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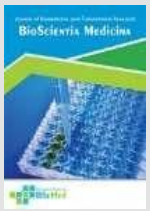

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# Male Breast Cancer in Dr. Hasan Sadikin General Hospital: A Serial Case

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**A B S T R A C T**

**Background:** Male breast cancer is a rare case. It accounts for 1% of all breast cancer cases. Both female and male breast cancers were influenced by the same risk factors. Male breast cancer patients are typically associated with advanced stages, higher grades, higher prevalence of hormone receptor-positive, and a worse prognosis. Many factors can explain the late diagnosis in men: absence of screening programs, lack of awareness about the condition by the male population, embarrassment due to a stigmatization of the disease, and misjudgment by primary care physicians. The aim of study is to improve the knowledge about the biology tumor and characteristics, risk factor, and management of male breast cancer. **Case presentation:** Two patients who were studied were a man with 50 years old, without malignancy on their family and testicles disease. First patients was diagnosed with mucinous adenocarsinoma grade II on right breast luminal A subtype T4bN0M0 and second patient was diagnosed with Ductal carcinoma in situ on right breast luminal B Her2 negative subtype TisN0M0 as preoperative diagnosis and Invasive solid papillary carcinoma grade III on right breast T2N0M0 as post operative diagnosis. Both of them were operated with modified radical mastectomy. First patient was given neoadjuvant chemotherapy, adjuvant chemotherapy and tamoxifen as endocrine therapy. Second patient was given adjuvant chemotherapy and tamoxifen as endocrine therapy. **Conclusion**: Both of patients on serial cases are male breast cancer with hormone receptor positive and they were given endocrine therapy. The majority characteristic of male breast cancer was hormone receptor-positive. Management of male breast cancer is similar overall to management of female breast cancer in modality surgery, chemotherapy, endocrine therapy, and radiotherapy.

## 1. Introduction

Breast cancer is one of the most common malignant tumors and the leading cause of cancer-related death in women worldwide. In 2018, there were an estimated 2.1 million new cases of breast cancer and 627,000 deaths from breast cancer worldwide. Though it is rare, breast cancer in men accounts for 1% of all breast cancer cases.[1] According to Surveillance, Epidemiology, and End Results (SEER) data, male breast cancer incidence rose by 40% from 1975 to 2015, exceeding that of women by 25%. The American Cancer Society estimated that in 2019, 2670 new cases of male breast cancer would be diagnosed in the United States, with 18% mortality. The number of diagnosed cases of male breast cancer increased over the past 2 decades, which highlights the need to raise awareness of this disease in the community.

Diagnosis of biomarkers such as ER, PR, and HER2 through early screening could guide clinicians for better prognoses and outcomes. In fact, some studies have suggested that more male breast cancer patients are diagnosed with advanced disease compared to women due to a lack of awareness of screening for breast cancer in men. In addition, there is a lack of

randomized trials aimed at patients with male breast cancer. Though male breast cancer is different from female breast cancer, some of the molecular markers are present in both sexes. Large multicenter trials are required to understand the disease and determine the most effective therapies. Additional information related to treatment, biological attributes, and lifestyle (e.g., smoking, drinking, body mass index) could be assessed to develop treatment tailored for men with breast cancer.[2]

## 2. Case Presentation

### Case 1

A man, 50 years old, was admitted on October 2022 due to a lump on his right breast. He had a chief complaint lump on his right breast since 1,5 years ago. He didn't feel pain and bloody discharge on his nipple, without malignancy in his family history and testicle disease. He didn't feel lumps on his right axilla, supraclavicle, infraclavicle, and parasternal. From the physical examination, we found nipple retraction, a lump with size 18x15x8 cm, regular margin, solid, hard consistency, skin dimpling, peau de orange, and it didn't attach to the chest wall. The patient was not coughing, had dyspnea, pain in his abdomen, headache, history of seizures, bone pain, and extremity weakness. Breast ultrasonography found a solid mass on the right breast, regular margin, posterior shadowing, calcification, and without lump on the left breast, right and left axilla, right and left parasternal, supraclavicle, and infraclavicle. Pathology anatomy results from core biopsy were mucinous adenocarcinoma with luminal A subtype. He was diagnosed with mucinous adenocarcinoma grade II right breast luminal A subtype. Chest radiography and liver ultrasonography were not found signs of metastasis. He was given docetaxel carboplatin 4 cycles with partial response, and then a right modified radical mastectomy (MRM) was performed. Pathology anatomy results from the operation sample found mucinous carcinoma, with 1 axillary lymph node invasion from 5 lymph nodes, and free tumor margin incision, without DCIS structure, microcalcification, and lymphovascular invasion. After the operation, the patient was given adjuvant chemotherapy docetaxel carboplatin 2 cycles and tamoxifen 20 mg for 5 years.

