and urethra which bleeds on touch measuring approximately 12 X 12 cm. The mass was anteriorly involving clitoris, laterally para-median and lateral vaginal vault is involved with involvement of upper vagina. Biopsies taken from multiple areas of the vulval mass, FNAC of the left breast lump was also done and the specimens were sent for cytological and histopathological examination.

Different sections from the vulval mass biopsy showed stratified squamous epithelium along with nests and sheets of atypical melanocytes in the dermis (Figure 1 & 2).

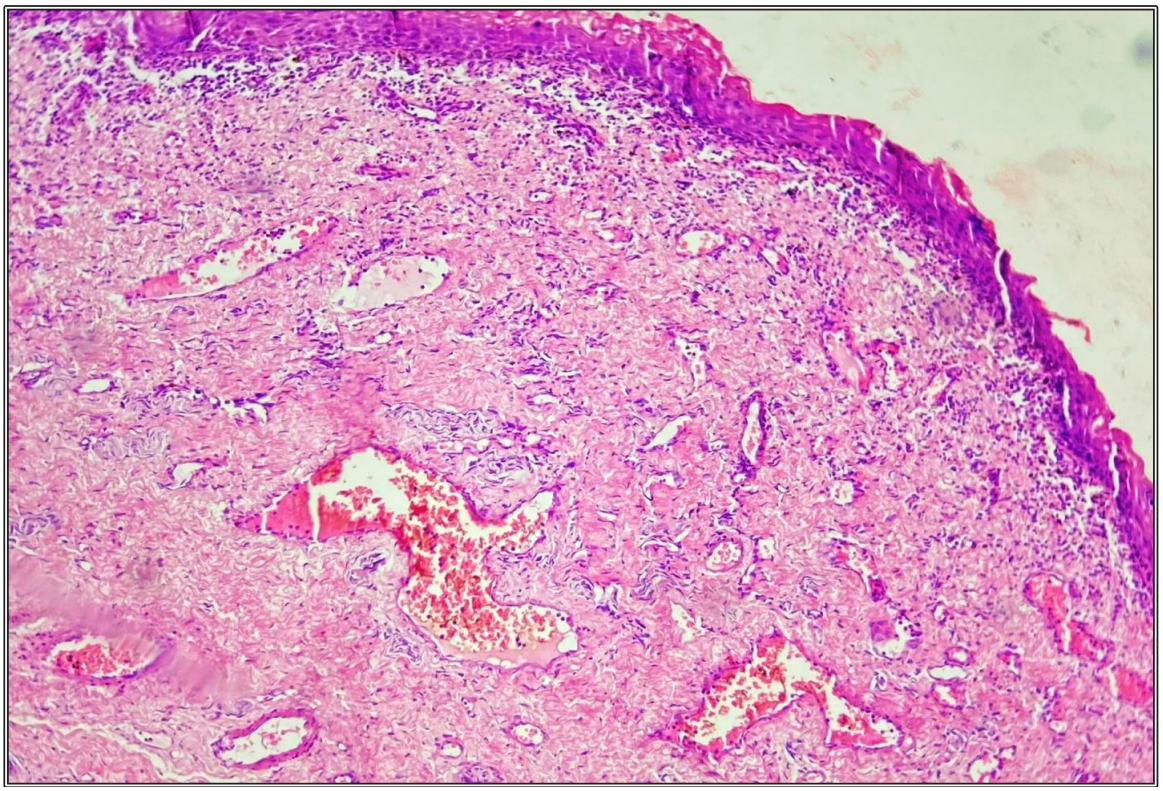

Figure 1: H&E,100X; Section showing tissue piece covered by ulcerated and partially denuded epidermis with atypical melanocytes and junctional activity.

