

Brain Metastasis from Breast Cancer in a Male Patient

Bir Erkek Hastada Meme Kanserinin Beyin Metastazı

^{ID} Bee Chen LUA^a, ^{ID} Wan Zainira WAN ZAIN^a, ^{ID} Kok Bing NELSON YAP^b,
^{ID} Andee Dzulkarnaen ZAKARIA^a, ^{ID} Firdaus HAYATI^c

^aDepartment of Surgery, Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, MALAYSIA

^bDepartment of Neurosurgical, Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, MALAYSIA

^cDepartment of Surgery, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Sabah, MALAYSIA

ABSTRACT Male breast cancer is a rare disease and has contributed to <1% of all cancers in the male population. Delay in diagnosis is common, due to its rarity and lack of awareness of the disease among the male patient and physicians. Most cases were detected at an advanced stage and up to 30% of them were diagnosed with metastasis on the initial presentation. The authors presented a case of a 60-year-old man who presented with seizure and right hemiparesis. In addition, he also has left breast mass for one year. Computed tomography of the brain showed a left frontal intra-axial brain lesion and biopsy of the breast lesion confirmed triple-negative invasive breast cancer. He was planned for whole-brain radiotherapy, however, he succumbed prior to the treatment.

Keywords: Male breast cancer; metastasis; triple negative breast cancer

ÖZET Erkeklerde meme kanseri nadir bir hastalıktır ve erkek nüfusta tüm kanserlerin %1'inden azına katkıda bulunur. Nadir görüldüğü için ve erkek hastalar ve doktorlar arasında farkındalık olmadığı için tanıda gecikme sıklıkla görülür. Olguların çoğu ileri evrede tanı alır ve %30'u ilk olarak metastazla karşımıza çıkar. Yazarlar nöbet ve sağ hemiparezi ile başvuran 60 yaşında bir erkek hastayı sunmuştur. Ayrıca, hastanın bir yıldır sol memede kitlesi vardır. Beynin bilgisayarlı tomografisinde sol frontal intra-aksiyal beyin lezyonu saptanmış olup memedeki lezyonun biyopsisi sonucunda üçlü negatif invazif meme kanseri tanısı doğrulanmıştır. Tüm beyin radyoterapisi planlanmıştır ancak hasta tedaviye başlamadan önce hastalığa yenik düşmüştür.

Anahtar Kelimeler: Erkeklerde meme kanseri; metastaz; üçlü negatif meme kanseri

Male breast cancer is rare and accounts for 1% of all malignant breast neoplasm cases.^{1,2} Male breast cancer has many differences from female breast cancer in terms of age of diagnosis, frequency of histological subtype and hormonal receptor expression frequency.³ Male breast cancer has a peak incidence at the age of 71 years in comparison to female breast cancer, which shows bimodal age frequency distribution with a peak incidence at the age of 52 and 72 years respectively.^{4,5} Oestrogen and progesterone receptor expression are higher in men (90% and 81%, respectively) than women (with 90% and 81% in men whereas 76% and 66.7%, respectively).⁴ Due to the absence of lobules in men, invasive lobular cancer is uncommon with an incidence of about 1%.⁶

Several risk factors including genetic, hormonal, occupational and/or environmental exposure are associated with male breast cancer.^{1,2,7} Nearly 15% of male breast cancers are familial with BRCA2 is the strongest.⁵ Apart from that, gene mutation of androgen receptor (AR), CHEK 2, and PTEN have been reported as well.⁵ Other associations of male breast cancer such as anti-androgen therapy in prostate cancer, liver cirrhosis, obesity, exposure exogenous estrogen and testicular trauma or abnormality which alter estrogen-testosterone ratio have increased the risk of developing breast cancer in men.⁷ Men with Klinefelter's syndrome, which are associated with low testosterone level, carry a 50-fold increase in the risk of developing breast cancer and had contributed

Correspondence: Firdaus HAYATI

Department of Surgery, Faculty of Medicine and Health Sciences, Kota Kinabalu, Sabah, MALAYSIA

E-mail: firdaushayati@gmail.com



Peer review under responsibility of Türkiye Klinikleri Journal of Medical Sciences.

Received: 06 May 2020 **Accepted:** 26 Jun 2020 **Available online:** 22 Sep 2020

2146-9040 / Copyright © 2020 by Türkiye Klinikleri. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

to 3% of all male breast cancer cases.⁷ Prolonged exposure to high ambient temperature may also lead to testicular failure and an increased risk of male breast cancer.⁷ Exposure to external radiation such as treatment of Hodgkin disease had been identified as one of the risk factors also.⁵

Subareolar mass is the most common clinical presentation and accounted for 80-95% of the cases. Skin ulceration and nipple discharge have been reported in 45% and 10% of the cases respectively.¹ These symptoms are more common in males due to the unique male breast anatomy.⁵ Herein, we describe a 60-year-old man with left breast triple-negative invasive ductal carcinoma who presented with seizure and right hemiparesis.

