MALIGNANT MELANOMA OF BREAST: A RARE CLINICAL ENTITY

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Abstract. The incidence of melanoma is very low in Asian country especially in Malaysia. Primary malignant melanoma of breast is even rarer, account for less than 5% of all melanomas. The breast can be a site for primary malignant melanomas arising from the overlying skin, primary non-cutaneous melanomas or metastatic lesions from other primary cutaneous sites. This paper aims to highlight our management strategy on manging a middle-aged woman with breast melanoma and raise awareness about this rare breast tumours. We present a case of 49 years old lady with primary malignant melanoma of the right breast. The patient presented to the clinic with a large palpable right breast lump extending to right axilla for almost 1 year. Otherwise, the physical examination shows no suspicious mole or skin lesions at the upper trunk or extremities as well as lower extremities. However, her final histopathology report from the core needle biopsy revealed a malignant melanoma of the breast. We review the relevant literature and a discussion regarding guidelines available for diagnosis, follow-up and surveillance of this rare case. The prognosis for patients with this rare tumour of the breast is somewhat poor. Early diagnosis, timely and precise comprehensive treatment, including surgical intervention, along with adjuvant therapy are the key procedures that may improve the patient survival rate.
Keywords: *malignant melanoma, breast carcinoma, primary, metastasis*

Introduction

Melanoma is an aggressive skin cancer, predominantly occurs in the skin, mucous membranes and the choroid. It is rare in Asian population and occurs predominantly among Caucasians. In Malaysia, the incidence of melanoma is very low. The prevalence rate in Malaysia is about 0.5 per 100,000 for males and 0.3 per 100,000 for females (Del Boz et al., 2009). There were 184 and 163 reported cases of melanoma in male and female, based on Malaysia National Cancer Registry Cancer in the years of 2012-2016, which from these results, 58.3% male and 52.3% female were diagnosed as stage IV melanoma. Melanoma of the breast on the other hand is particularly rare. The incidence of primary malignant melanoma of breast is less than 5% of all melanomas (Kurul et al., 2005). The breast may be involved in primary malignant melanoma arising from the overlying skin, primary non-cutaneous melanomas or as a site for metastatic lesions originating from other cutaneous melanomas. Primary non-cutaneous breast melanomas with-out evidence of a skin primary lesion are rarer and only a few cases have been reported in the literature (Rassouli and Voutsadakis, 2016). We present a case of 49-year-old lady with primary malignant melanoma of the right breast with no evidence of

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other cutaneous melanomas as well as no previous history of malignant melanoma. Herein we review the literature and discuss the diagnostic dilemma of this rare breast tumour.

Materials and Methods

We present a case of 49 years old lady with primary malignant melanoma of the right breast. The patient presented to the clinic with a large palpable right breast lump extending to right axilla for almost 1 year. Otherwise, the physical examination shows no suspicious mole or skin lesions at the upper trunk or extremities as well as lower extremities. The patient had no family history of breast cancer and no other risk factor of breast cancer. Mammography with complimentary ultrasound of right breast revealed a large mass at the right upper outer quadrant extending to the right axilla measuring 9.5 cm of its largest diameter with multiple satellite nodules in the rest of the quadrants of the right breast (*Figure 1*). An ultrasound guided core biopsy of the lesion was done and histology revealed multiple cores of breast tissue with malignant cells arranged in solid sheet accompanied by desmoplastic stroma. The cells are markedly pleomorphic, hyperchromatic nuclei with moderate eosinophilic cytoplasm. Many of the cells show intranuclei inclusion and cytoplasmic vacuolation with melanin pigment. Mitotic figures are seen. Occasional lobules of benign breast ducts are seen intermingle with the malignant cells and at the periphery of the lesion. The malignant cells are immunopositive for S100, Melan A and HMB45 immunostains which is consistent with malignant melanoma (*Figure 2*). Staging computed tomography (CT) revealed primary right breast malignancy with ipsilateral axillary nodal lymphadenopathy and distant metastases to the pleura, lungs, liver and bones (*Figure 3*). No enhancing subcutaneous nodules seen. Given the tumour's significant size and the late-stage diagnosis of the disease, the multidisciplinary team discussion includes breast surgeon, radiologist, oncologist and breast histopathologist has recommended for systemic chemotherapy with Dacarbazine before surgery, contingent on the patient's response to treatment. Unfortunately, the patient passed away shortly after starting chemotherapy.