Figure 1. Physical examination. A lump on the right breast with nipple retraction, size 18x15x8 cm, regular margin, solid, hard consistency, and it didn't attach to the chest wall.

Figure 2. Sample from right modified radical mastectomy with nipple retraction, skin dimpling, peau de orange, and no lymph node palpable.

**Case 2**

A man, 50 years old, was admitted on February 2023 for controlling a lump in his right breast to the oncology surgery department. He was referred from Bandung General Hospital with a chief complaint lump on his right breast 1 year ago. He didn't feel pain and bloody discharge on his nipple without malignancy in his family history and testicle disease. From the physical examination, we found a lump with size 3x3x2 cm, regular margin, solid, hard consistency, without nipple retraction, skin dimpling, and peau de orange, and it didn't attach to the chest wall. We didn't find a lump on his right axilla, supraclavicle, infraclavicle, dan parasternal. The patient didn't sigh, cough, dyspnea, pain in his abdomen, headache, history of seizures, bone pain, and extremity weakness. Breast ultrasonography found an iso echoic mass on the right breast with size 34,4x22,4x33 mm, strict lines with internal echo on the right subareolar breast, suspicious of breast cancer. Pathology anatomy results from incision biopsy was ductal carcinoma in situ (DCIS) in gynecomastia on the right breast with Luminal B Her2 negative subtype. He was diagnosed with ductal carcinoma in situ on the right breast Luminal B Her2 negative subtype. Chest radiography and liver ultrasonography were not found signs of metastasis. Right-modified radical mastectomy (MRM) was performed. Pathology results from the operation sample were different from incision biopsy. The pathology anatomy result was invasive solid papillary carcinoma grade III with lymphovascular invasion and without axillary lymph node invasion, with a free tumor margin incision. After the operation patient was given adjuvant chemotherapy doxorubicin and cyclophosphamide 6 cycle, and then tamoxifen was given 20mg for 5 years.

Figure 3. Physical examination. a lump with size 3x3x2 cm, regular margin, solid, hard consistency, without nipple retraction, skin dimpling, peau de orange, and it didn't attach to the chest wall.

Figure 4. Sample from a modified radical mastectomy. The size was 19x11x2 cm, with nipple retraction, without skin dimpling, peau de orange, and lymph node palpable.

