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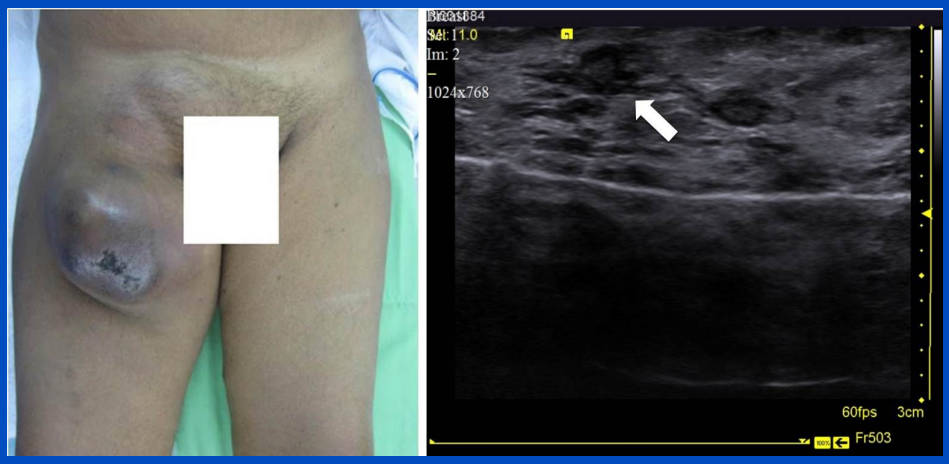
# GIANT MALIGNANT MELANOMA WITH BILATERAL SYNCHRONOUS BREAST CARCINOMAS: A CASE REPORT AND REVIEW OF LITERATURE .

**Bing Wui NG, Mohamed Haflah NOR HAZLA, Mohd Kassim ABDUL YAZID, Sivasamy PARTHIBAN**
**Orthopaedic Oncology Unit, Department of Orthopedics and Traumatology, Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia.**




## ABSTRACT

Incidences of giant melanoma have been well documented. However, the presence of giant melanoma with coexisting breast cancer is scarce. We present a case of a giant malignant melanoma over the right thigh with synchronous presentation of bilateral breast carcinoma in a patient. Unfortunately, excision of the melanoma and mastectomy did not prevent disease progression and resulted in metastasis of the melanoma to the lungs and brain. Despite aggressive treatment involving surgery, immunotherapy and chemoradiotherapy, this patient succumbed to the illness fourteen months after the detection of the lumps. This case serves to highlight the sinister nature of the disease, possible association of melanoma with breast cancer and its high recurrence and mortality rate.

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## ABSTRACT

Incidences of giant melanoma have been well documented. However, the presence of giant melanoma with coexisting breast cancer is scarce. We present a case of a giant malignant melanoma over the right thigh with synchronous presentation of bilateral breast carcinoma in a patient. Unfortunately, excision of the melanoma and mastectomy did not prevent disease progression and resulted in metastasis of the melanoma to the lungs and brain. Despite aggressive treatment involving surgery, immunotherapy and chemoradiotherapy, this patient succumbed to the illness fourteen months after the detection of the lumps. This case serves to highlight the sinister nature of the disease, possible association of melanoma with breast cancer and its high recurrence and mortality rate.

**Keywords: Breast Neoplasm, Immunotherapy, Melanoma, Radiotherapy, Synchronous Neoplasm.**

## INTRODUCTION

The natural history of melanoma should not be underestimated due to its misnomer. Neglected naevi has the potential to grow to enormous size, giving rise to 'giant melanoma'. Various authors have defined giant melanoma as lesion greater than ten centimetres in size regardless of tumour depth.[1] A growing tumour this size is hard to be ignored by patients thus making giant melanoma a rare entity. Case reports have been published on giant melanoma found on scalp, anterior chest wall and abdomen.[2,3] Recurrence and survival rate of patients with melanoma is closely associated with tumour depth and presence of metastasis.[4,5] Presence of melanoma with other malignancies has been reported. Studies have shown that the incidence of melanoma is closely related to breast cancer.[1] We would like to present a case of giant melanoma of the extremity which presented concurrently with breast cancer.

**Correspondence**: Dr. Ng Bing Wui, Orthopaedic Oncology Unit, Department of Orthopedics and Traumatology, Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia.
email address: bingwuing@gmail.com

## CASE REPORT

A 59 years old lady presented to our centre on February 2017 with chief complaint of right thigh swelling which was progressively increasing in size for the past 4 months. Additionally, she also complaint of bilateral breast swelling and constitutional symptoms. Further family history revealed that patient's mother had breast cancer. On examination, there was a multi-lobulated swelling at the right thigh

extending up to the right inguinal region measuring 20cm x 10cm (Figure 1a). The overlying skin was bluish with an area of ulceration over the tip of the swelling. The margins were well defined, firm on palpation, adhered to the overlying skin and fixed. Both left and right inguinal lymph nodes were not palpable. Examination of the breasts showed multiple swellings over right upper quadrant of right breast with the biggest measuring 2cm x 3cm, firm, mobile with no overlying skin changes. No palpable swelling of left breast. Both axillary lymph nodes were palpable.