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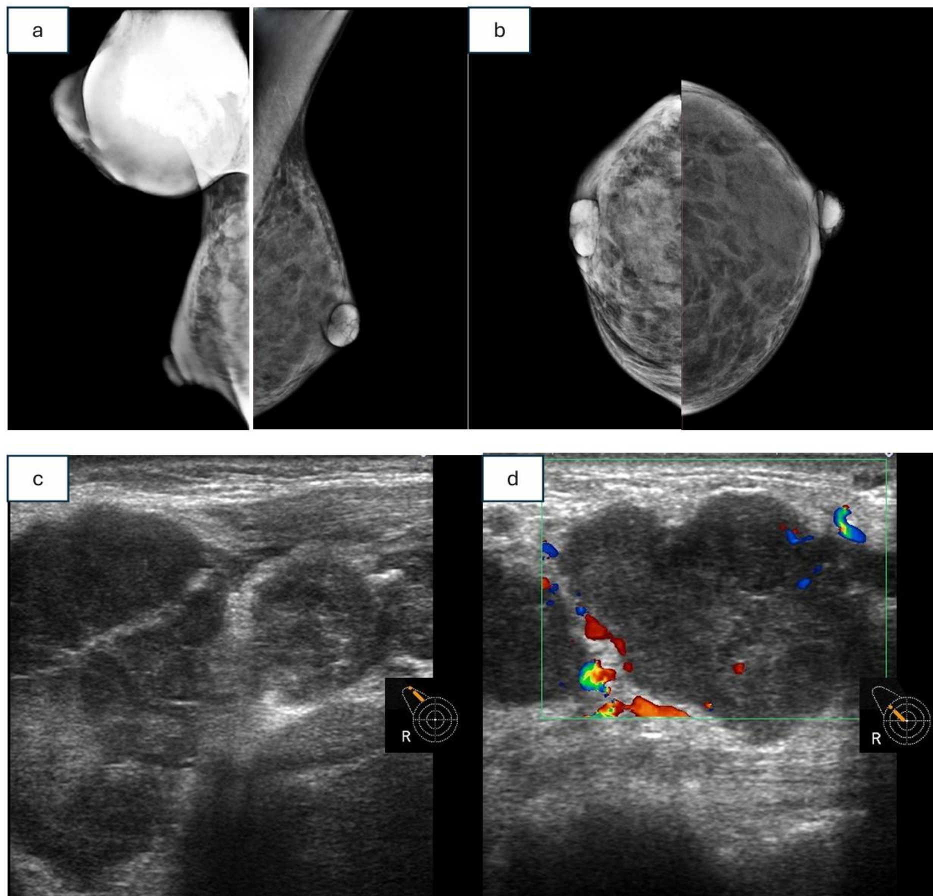

Figure 1. *Mammography features (a) MLO view: Large high-density mass at right upper outer quadrant extending to axilla; (b) CC view: Few high density mass with some indistinct margin of right breast. Ultrasound features; (c) & (d) Lobulated hypoechoic masses at right upper outer quadrant extending to axillary region with increased vascularity on color Doppler flow.*