CASE REPORT

A 60-year-old male smoker presented with 6 episodes of generalized tonic-clonic seizures, each lasted for 5 minutes and self-aborted before admission. He also complained of progressive right-sided body weakness for the past 1 month and required some assistance in daily activities. On further questioning, he was learned to have a left breast swelling for a 1-year duration which had been increasing in size for the past 5 months (Figure 1). He also had a loss of appetite and loss of weight. There was no family history of breast cancer and other risk factors.

Upon examination, his vital signs were normal. There was a left breast mass measuring 10 x 10 cm in size with irregular surface, hard in consistency, fixed to both underlying muscle and overlying skin. There was no axillary lymph node palpable. Neurological examination showed hypertonia and hyperreflexia

over the right upper and lower limbs. Muscle power over the right upper and lower limb was 1/5. Babinski sign was positive and clonus was present over his right lower limb.

Trucut biopsy of his left breast lesion was consistent with triple-negative invasive breast carcinoma. Contrast-enhanced computed tomography (CT) showed a left breast lesion with an erosion of adjacent ribs, intrathoracic extension, and distant metastases to the adrenal gland, lungs, and spine (Figure 2). A CT of the brain revealed left frontal intraaxial lesion measuring 1.6 x 2.3 x 1.6 cm with perilesional edema (Figure 3).

He was initially offered surgical resection of the brain lesion but he refused and subsequently discharged against medical advice. Two weeks later, he presented again with fever and another episode of seizures. He was admitted and treated as hospital-acquired pneumonia. He became confused and was unable to obey a command. His general condition deteriorated further. Repeat brain CT showed worsening of cerebral edema with a midline shift of 2 cm. He was then planned for whole-brain radiotherapy (WBRT). Unfortunately, he succumbed to his illness before radiotherapy was rendered.

DISCUSSION

It has been reported that about 93% of the male breast cancers were diagnosed at an advanced stage, in which 30% were diagnosed with metastasis as the first presentation.¹ This was probably because of a lack of awareness among men leading to the delay in seeking treatment. The reported common sites of metastasis in male breast cancer are bones (48.78%),

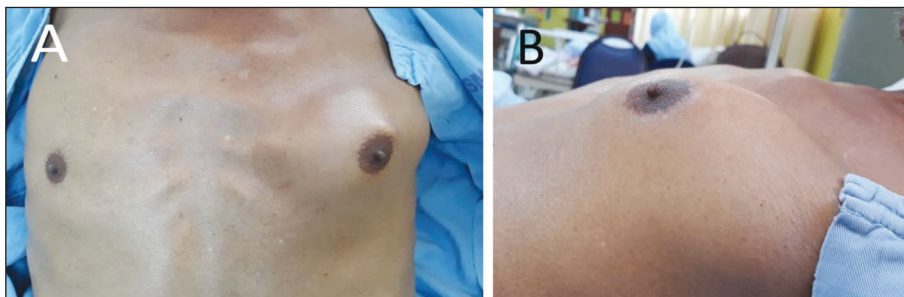


FIGURE 1: Examination showing an anterior (A) and lateral (B) view of left breast lesion which measures 10x10 cm, without ulceration and satellite nodules.

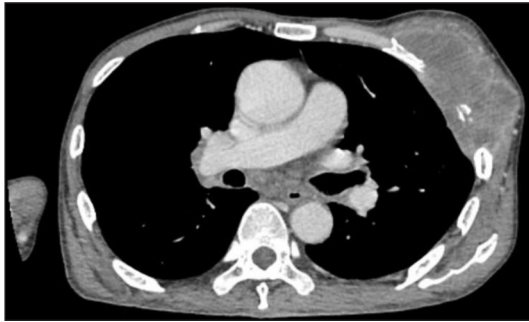


FIGURE 2: Contrast enhanced CT of the thorax showing a lobulated, heterogeneously enhancing mass occupying the whole left breast measuring 11.1x4.7x9.2 cm with ribs erosion and intrathoracic extension.

