

## Primary Malignant Melanoma of the Breast: A Case Report

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### Abstract

Malignant melanoma predominantly is a malignancy of cutaneous and mucous membrane. Primary malignant melanoma of the breast (PMMB) is a rare tumor, accounting for <5% of all malignant melanomas. In this report, we tried to explore and share our local experience of PMMB and discussed a literature review on this rare entity to stimulate physician awareness. We found that, data on this topic is scarce in the academic literature; moreover, there are no standard guidelines or consensus statements available on the management of primary malignant melanoma of the breast. Therefore, we, herein, present a very rare case of a 43 years old female with the primary non-cutaneous malignant melanoma of left breast (PNCMB).

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**Keywords:** Malignant melanoma, Modified radical mastectomy, Primary non-cutaneous malignant melanoma.

### Introduction

Malignant melanoma is a malignant neoplasm of melanocytes predominantly involving the skin; other sites of origin include oral, gastrointestinal and genitourinary mucosal surface, meninges, uvea of eye etc. In breast, melanomatous lesions may develop as metastatic lesion of primary cutaneous melanoma or as primary malignant melanoma of the breast (PMMB) arising from the breast parenchyma or from overlying skin.<sup>1</sup> Metastasis from cutaneous malignant melanoma represents the majority cases melanoma involving the breast. PMMB is very rare; and accounting for 3-5% malignant melanoma of all tissue types and only <0.5% of malignant breast tumors.<sup>2</sup> Thorough

clinical and radiological evaluation, routine histopathology and immunohistochemical staining method (IHC) are required to confirm primary malignant melanoma of the breast, as well as other types of breast tumor. Surgical resection followed by chemo-, radio- and/or immunotherapy is the commonly adopted treatment method for malignant melanoma.<sup>3</sup> Regional lymph nodes metastasis is the most significant prognostic variable to predict survival of patients with melanomas.<sup>4</sup> The clinical course of melanoma also depends on the thickness, ulceration, localization, tumor immunity and histology of the primary tumor, as well as the sex of the patient.<sup>5</sup> Here, we report a patient who underwent mastectomy for a primary malignant melanoma of breast.

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### Case presentation

A 43 years old female presented with complaints of painless mass in her left breast for 5 months. The patient mentioned that the mass had grown rapidly and recently a painful ulceration over the skin of left breast had developed. There was no notable medical history as well as personal and family history of previous diagnosis of malignancies. Clinical examination revealed a 10x8 cm firm irregular mass involving all four quadrants of the left breast associated with ulceration and bleeding from overlying skin. The nipple was retracted. A mobile 1×1 cm lymph node was palpable in the left axilla. Examination of right breast, right axilla and both supraclavicular fossa revealed nothing abnormal. Routine investigation of blood, chest X-ray and ultrasound abdomen and pelvis failed to reveal any abnormality. Trucut biopsy was attempted but could not be done due to severe bleeding. Touch imprint cytology smears were made from ulcerated skin and malignant cells were found. No other

cutaneous, mucosal or ocular lesion was detected and all other systems on physical examination were unremarkable. She underwent left modified radical mastectomy with axillary node dissection. On cut section of mastectomy specimen, irregular, firm, tarry-black growth was found that replaced whole breast parenchyma (Fig 1 & 2). Histopathological examination showed a high grade malignant neoplasm composed of sheets and strands of discohesive cells with a high degree of pleomorphism, large vesicular nuclei and prominent nucleoli (Fig 3 & 4). Abundant cytoplasm with significant intracellular pigmentation was also observed. So the tumor was histomorphologically consistent with primary non-cutaneous malignant melanoma of left breast (PNCMB). Five axillary nodes were dissected and one lymphnode showed metastatic melanoma, other four lymph nodes showed reactive changes. Patient was advised to do IHC panel of malignant melanoma but they refused. Post-operative period was uneventful.



Figure 1. Resected breast with surface ulcer



Figure 2. Resected breast showing base

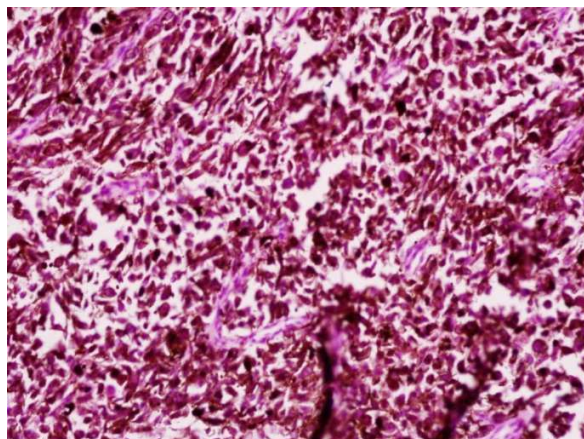


Figure 3. Malignant melanocytes and melanophages H& E stain (200X magnification)

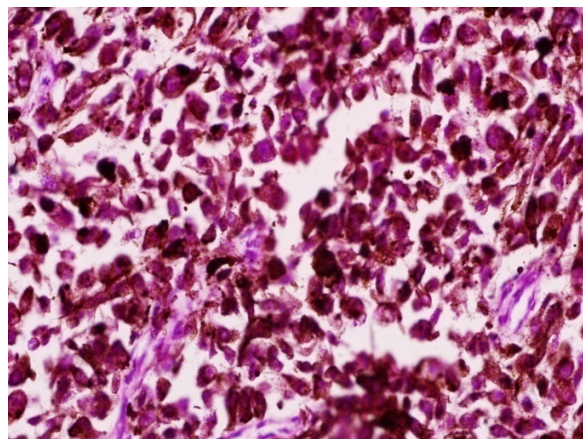


Figure 4. Malignant melanocytes and melanophages H& E stain (400X magnification)