**3. Discussion**

In the first case, a man, 50 years old, was diagnosed with mucinous adenocarsinoma grade II on the right breast luminal A subtype T4bN0M0. The diagnosis was based on pathological anatomy results from a core biopsy and a sample from a mastectomy. The subtype was determined by immunohistochemistry. Staging T4bN0M0 was based on physical examination and imaging, with nipple retraction, size 18x15x8 cm, regular margin, solid, hard consistency, skin dimpling, peau de orange, and it didn't attach with the chest wall. The patient didn't sigh, cough, dyspnea, pain in his abdomen, headache, history of seizures, bone pain, and extremity weakness. Breast ultrasonography found a solid mass on the right breast, regular margin, posterior shadowing, calcification, and without lump on the left breast, right and left axilla, right and left parasternal, supraclavicle, and infraclavicle. Chest radiography and liver ultrasonography were not found signs of metastasis. Due to the tumor size being T4b, the patient was given systemic preoperative chemotherapy or neoadjuvant with docetaxel carboplatin 4 cycles. It was suitable with NCCN guidelines 2023. The aim of neoadjuvant chemotherapy was to facilitate breast conservation, can render inoperable tumors operable, treatment response provides important prognostic information at an individual patient level, particularly in patients with TNBC or HER2- positive breast cancer, identifies patients with residual disease at higher risk for relapse to allow for the addition of supplemental adjuvant regimens, particularly in patients with TNBC or HER2-positive breast cancer. Besides that, neoadjuvant chemotherapy has an advantage for downsizing bulky tumors.[9] Unfortunately, after neoadjuvant chemotherapy, there was no ultrasonography or MRI for evaluating anatomical response from the treatment. But, from anamnesis and physical examination, the tumor shrank by 50% volume if it was compared with tumor volume before chemotherapy was given. After neoadjuvant chemotherapy, the patient was operated with a modified radical mastectomy. Breast-conserving surgery was not performed due to the tumor size was bigger than the breast size. Besides that, the position of the tumor was not only on the perifer but in the central too. Pathology anatomy results from the operation sample found mucinous carcinoma, with 1 axillary lymph node invasion from 5 lymph nodes, and free tumor surgical margin, without DCIS structure, microcalcification, and lymphovascular invasion. After the operation patient was given adjuvant chemotherapy docetaxel carboplatin 2 cycles and tamoxifen 20 mg for 5 years. The patient has not performed radiotherapy due to the incision margin being a free tumor. Adjuvant chemotherapy was given due to there being 1 axillary lymph node invasion from 5 axillary lymph nodes.

Tamoxifen 20 mg each day for 5 years was given to patient due to immunohistochemistry was luminal A. Since over 90% of male breast cancer patients have hormone receptor positive disease, endocrine therapy is an important part of male breast cancer treatment. Tamoxifen has, so far, been the most widely used anti-estrogen therapy in both female breast cancer and male breast cancer.[2]

In the second case, a man 50 years old was diagnosed with Ductal carcinoma in situ on the right breast luminal B Her2 negative subtype TisN0M0 as a preoperative diagnosis. The diagnosis was based on pathology anatomy results from the core biopsy. The subtype was determined by immunohistochemistry. Staging TisN0M0 was based on pathology anatomy results and a lump with size 3x3x2 cm, regular margin, solid, hard consistency, without nipple retraction, skin dimpling, and peau de orange, and it didn't attach with the chest wall. He didn't sign a lump on his right axilla, supraclavicle, infraclavicle, dan parasternal, and no cough, dyspnea, pain in his abdomen, headache, history of seizures, bone pain, and extremity weakness. Chest radiography and liver ultrasonography were not found signs of metastasis. Due to the size and luminal A subtype, the patient was not given neoadjuvant chemotherapy. The patient was operated with a modified radical mastectomy. The sample from the mastectomy was different from the incision biopsy. The pathology anatomy result was invasive solid papillary carcinoma grade III, with lymphovascular invasion, without axillary lymph nodes invasion, and with free tumor margin incision. The differentiation between before and after operation can happen because of a mass of tumor can have some histopathology description, and sample from core biopsy was a little part of a mass than sample from mastectomy as a full mass from one breast which was more representative. After operation patient was given adjuvant chemotherapy doxorubicin and cyclophosphamide 6 cycles and then tamoxifen was given 20mg for 5 years. Patients was given adjuvant chemotherapy due to pathology anatomy results from mastectomy sample was grade III, with lymphovascular invasion, without axillary lymph node invasion. It was suitable with risk cathegory according clinicopathology parameter for determining the necessary of chemotherapy adjuvant. If axillary lymph nodes negative and there was minimal one of the poor prognostic features (pT>2cm, Grade 2-3, Lymphovascular peritumoral invasion, ER and or PR (-) / weak positive (1-9%), Ki67 intermediate (10-20%), Her2 overexpressed, age > 35 years old), adjuvant chemotherapy was given.[3] After adjuvant chemotherapy was given, tamoxifen was given to the patient. It was caused by the luminal B Her2 negative subtype. It was suitable with the guidelines, and endocrine therapy is an important part of male breast cancer treatment. Tamoxifen has, so far, been the most widely used anti-estrogen therapy in both female breast cancer and male breast cancer.[2,9]