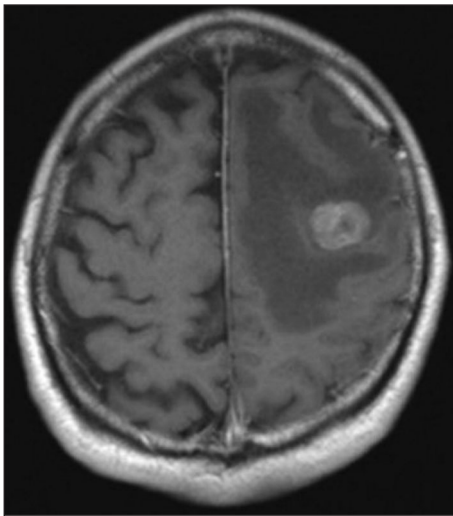


FIGURE 3: Contrast enhanced CT of the brain at axial cut showing a space-occupying lesion measuring 1.6x2.3x1.6 cm over the left precentral gyrus with perilesional edema.

lungs (29.26%), liver (17.07%), spine (30%) skin and pleura.¹ Metastasis to the brain (11.8%) had been reported in the study conducted by Uslukaya et al.⁶ Due to the anatomy of the male breast, skin involvement is common.⁴ In this case, the patient had a breast lump for a few months, but he sought treatment only after he developed seizures due to brain metastasis.

Brain metastasis in breast cancer carries significant mortality and morbidity rates. Hence, a few prognosis scoring systems have been developed to predict overall survival for breast cancer patients with brain metastasis in order to prevent overtreatment in poor prognosis patients and allowing more aggressive therapy to be chosen for the patient with

a better prognosis.⁸ These scoring systems were breast-specific Graded Prognostic Assessment (Breast-GPA) which was developed by Sperduto et al. and modified-GPA which was used in a study conducted by Subbiah et al. Breast specific GPA consists of age (<60 years old or above), tumour subtype (basal, luminal A, HER 2, luminal B) and Karnofsky performance status, whereas in modified breast-GPA index which includes number of brain metastasis (>3 or 1-3) as the variable into breast specific GPA.⁹⁻¹¹

There are lacking reports on male breast cancer with brain metastasis. Therefore, the treatment of it is deemed reasonable based on the information of female breast cancer treatments.^{4,11,12} Treatment options for brain metastasis in breast cancer patients are surgery, radiotherapy (WBRT or stereotactic radiosurgery), systemic therapy or a combination.¹³ Surgery is recommended in large (>3 cm) solitary brain lesions with surgically accessible location.^{8,14} Surgical excision is able to reverse neurological deficit rapidly, provides tissue diagnosis and able to reduce the duration of steroid dependency as well.¹⁴ Stereotactic radiosurgery is used in multiple metastases.¹⁻⁴ with a diameter of 3 cm or less or inoperable tumour (deep eloquent brain area).^{8,14} For a patient with poor prognosis or poor performance status and multiple metastases, WBRT remains the standard treatment to control symptoms and improve neurological deficit. WBRT has also been used in the treatment of disease with leptomeningeal involvement. Systemic treatment includes chemotherapy, HER-2 targeted therapy for HER-2 positive breast cancer and endocrine treatment for the hormonal receptor-positive disease.¹⁴

In the aforementioned case, the excision of the brain tumour was planned initially as it is a solitary lesion with significant perilesional oedema causing the neurological deficit. Surgery could reduce cerebral oedema rapidly after tumour removal, improve his hemiparesis and reduce the frequency of seizure, thus improving the quality of life. However, his general condition deteriorated on the second admission and his modified breast-GPA index was 0.5 (Karnofsky score 20, triple negative, 60 years old and 1 brain metastasis). The overall survival for a patient with a

modified breast GPA score 0-1 is 2.6 months.¹¹ In view of his poor performance state and poor prognosis, WBRT was planned.

Mastectomy with axillary lymph node dissection is the primary local regional treatment for male breast cancer. Sentinel lymph node has been accepted as one of the treatments for a patient with clinically negative axillary lymph node disease.^{2,13} Axillary lymph node involvement is a strong predictor for the risk of local and distant recurrence.⁶ The 5 years overall survival rate in negative lymph node disease is 100%, whereas the overall survival rate reduced to 79.9% in N1 disease, 66.7% in N2 and 25% in N3 disease.³ Post-operative radiotherapy reduces the local recurrence rate. It is recommended for a patient with skin or pectoralis muscle or areolar involvement, inadequate surgical margin and lymph node involvement.⁵ Adjuvant or neoadjuvant systemic therapy such as chemotherapy with or without HER-2 targeted therapy can be considered in male breast cancer. Tamoxifen or GnRH analog with aromatase inhibitor is the option of adjuvant endocrine therapy in male breast cancer. The use of an aromatase inhibitor alone is not recommended because of its inferior outcome.¹³ Tamoxifen has few side effects such as venous thrombosis, cataract, hot flush and sexual dysfunction.²

The patient, in this case, had triple-negative stage IV breast cancer, treatment for him was chemotherapy. However, initiation of chemotherapy depends on the patient's general condition. The overall prognosis in male breast cancer is worse than female breast cancer due to the old age of diagnosis, multiple comorbidities and extent of disease at diagnosis.^{3,5}

CONCLUSION

Awareness of male breast cancer among physicians and populations is important in order to detect and treat the disease at an early stage. Late presentation correlates with poor prognosis. Tumour subtype in breast cancer is an important prognostic parameter in brain metastasis patients and it guides the treatment options as well.