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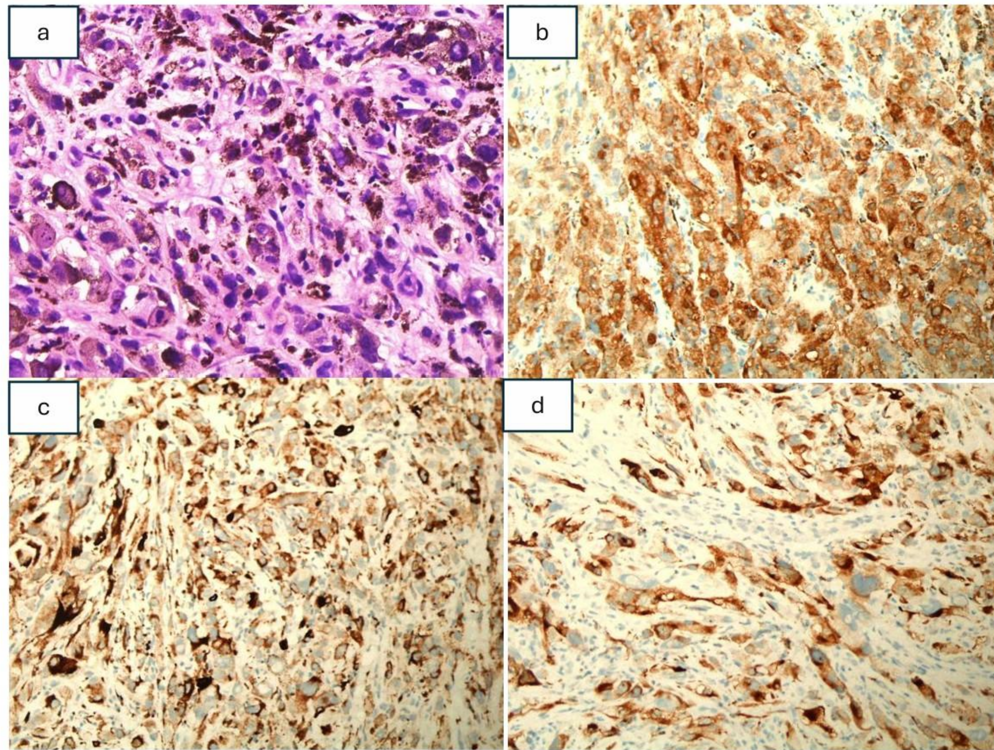

Figure 2. *Pathological morphology features and immunohistochemistry results of the patient. (a) Haematoxylin and eosin-stained section shows presence of markedly pleomorphic, hyperchromatic nuclei with moderate eosinophilic cytoplasm of cells. Several cells demonstrate intranuclei inclusion, cytoplasmic vacuolation and melanin pigmentation. Mitotic figures is evident. Immunohistochemical staining of the tumour cells; (b) S-100, showing nuclear and cytoplasmic positivity. The malignant cells are immunopositive for; (c) HMB-45; and (d) melan-A immunostains.*

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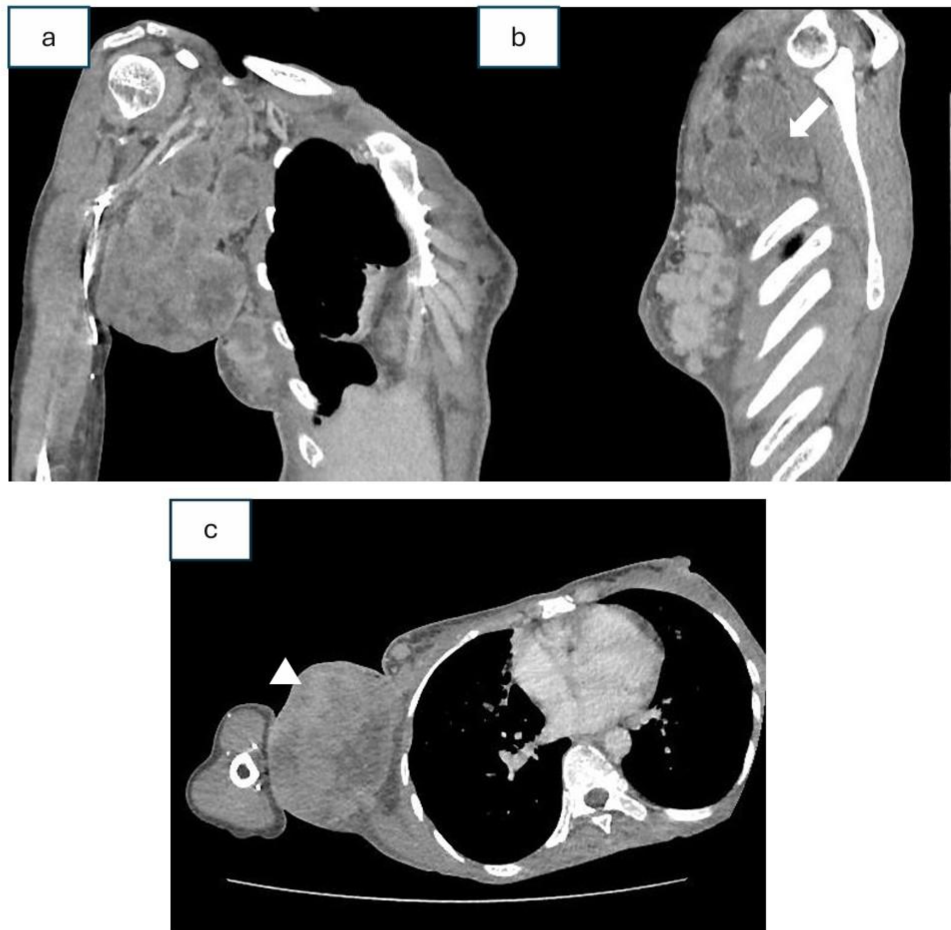