In both of these cases, there were some similar items. First, they are 50 years old, without malignancy in his family history, and they didn't have testicle disease. From the age, these cases were suitable with the incidence rate of male breast cancer that increases at 50 years old. Second, both of them were operated with mastectomy. The majority of male breast cancer patients undergo mastectomy, leaving a small percentage of men (10–24%) who are treated with breast-conserving surgery (BCS). The first case was performed a mastectomy due to tumor size was still big, although he had received neoadjuvant chemotherapy with partial response, and the second case due to comparison of tumor and breast size was big. Third, Both of these patients received adjuvant chemotherapy, and determination for receiving adjuvant chemotherapy between female and male breast cancer was similar, according to clinicopathology parameter. Forth, their breast cancer were hormone receptor positive, though first case was luminal A and second case was luminal B HER2(-). 90% male breast cancer was hormone receptor positive and they were given tamoxifen as endocrine therapy for 5 years. Fifth, Both of patient will be followed up like as female breast cancer, with history and physical examination 1–4 times per year as

clinically appropriate for 5 years, screening for metastases, and in the absence of clinical signs and symptoms suggestive of recurrent disease, there is no indication for laboratory or imaging studies for metastases screening.[2,10] The differentiation between the first and second cases was that the first patient was admitted to the hospital with the chief complaint of a lump on his right breast bigger than the patient from the second case. And it happened because of a lack of awareness about male breast cancer, many people in our population thought of gynecomastia with a lump on the male breast without clinical examination, whereas the normal anatomy of the male breast was not big and had no lump. And due to T4b size in the first case, he received neoadjuvant chemotherapy with the aim of downsizing a mass and knowing chemotherapy drug responses.[2,10]

Breast cancer is a common cancer in women but relatively rare in men, with male breast cancers accounting for less than 1% of all diagnosed cases. Similar to female breast cancer, the incidence rate continues to rise. It is estimated that there will be 2620 new cases of male breast cancer diagnosed in the United States in 2020, compared to only 900 cases in 1991. The age-adjusted incidence rate increased to 1.32 per 100,000 men in 2017 from 0.90 per 100,000 in 1980, as outlined by the surveillance, epidemiology, and end results (SEER).[1,2] Male breast cancer biological is different from female breast cancer. Male breast cancer patients are typically associated with advanced stages, higher grades, higher prevalence of hormone receptor-positive, and worse prognosis. Furthermore, studies have proposed that male breast cancer patients are insensitive to adjuvant therapy and underutilization of therapy in male breast cancer patients compared with female breast cancer patients. Therefore, it may be inappropriate to adopt the clinical applications of female-to-male extrapolation.[5] The most common symptom of breast cancer is a painless retroareolar mass which is present alone or with other symptoms in 75% of all cases. The mass is found more frequently on the left than on the right, and pain is present with the mass in 5% of all patients. Because of the smaller size of breast tissue in males, nipple involvement is seen early in the course of the malignant process, with ulceration in 6% of the patients, discharge in 6%, and retraction in 9%. When there is only bloody nipple discharge without a palpable mass, the diagnosis can be made early and is usually ductal carcinoma in situ of low or intermediate grade. Paget's disease is rare, presenting in only 1% of patients, with a mean age of onset of 60 years, similar to that of other males with breast cancer. Axillary lymph node involvement at presentation is more common in men than in women. In rare cases, male breast cancer presented as an occult primary with lymph node metastases. In summary, clinical presentation extends a spectrum of the most common painless breast mass, or mass with variable symptoms, to the least common metastatic disease.[8]