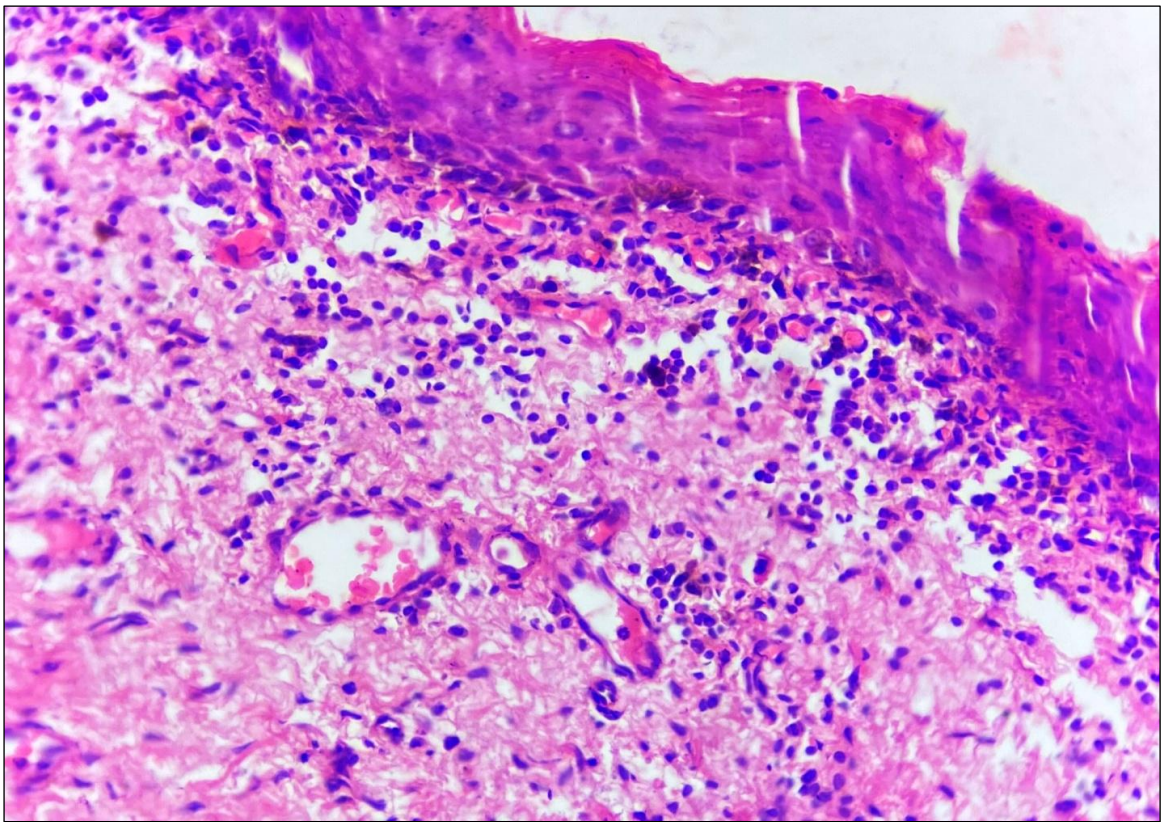

Figure 2: H&E, 400X; Section showing atypical melanocytes with cellular and nuclear pleomorphism, cytoplasmic pigments, high nuclear: cytoplasmic ratio and hyperchromatic nucleus with irregular nuclear membrane.

Atypical melanocytes are large pleomorphic cells with oval vesicular nuclei, prominent nucleoli and eosinophilic cytoplasm. Dense pigmentation noted. Junctional activity is seen (Figure 3). Inflammation is seen in the surrounding tissue. Immunostaining with HMB 45 and S 100 came strongly positive. The reporting was done following the CAP Protocol for Malignant Melanoma[4].