In view of high index of suspicion for malignancy, urgent radiological imaging was done. Radiographs of the right femur showed soft tissue opacity over the proximal femur with no bony changes. Staging computer tomography of thorax, abdomen and pelvis revealed multiple lobulated heterogeneously enhancing subcutaneous mass over the right inguinal region with necrotic centre. No distant metastasis was found. Magnetic resonance imaging of the lower limb and pelvis showed multiple large complex subcutaneous solid cystic mass with necrotic areas at the right hip suggestive of soft tissue sarcoma with adjacent nodal metastasis. An urgent incisional biopsy was performed under local anaesthesia and immunohistochemical studies of the sample showed malignant cells suggestive of melanoma.

She was referred to the Breast and Endocrine unit for management of breast lumps. Both mammogram and ultrasound showed irregular high-density mass over right upper quadrant of right breast associated with micro and macrocalcification (Figure 1b). There was also an irregular hypoechoic lesion at 2 o'clock position of left breast. Ultrasound guided biopsy of both breast lumps were carried out and histology confirmed invasive carcinoma of no special type Bloom and Richardson grade 1 for the right breast lump and intraductal papilloma with ductal hyperplasia for the left breast lump.

Patient underwent excision of the right thigh giant melanoma under general anaesthesia. Due to limitation of tissue for closure, the tumour was excised en-bloc with minimal margins of 1mm. Intra-operatively, the swelling was found to be adhering to the underlying fascia of the right thigh (Figure 2a and 2b). Proximally, the mass extended up to

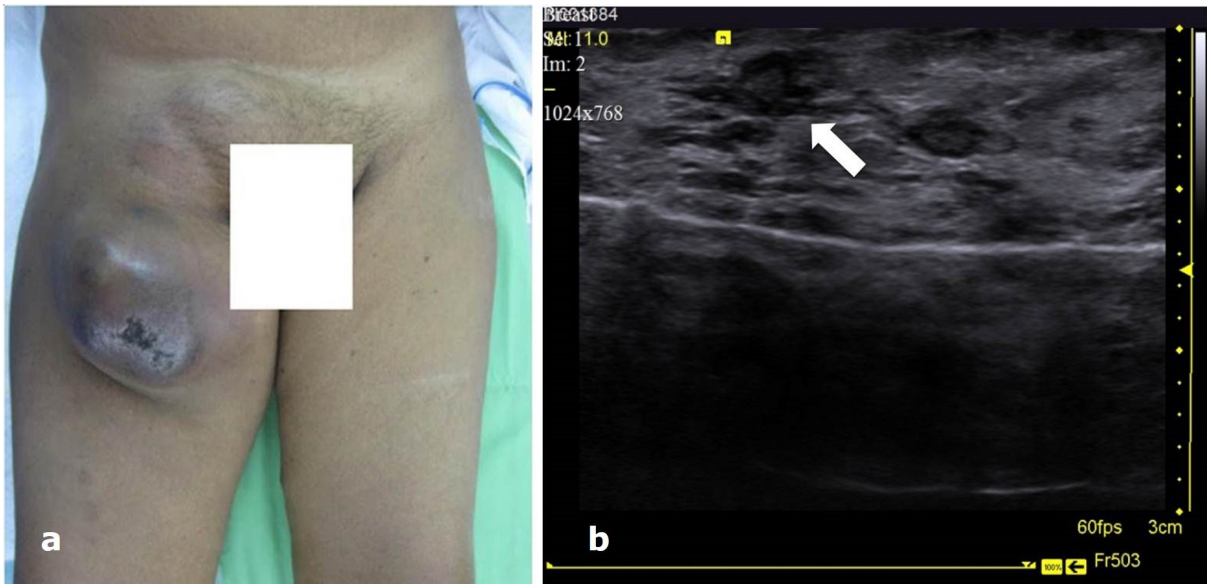


**Figure 1: (a) Clinical picture showing large bluish mass over anterior aspect of right proximal thigh with lobules extending up to right inguinal region, : (b) Ultrasound images showing irregular high density mass at right breast.**

**Figure 2: (a) Excised giant melanoma of the right thigh measuring approximately 27cm x 15cm, (b) bisected tumour with black tarry gelatinous centre.**

the inguinal region close to the femoral neurovascular bundle. Inguinal lymph nodes could not be identified intraoperatively. Immunohistochemical studies show that the malignant cells are diffusely positive for S-100, HMB-45 and Melan A consistent with melanoma.