Figure 3. *CT features: (a) coronal oblique; (b) Sagittal; (c) axial: Large lobulated heterogeneously enhancing masses seen predominantly at the outer aspect of the right breast (arrowhead) extending to the right axillary region with some demonstrate hypodensities within suggestive of necrotic centre. Multiple enlarged matted lymph nodes with areas of necrosis within the right axilla (arrow).*

Results and Discussion

Malignant melanoma is a type of cancer involving the melanocyte. It can occur anywhere in the body but is most commonly found in the skin, mucous membranes and choroid. The aetiology of malignant melanoma remains unknown; however, it is generally hypothesised that the accumulation of DNA mutations, most often secondary to UV light radiation from excessive sun exposure, contributes to the melanocyte's loss of division inhibition (Greene and Kunesh, 2024). The occurrence of primary melanoma in the breast is particularly rare, with an incidence of <5% of all malignant melanomas (Rassouli and Voutsadakis, 2016; Alzaraa and Sharma, 2008; Kurul et al., 2005). Malignant melanomas occurring in the breast may be categorised in these three broad categories: (i) Primary cutaneous melanomas of the skin overlying the breast; (ii) primary non-cutaneous melanomas of the breast parenchyma; and (iii) metastatic melanomas to the breast from primary tumours in other cutaneous locations (Rassouli and Voutsadakis, 2016). Extramammary malignancies which metastasis to the breast are rare. More common primary tumours for breast metastases other than primary carcinoma of the contralateral breast are lymphomas, melanomas, rhabdomyosarcomas,

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lung and ovarian tumours (Al Samaraee et al., 2012). Metastatic melanoma lesions may present without skin involvement in the breast. Upper trunk and extremities are the most prevalent primary sites of melanoma metastasize to the breast, whereas the primary lesion involving the lower extremities rarely metastasizes to the breast (Ramli Hamid et al., 2020). Hence, a thorough complete skin examination should be performed in order to exclude the presence of primary. Additional fundoscopic examination, ear nose and throat examination, upper and lower endoscopy may be prudent to exclude breast metastases from mucosal or ocular melanomas (Rassouli and Voutsadakis, 2016). Metastatic malignant melanoma to the breast are more commonly found in the upper outer quadrant due to the presence of more fibroglandular breast tissues and better vascularity as metastasis from melanoma usually occur through haematogenous spread (Al Samaraee et al., 2012). However, up to 66% of primary breast carcinomas are also occur in the upper outer quadrant. Upon presentation of our patient, a palpable right breast lump at upper outer quadrant with no any primary skin lesions mole overlying the breast parenchyma, upper trunk or extremities as well as no prior history of malignant melanoma.

Breast metastases can closely resemble primary breast carcinoma both clinically and on imaging studies, posing diagnostic challenges. On mammography, metastatic melanoma typically appears as well-circumscribed nodular opacities, lacking spiculation, microcalcifications, architectural distortion, or secondary skin and nipple changes (Ramli Hamid et al., 2020). These features reflect the absence of a desmoplastic response, a characteristic feature of primary breast carcinoma. In our patient, the lesion appears to be high-density lesion , lobulated with overlying skin changes and none was associated with microcalcifications, spiculation or architectural distortion. On ultrasound, primary breast malignancies, which often exhibit irregular shapes, heterogeneity, and posterior acoustic shadowing while metastatic melanoma is commonly visualized as rounded or oval hypoechoic masses with well-defined or indistinct margins (Ramli Hamid et al., 2020). The right breast mass at the upper outer quadrant of our patient, appears irregular, hypoechoic with intralesional vascularity. Both primary and metastatic malignancies, however, generally present as hypoechoic, making it difficult to differentiate between benign and malignant lesions or to distinguish metastatic disease from primary carcinoma based on sonographic imaging alone. Despite these imaging characteristics, the radiological findings of metastatic melanoma can overlap with those of primary breast carcinoma. Therefore, histopathological examination, including immunohistochemical staining, is essential for a definitive diagnosis.