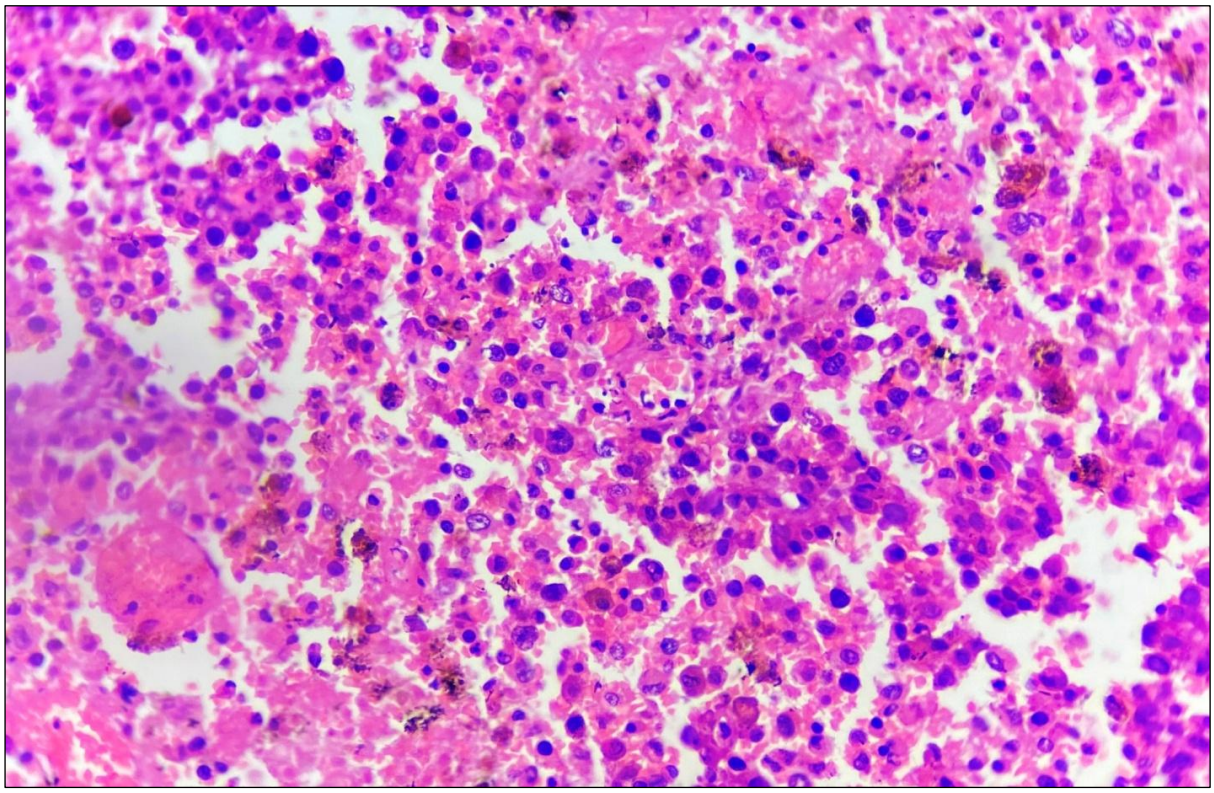

Figure 3: H&E, 400X; Section showing sheets of atypical melanocytes invading the dermis with pigment incontinence.

Lymphovascular invasion and neurotropism were not identified. Non-brisk tumour infiltration lymphocytes were present. Breslow thickness was 6 mm with no ulceration or macroscopic satellite nodules. Clark level was IV, Melanoma invades reticular dermis. Mitotic rate was 6 per mm^2. No identifiable microsatellism. Tumour regression was not identified. Margins cannot be commented as tissues were fragmented and no lymph node was submitted with the main specimen. Immunohistochemistry was done for S100, HMB45 and Melan A that came strongly positive in the malignant cells.

FNAC was done from the left breast lump concurrently. A (4X3) cm mobile, non-tender firm swelling was palpable at lower inner quadrant of left breast. Brownish material was aspirated.

Microscopic examination revealed smears are highly cellular showing largely dispersed cells and occasional clusters of pleomorphic cells having oval to spindle shape with nuclear hyperchromasia, high nuclear-cytoplasmic ratio, nucleomegaly , anisonucleosis and prominent nucleoli (Figure 4). Cytoplasm of these atypical cells shows brownish pigmentation. Few multinucleated cells are also seen. Hence the cytomorphological features are suggestive of malignant epithelial neoplasm with possibility of malignant melanoma.