### Discussion

Malignant melanoma usually presents as a primary cutaneous malignancy. It is a neoplasm of neural crest-derived melanocytes that can develop both in sun-exposed and unexposed areas of the skin.<sup>5</sup> Apart from the skin, it also arises in the oral mucosa, paranasal sinuses, leptomeninges, esophagus, larynx, vagina, anorectal region and elsewhere in the body. Approximately 15% of all malignant melanomas originate from primarily non-cutaneous sites.

It is highly malignant due to its rapid growth and early metastasis. Approximately, 160,000 new cases of malignant melanoma are detected worldwide every year.<sup>6</sup> Malignant melanoma of the breast has diversified manifestations and can present as: i) malignant melanoma metastasis to the breast; ii) Primary cutaneous malignant melanoma of the breast iii) in-transit metastases between breast tissue and skin; and iv) primary malignant melanoma of the breast gland and parenchyma (PNCMB).<sup>3</sup> Primary malignant melanoma of the breast (PMMB) is a very rare condition accounting for <0.5% of malignant breast tumors. The PMMB may arise from the cutaneous aspect of the breast or from breast parenchyma. According to our

literature search, less than 200 cases of PMMB are reported till date.<sup>6</sup>

Malignant melanoma develops metastasis via hematogenous or lymphatic routes. Melanoma can spread to lymph nodes, secondary sites in the skin and distant organs such as the breast. Trunk and upper limb are the most common primary sites for melanoma metastasis in the breast in premenopausal women.<sup>7</sup> The etiology of malignant melanoma is still unknown. One of the hypotheses that favored to be associated with excessive exposure to ultraviolet radiation from the sun. Ethnicity, the endocrine and immune systems, chronic stimulation and improper surgery are also considered as causes of progression of nevus into malignant melanoma.<sup>[8]</sup> Pathogenesis of PMMB is based on few debatable hypotheses. Some authors have suggested that it may be a metastatic tumor from an unknown primary or a primary tumor that has completely regressed. True primary tumor arising from ectopic melanocytes in the breast epithelium or metaplastic transformation of a normal mammary duct precursor could be other alternative pathogenic pathways.<sup>9</sup>

PMMB is a very rare entity and offers diagnostic challenge both to the histopathologist and the clinician. It has to be

differentiated from metaplastic carcinoma of breast with melanocytic differentiation, pigmented Paget's disease of the breast, epithelioid angiosarcoma of breast and metastatic malignant melanoma from extra mammary site. In metaplastic carcinoma of the breast, several lineages of differentiation may concomitantly present in the tumor along with melanocytic differentiation. It has components of both ductal carcinoma and melanoma with morphological transition. In epithelioid angiosarcoma, tumor cells mimic malignant melanoma associated with wide areas of hemorrhage and tubular vasoformative architecture. Clinically in almost all the cases of pigmented Paget's disease, the nipple and areola are involved and in 35% - 50% of patients are associated with invasive ductal carcinoma of breast. Pagetoid spread of malignant epithelial cells with phagocytosed melanin pigment mimicks malignant melanoma. Immunohistochemical evaluation may guide to solve the diagnostic dilemmas.<sup>9,10</sup>

Diagnosis of PMMB is complex and based on a combination of morphological and immunohistochemical features. Melanoma cells have a diverse appearance; epithelioid feature, spindled cells, signet ring cells, clear cells and other cytoplasmatic morphologies. Large architectural variations including trabeculae, rosettes, glands, papillae, sheets etc are frequently noted. To distinguish melanomas from epithelial, hematological, mesenchymal and neural tumors and from metastases of extra-mammarian malignancies IHC panel may require. S100, melan-A, tyrosinase and HMB-45 are sensitive and specific markers for melanoma. Ki-67 or Mib-1 immunostain may be used to distinguish between benign and malignant tumors.<sup>11</sup>

In view of the rarity of the disease and the complex anatomy of the breast, treatment of PMMB requires special attention. Radical

surgical resection combined with free margins and axillary node resection constitutes the primary modality of treatment in PMMB patients. Adjuvant treatment strategies for PMMB usually follow treatment approach suggested by the standard melanoma guidelines. Interferon alpha is considered as the standard immunotherapy in high-risk patients. Other immunotherapies for primary advanced and recurrent PMMB include ipilimumab, vemurafenib and systemic chemotherapy with dacarbazine, temozolomide, cisplatin, and paclitaxel. Adjuvant radiotherapy does not improve overall survival and therefore, remains debatable.<sup>6</sup>

#### *Conclusion*

We report a very rare case of PNCMB with distinct clinical manifestations. Such cases are always diagnostic challenge for pathologists. PNCMB can present as an amelanotic neoplasm without skin involvement; so poorly differentiated neoplasms within the breast parenchyma should be included in the differential diagnosis. The IHC panel of multiple melanocytic markers is an ancillary test for the diagnosis of PMMB.

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