The diagnostic approach for male breast cancer was similar to female breast cancer. That was a physical examination, imaging (ultrasonography and mammography), and pathological anatomy results from the biopsy. Sometimes there was nipple involvement in 40-50% of cases. The chest was asymmetric due to there being a mass on the breast. Imaging examination was generally performed through ultrasonography and mammography. Mammography can differentiate benign lesions (sensitivity 92% and specificity 90%). Mammography showed an abnormality for 80-90% of male breast cancer cases and can differentiate between malignant and gynecomastia. The male breast consisted of fat and less of a secretory canal. Besides that, there was no cooper ligament and interlobular connective tissue. Mammography showed a radiolucent description. The tumor will show hyperdense, lobulated mass with spiculated margin or structure distortion. Gynecomastia will show a round area description or symmetric triangular with increasing density on retroaerola. Ultrasonography examination for male breast cancer showed a solid mass with irregular hypoechoic and posterior acoustic shadow. Ultrasonography will give information about axillary lymph node involvement.[3]

Core biopsy is preferred over fine-needle biopsy because it enables a definitive diagnosis of invasive breast cancer. The presence of malignant cells on a cytology specimen may be the result of ductal carcinoma in situ rather than an invasive disease, and the treatment of the two diseases is completely different. In addition, a core biopsy yields a tissue sample similar to that of an open biopsy without the need for a formal surgical procedure. The most common histological type of male breast cancer is invasive ductal carcinoma, which represents more than 90% of all cases. The stadium for male breast cancer was similar to female breast cancer. The determination stadium system was from American Joint Committee on Cancer (AJCC) 2018.[3] According to NCCN 2023, recommendations regarding the management of breast cancer in males are generally extrapolated from findings of clinical trials focusing on breast cancer in females. Although there are some biological and clinical differences between breast cancer in males and females, the management of breast cancer in males is similar overall to the management of breast cancer in females, with the following special considerations pertinent to male patients. Historically, males with breast cancer have undergone mastectomy more often than breast-conservation therapy. However, breast-conservation therapy is increasingly being performed in males, and evolving data indicate that breast conservation in males is associated with equivalent outcomes to mastectomy and that it is safe and feasible. Decisions about breast conservation versus mastectomy in males should be made according to similar criteria as for females.[9]

As in females, SLNB should be performed in the setting of male breast cancer with a clinically node-negative axilla. Indications for radiation after breast surgery in males with breast cancer are the same as for females with breast cancer. Chemotherapy with/without HER2-targeted therapy should be recommended for males with breast cancer, according to guidelines for females with breast cancer. Options for adjuvant endocrine therapy for males with breast cancer include tamoxifen for 5–10 years or, if tamoxifen is contraindicated, a GnRH analog plus an aromatase inhibitor. In males, single-agent adjuvant treatment with an aromatase inhibitor has been associated with inferior outcomes compared to tamoxifen alone, likely due to inadequate estradiol suppression, and is not recommended. The NCCN Panel recommends that bone density be assessed at baseline and every 2 years in males with breast cancer who receive adjuvant GnRH analog therapy. Low bone density should be managed according to standard guidelines. Systemic therapy for advanced disease and management of advanced breast cancer in males is similar to that in females. However, it is preferred that when an aromatase inhibitor is used, a GnRH analog should be given concurrently. Available data suggest that single-agent fulvestrant has similar efficacy in males as in females. Newer agents such as CDK4/6 inhibitors in combination with an aromatase inhibitor or fulvestrant, mTOR inhibitors, and PIK3CA inhibitors have not been systematically evaluated in clinical trials in males with breast cancer indications for and recommendations regarding chemotherapy, HER2-targeted therapy, immunotherapy, and PARP inhibitors for advanced breast cancer in males are similar to those for advanced breast cancer in females.[9]

**4. Conclusion**

Male breast cancer was a rare case, and it was estimated 1% of all breast cancer. Male breast cancer patients are typically associated with advanced stages, higher grades, higher prevalence of hormone receptor-positive, and a worse prognosis. Both of the patients on serial cases are male breast cancer with hormone receptor-positive, and they were given endocrine therapy. The majority characteristic of male breast cancer was hormone receptor-positive. Management of male breast cancer is similar overall to the management of female breast cancer in modality surgery, chemotherapy, endocrine therapy, and radiotherapy.

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