Informed Consent

Informed consent was taken from the next of kin for this case report.

Acknowledgement

We would like to thank those who have involved in preparation of this manuscript.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Bee Chen Lua; **Design:** Wan Zainira Wan Zain; **Data Collection and/or Processing:** Kok Bing Nelson Yap; **Literature Review:** Kok Bing Nelson Yap; **Writing the Article:** Bee Chen Lua; **Critical Review:** Andee Dzulkarnaen Zakaria; **Other:** Firdaus Hayati.

REFERENCES

1. Badke GL, de Aguiar GB, de Almeida Silva JM, Campos Paiva AL, da Silva EU, Esteves Veiga JC. Cerebral metastasis from breast cancer in a male patient with HIV. *Case Rep Neurol Med.* 2015;2015:482839. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
2. Giordano SH. Breast cancer in men. *N Engl J Med.* 2018;378(24):2311-20. [[Crossref](#)] [[PubMed](#)]
3. Yoney A, Kucuk A, Unsal M. Male breast cancer: a retrospective analysis. *Cancer Radiother.* 2009;13(2):103-7. [[Crossref](#)] [[PubMed](#)]
4. Madeira M, Mattar A, Passos RJB, Mora CD, Vilar Mamede LHB, Kishino VH, et al. A case report of male breast cancer in a very young patient: what is changing? *World J Surg Oncol.* 2011;9:16. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
5. Zygiogianni AG, Kyrgias G, Gennatas C, Ilknur A, Armonis V, Tolia M, et al. Male breast carcinoma: epidemiology, risk factors and current therapeutic approaches. *Asian Pac J Cancer Prev.* 2012;13(1):15-9. [[Crossref](#)] [[PubMed](#)]
6. Uslukaya Ö, Gümüş M, Gümüş H, Bozdağ Z, Türkoğlu A. The management and outcomes of male breast cancer. *J Breast Health.* 2016;12(4):165-70. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
7. Johansen Taber KA, Morisy LR, Osbahr 3rd AJ, Dickinson BD. Male breast cancer: risk factors, diagnosis, and management (Review). *Oncol Rep.* 2010;24(5):1115-20. [[Crossref](#)] [[PubMed](#)]
8. Frisk G, Tinge B, Ekberg S, Eloranta S, Bäcklund LM, Lidbrink E, et al. Survival and level of care among breast cancer patients with brain metastases treated with whole brain radiotherapy. *Breast Cancer Res Treat.* 2017;166(3):887-96. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
9. Sperduto PW, Kased N, Roberge D, Xu Z, Shanley R, Luo X, et al. Summary report on the graded prognostic assessment: an accurate and facile diagnosis-specific tool to estimate survival for patients with brain metastases. *J Clin Oncol.* 2012;30(4):419-25.
10. Grubb CS, Jani A, Wu CC, Saad S, Qureshi YH, Nanda T, et al. Breast cancer subtype as a predictor for outcomes and control in the setting of brain metastases treated with stereotactic radiosurgery. *J Neurooncol.* 2016;127(1):103-10. [[Crossref](#)] [[PubMed](#)]
11. Subbiah IM, Lei X, Weinberg JS, Sulman EP, Chavez-MacGregor M, Tripathy D, et al. Validation and development of a modified breast graded prognostic assessment as a tool for survival in patients with breast cancer and brain metastases. *J Clin Oncol.* 2015;33(20):2239-45. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
12. Nieder C, Jost PJ, Grosu AL, Peschel C, Molls M. Report of a male patient with brain metastases from breast cancer. *Breast.* 2003;12(5):345-7. [[Crossref](#)]
13. NCCN (National Comprehensive Cancer Network). "Breast Cancer Guidelines." 2019. Retrieved on 1 May, 2020, from [[Link](#)]
14. Zagar TM, Van Swearingen AED, Kaidar-Person O, Ewend MG, Anders CK. Multidisciplinary management of breast cancer brain metastases. *Oncology (Williston Park).* 2016;30(10):923-33.