Diagnosing primary malignant melanoma of the breast relies heavily on the pathological morphology, immunohistochemistry, electron microscopy, and other diagnostic methods. The following should be noted during diagnosis (He et al., 2014). (i) Pleomorphism and nuclear atypia which the tumour cells exhibit variability in size and shape, along with nuclear abnormalities. (ii) Presence of intracellular pigment granules, however, 6-10% of malignant melanomas have a lack of pigmentation and are classified as amelanotic melanomas (He et al., 2014; Duggal and Srinivasan, 2010). (iii) Immunohistochemical findings with positive expression of S-100, HMB-45, and Melan-A proteins (Bonetti et al., 1991). (iv) Presence of melanosomes and premelanosomes in electron microscopy observations (Taatjes et al., 1993). (v) Absence of transitional tissues between the edge of tumour tissue and normal breast tissue. (vi) Exclusion of metastasis and invasion from adjacent site. Though positive S-100 protein is highly

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sensitive for malignant melanoma, it is also expressed in about 50% of breast cancer cases. Thus, its expression must be confirmed in conjunction with positive results for HMB-45 and Melan-A to establish a definite diagnosis of primary melanoma of breast (He et al., 2014). Based on the clinical examination, histopathological features and results from immunohistochemical staining, the patient was diagnosed with a primary malignant melanoma of the breast. Surgical resection with an appropriate combination of chemotherapy, radiotherapy, immunotherapy and targeted therapy are the primary treatment method of primary malignant melanoma of breast. Our patient is not suitable for surgery as she exhibit extensive right breast mass extending to the axilla with widespread of metastasis, pre-operative chemotherapy was given, Dacarbazine-based treatment plan, though the chemotherapy programme effective rate is only 7-13% (He et al., 2014).

Conclusion

In conclusion, primary malignant melanoma of the breast is an exceptionally rare and aggressive malignancy, presenting unique diagnostic and therapeutic challenges. Its rarity, coupled with clinical and histopathological overlap with other breast tumors, underscores the importance of a thorough, multidisciplinary diagnostic approach. Accurate identification requires the integration of histopathological assessment, immunohistochemical analysis, detailed clinical history, and careful physical examination. Early detection remains pivotal, as timely surgical intervention, complemented by appropriate adjuvant therapies, has a direct impact on patient prognosis and overall survival. The management of this malignancy highlights the necessity for coordinated care among surgeons, oncologists, radiologists, and pathologists. Surgical excision with clear margins, together with sentinel lymph node assessment when indicated, remains the standard of care. Adjuvant modalities, including targeted therapy, immunotherapy, and radiotherapy, can further improve outcomes, particularly in advanced or high-risk cases. Despite these strategies, prognosis continues to be guarded, reflecting the aggressive biology of the tumor and the limited clinical experience due to its infrequency. Advances in molecular profiling and the development of personalized targeted therapies offer promising avenues to enhance management and survival. However, evidence remains limited, emphasizing the need for continued research, prospective studies, and inclusion of patients in clinical trials. A deeper understanding of tumor biology, prognostic markers, and therapeutic responsiveness is essential to refine treatment strategies and optimize patient outcomes. Ultimately, primary malignant melanoma of the breast exemplifies a clinical scenario in which rarity amplifies complexity. Its study demands not only rigorous diagnostic and therapeutic approaches but also collaborative, multidisciplinary engagement. Ongoing research and clinical innovation are crucial to improving understanding, guiding evidence-based management, and ultimately enhancing survival and quality of life for affected patients.

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Conflict of interest

The authors have no conflicts of interest to declare.

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