In addition, right mastectomy with axillary lymph nodes clearance and left hook wire localization with wide local excision and sentinel lymph node biopsy was performed by breast and endocrine team 2 weeks after the initial surgery. Immunohistopathological examination showed right breast ER-negative, PR-negative and HER-positive (2+). Right axillary lymph nodes dissection was negative for malignancy. No malignancy was found in sentinel lymph nodes.

Two months post-surgery, patient noted multiple hyperpigmented nodules over right thigh and along the surgical scar (Figure 3a). Positron Emission Tomography (PET) was performed which showed large melanomatous mass at the right inguinal and upper thigh region with local and distant extensive metastases to the thigh, lymph nodes of right femoral, right external iliac, popliteal, mediastinal, supraclavicular and lung (Figure 3b). The patient was started on immunotherapy by the oncologist in view of disseminated disease. One cycle of Pembrolizumab 100mg was prescribed as first line but as a result of poor response to treatment she was then put on 4 cycle of IV Dacarbazine 500mg/m$^2$. Sadly, swift clinical progression of disease was noted with rapid increase of cutaneous lesion and worsening of ulceration (Figure 4a and 4b). CT brain was done in October 2017, 4 months after the initiation of chemotherapy as patient developed fluctuating consciousness. It showed multiple brain metastases. Radiotherapy was commenced but with minimal clinical improvement. Patients' family opted for palliative care in view of her deteriorating condition and poor response to treatment. Regrettably, she succumbed to the illness on December 2017, 14 months after first noticing the swelling over her right thigh.

## DISCUSSION

Giant melanoma is defined as a melanoma with size greater than 10cm.[1] Such lesions

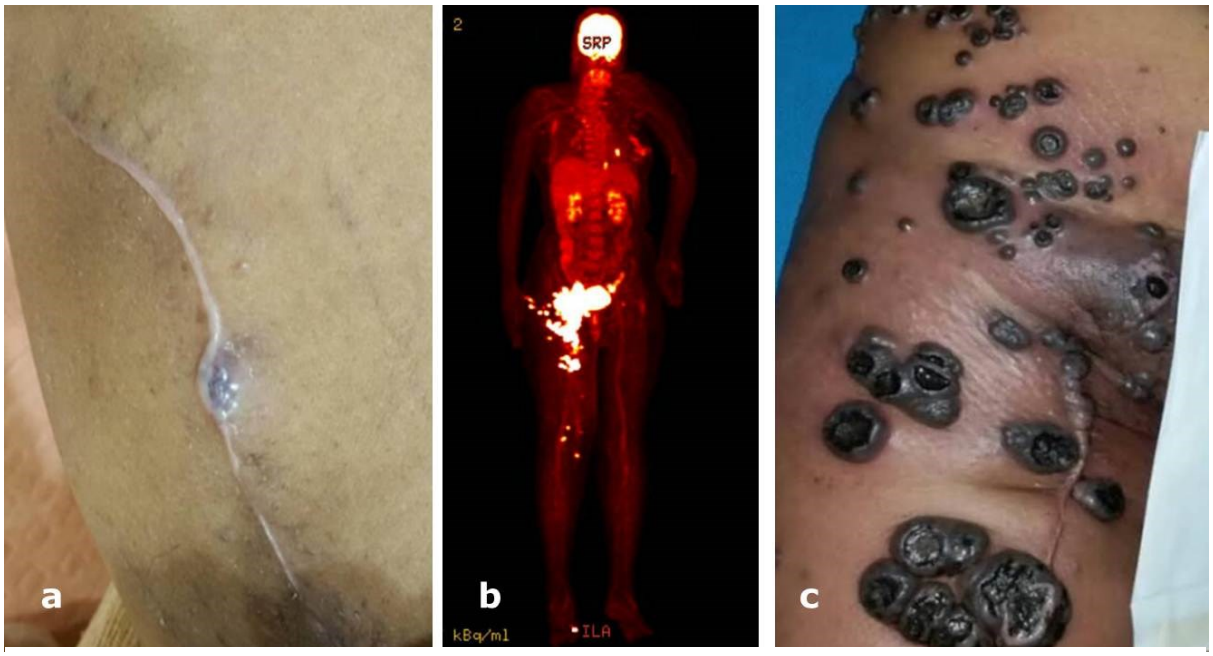


**Figure 3: (a) Pigmented naevus along surgical scar noted 2 months after surgery, (b) PET CT scan showing recurrence of melanoma deep in the right thigh with distant metastases, (c) recurrence of multiple hyperpigmented and ulcerated skin melanomas 4 months after surgery, despite receiving chemotherapy.**