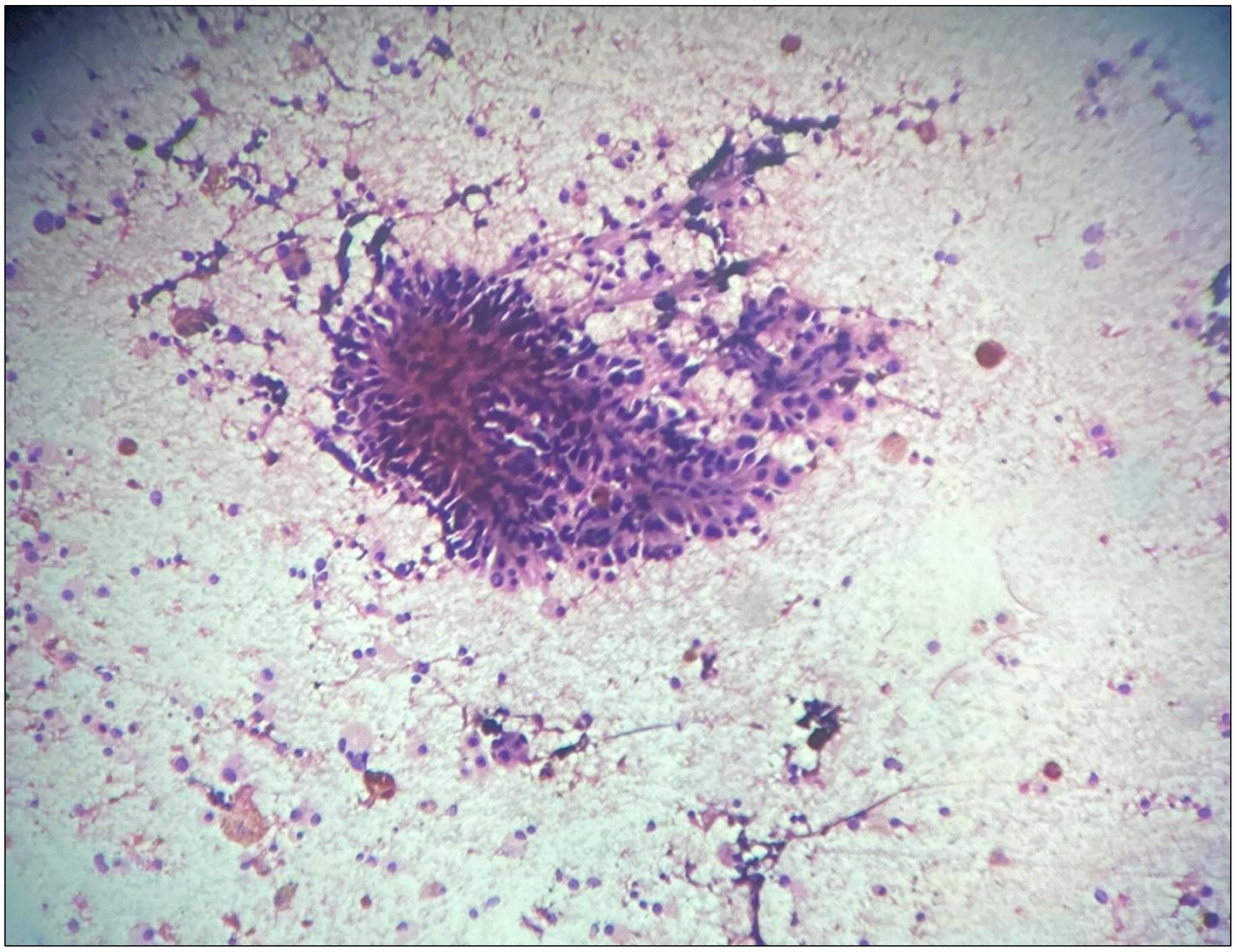

Figure 4: Leishman-Giemsa,100X; Smear shows hypercellularity with papillary core consisting of pigmented atypical melanocytes.

Outcome & Management: The patient was advised for radical excision but unfortunately she passed away due to cardiac failure.

3. Discussion

Considering the presentations, two possibilities could be taken into account. First, the vulval growth is the primary malignancy that has metastasised in the breast. Second, the breast lump and the vulval growth are unrelated and the patient is having synchronous carcinomas.

In the process of histopathological and cytomorphological examination of the vulval growth and breast lump respectively it was evident that the vulval lesion to be Invasive malignant melanoma with secondaries in the left breast.

The close differentials of melanoma of the vulva were Paget's disease of vulva and high grade squamous intraepithelial lesion. But in both the cases HMB 45 and Melan A would be negative.

It was important to sub classify further the diagnosis of melanoma according to WHO classification[5]. The vulval growth was not at all superficial and neither shows pagetoid growth pattern of the neoplastic melanocytes nor acanthosis or parakeratosis were present. Thus, excluding superficial spreading melanoma and acral lentigo melanoma. There was no previous history of nevus in the site of melanoma, thus excluding other subtypes of melanoma associated with nevus, and the diagnosis of Melanoma, not otherwise classified, was made.

A pigmented skin lesion can have multiple differential diagnoses that include nevus, melanoma, dysplastic melanocytic nevus, seborrhoeic keratosis, pigmented basal cell carcinoma (BCC), and pigmented actinic keratosis[6]. Melanoma differs from non-melanoma cutaneous malignancy in that it can spread locally, regionally, and to distant areas. The risk of metastasis in an individual is closely linked to the depth and ulceration of the primary tumor. Early cancer metastasis involves several processes, such as invasion, angiogenesis, extravasation, dissemination, and colonization of the target organ. Even patients with clinically node-negative disease or those with a negative sentinel lymph node biopsy can still develop distant metastatic disease[7]. Additionally, performing a complete lymph node dissection has not shown a survival advantage for patients with node-positive disease. There have been instances of melanoma being transferred from a donor to a recipient following an organ transplant, even years after the donor was diagnosed with melanoma, suggesting the possibility of early subclinical micrometastasis[8]. According to the American Society of Clinical Oncology (ASCO), only about 4% of melanomas are diagnosed with metastasis.

As malignant melanoma is a highly aggressive tumour prompt diagnosis should be made and all the potential sites of metastasis should be looked for. Melanoma cells often acquire mutations that enable them to detach from the primary tumor, invade surrounding tissues, and enter the bloodstream or lymphatic system, leading to metastasis in distant organs. Key molecules involved in metastasis include E-cadherin (cell adhesion), integrins, and matrix metalloproteinases (which break down the extracellular matrix).

Understanding these molecular factors has led to the development of targeted therapies, such as BRAF inhibitors (e.g., vemurafenib) and immune checkpoint inhibitors (e.g., pembrolizumab and nivolumab), which have significantly improved the prognosis for patients with advanced melanoma.

Vulval malignant melanoma is a well known entity and many cases have been reported so far [9,10]. G Kobayashi et.al reported a case of breast and axillary lymph node metastases of amelanotic spindle cell melanoma where a postmenopausal female presented with a skin lesion over her back, diagnosed as malignant melanoma with epithelioid features that had a breast metastasis[11]. Emilio Mayayo Artal also reported a similar case of malignant melanoma of back with breast metastasis[12].
Now theoretically malignant melanoma can metastasise to any organ but by far lung, liver, brain, bone and gastro intestinal system are known to be the sites of metastasis in order of common occurrance[3].

Breast is an uncommon site of metastasis. Commonest aetiology being the malignancy of contralateral breast. Apart from the haematological malignancy, common primary sites are lung carcinoma, gastric carcinoma, cutaneous melanoma and female genitor-urinary carcinoma[13]. Breast metastasis from vulval carcinoma is a very rare occurance. To our knowledge only three cases have been reported so far. D C Papatheodorou et al. reported a case of bilateral breast metastasis from invasive squamous cell carcinoma of vulva[14]. Vicus D et. al and Khouchani M et. al reported squamous cell carcinoma metastasizing to unilateral breast[15,16]. But malignant melanoma of vulva with breast metastasis is very rare and so far unreported. Because of such rarity provisionally the breast lesion was thought to be synchronous neoplasm but with the progression of investigations breast metastatis of vulval melanoma was established. Thus, making the case to be rare and possibly first of its kind.

4. Conclusion

Malignant melanoma is always an important differential to be considered while investigating a pigmented lesion and all the unusual sites of metastasis to be kept in mind and not to be overlooked as the tumour itself is much aggressive and a diagnostic delay can be proven life taking. This case report is significant in adding information of probable site of metastasis in cases of vulval melanoma.

Ethical Approval: Not applicable.

Conflicts of interest: None.

Disclosure: The authors state that they do not have any financial conflicts of interest related to the content discussed in this report.

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