were reported to take 6 months to 15 years to reach the mentioned size.[1] Most cases would present with extensive regional lymph nodes involvement by the time of diagnosis. Sentinel lymph nodes dissection as a staging procedure was suggested in patients with no palpable lymph nodes or lymph node not picked up by sonography. However the practise is not standardized as it depends heavily on surgeon expertise and histological techniques.[6] Radical dissection of clinically-identified lymph node with metastasis is considered a standard procedure but was not found to improve overall survival.[7] Wide local excision of the primary tumour was found to be effective and carries good prognosis if no metastatic lesion was detected.[6,8] Based on guidelines published by multiple countries, the excision margin recommended for a melanoma with Breslow thickness of more than 2.0mm is 2cm.[6] Studies have also shown that incisional biopsies does not worsen prognosis when compared with immediate complete excision. Few studies suggested that margin of excision has a direct effect on local and regional recurrence but more research is still needed to support the effect of margin on patient survival.[6] Complete removal of distant metastasis should be the choice of treatment when possible especially in cases with normal range protein S100B and tumour markers LDH.[9]

Radiotherapy could help to reduce recurrence of melanoma after surgical excision but could not prolong prognosis. Radiotherapy to primary tumour is also rarely indicated.[6] Indications for radiotherapy includes extra-nodal disease and involvement of multiple or large nodes.[10] Radiotherapy is also used to control symptom in patients with brain metastases. Both surgical excision or radiotherapy can be used for solitary or small sized brain lesion.[6]

Adjuvant therapy is used in patients with possible microscopic metastases. Various drugs have been researched for the use of melanoma treatment. In recent years, the use of interferon-alpha has been declining due to lack of clear survival benefit but was offered for the reduction in relapse-free survival.[11] Ulceration of primary tumour was found to be one of the factors in determining Interferon

sensitivity. Low effectiveness of interferon was found in patients with a non-ulcerated primary tumour.[12] Checkpoint inhibitor such as anti-cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) has shown to improve overall survival for patients with unresectable metastatic melanoma.[13] PD-1 antibodies such as Pembrolizumab and Nivolumab have shown improvement in progression free survival and overall survival in clinical trials.[14,15] Meanwhile, studies of new agents such as the use of Vemurafenib alone or Dabrafenib and Trametinib is still on going. Chemotherapy using Dacarbazine is still used in some country where the newer drugs are not available.[6]

Recent publications have shown the possible bi-directional association of malignant melanoma and breast cancer. Murphy et al did a cross-reference analysis from the National Irish Cancer Registry in 2009 and found a fourfold increase in number of cases of patients having both malignant melanoma and breast cancer.[16] Scientists have searched for possible genetic and hormonal causes to this association. Goggins et al in his study found that female patients with breast cancer (below 50 years of age) has a 46% risk of having a subsequent cutaneous melanoma. They also detected a 19% increase risk of a patients with cutaneous melanoma to get a second breast cancer.[17] Few other studies have explored the possibility of a genetic influence, specifically the BRCA2 genes and mutation of CDKN2A genes.[18,19] Cooper et al in their study found that up to 70% of patients with history of melanoma who underwent fine-need biopsy looking for possible melanoma metastatic disease has another epithelial tumour such as carcinoma of the breast, prostate or large bowel.[20]

In this case, a PET scan during the earlier stage for diagnosis of metastasis would be advantageous however it could not be done due to financial constraint. Post-operative radiotherapy for the inguinal region was not scheduled as patient had to undergo excision of breast lumps 2 weeks after the initial surgery and there are concerns regarding possibility of bleeding at the operation site.

## CONCLUSION

In conclusion, we would like to emphasize that public should be aware of the highly malignant nature of melanoma that warrants early detection and aggressive multidisciplinary management needed to ensure success in treatment and prevent recurrence. It is of utmost importance that a melanoma should not be taken lightly as a benign lesion. Signs suggesting of a sinister naevus include changing in colour, increase in size, bleeding, pruritus, ulceration and pain. First line treatment of extensive surgical excision, amputation of distal digits or limb during the early stage of localized disease could markedly improve patients' outcome. With this case report, we too stress upon the importance of medical fundamentals such as detailed history taking and thorough examination for detection of synchronous carcinoma as evident in this patient.

**Declaration:**
**There is no financial or other relationships which is present that might lead to a conflict of interest.**

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