



Case Report

A SCITECHNOL JOURNAL

Male Breast Cancer

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Abstract

Breast cancer is one of the most common malignancies in women but is relatively rare in men with an incidence rate of 0.5% compared to female breast cancer. The risk of breast cancer in male increases with age and men usually present with later stage of disease that results in a worse outcome.

Keywords

Breast cancer; Malignancies; Left gynecomastia

Introduction

Breast cancer is one of the most common malignancies in women but is relatively rare in men with an incidence rate of 0.5% compared to female breast cancer. The risk of breast cancer in a male increase with age and men usually present with later stage of disease that result in a worse outcome. The surgical approach to women with breast cancer has become more conservative through the years with approximately 66% of the women having breast preservation with a lumpectomy and all women having their nodal staging performed with the lymphatic mapping and sentinel lymph node biopsy technique. These more conservative surgical procedures are now being applied to men with breast cancer. Although the number of men that are candidates for the procedure are less due to larger tumor size/breast size ratios, more men are opting for this conservative approach. In addition because of its rarity and the fact that men with mutations in the BRCA II gene are at an increased risk compared to the normal population for breast cancer development, men with breast cancer is now a listed indication for genetic testing. This case report and review examines this changing landscape for the treatment of breast cancer in the male population.

Case Presentation

The patient was a 49 year old Caucasian male who presented to the local emergency room with the chief complaint of uncontrolled diabetes and a painful left breast mass. The left breast mass had been present for 8 months and had been increasing in both size and tenderness. He had also experienced a 30 lb weight loss over the past year which was unexplained. He had no allergies and his past medical history was significant for diabetes and hypertension. His current medications were Metformin and Lisinopril. The patient had a 30-pack year history of smoking and continued to smoke. He denied drinking. Family history was remarkable for a sister who died of

pancreatic cancer and a mother who died of lung cancer. On physical exam, the patient had a 2 cm left breast mass that was movable with slight tenderness (Figure 1). The mass was located in the lower, outer quadrant 2 cm from the retroareolar area. There was a palpable 2 cm left axillary node that was suspicious for metastases. The patient was admitted through the ER on 04/08/2016 for diabetes control and a CT scan of the chest, abdomen and pelvis was ordered. These studies were interpreted as normal except for left gynecomastia. In retrospect, the CT scan of the chest showed a chest wall density that was lateral to the retroareolar area (Figure 2) and the left axilla showed nodes suspicious for metastases (Figure 3). A mammogram and left breast ultrasound was denied by insurance. The patient was taken to the OR on 04/11/2016 for a left breast biopsy (Figure 4) and possible left modified radical mastectomy (LMRM). The intra-operative frozen section showed a sclerotic mass (Figure 5) and, histologically, an infiltrating ductal carcinoma. The patient was converted to a LMRM with an en bloc resection (Figure 6). A gross examination of the axilla showed a number of suspicious nodes (Figure 7). Figure 8 shows the transverse chest wall incision. Final pathology showed a 2.0 cm infiltrating ductal carcinoma (Figures 8 and 9) with clear margins. The tumor was estrogen receptor and was estrogen receptor positive on immunostains (Figure 10). Peri-arteriole stranding of the tumor cells (Figure 11) and lymphovascular invasion (Figure 12) was noted in the primary tumor. Examination of the left axilla showed 10 of 12 lymph nodes positive for metastases (Figure 13) with extra-nodal extension. The Mammoprint (70-gene assay) showed the tumor to be high risk for recurrence, luminal B subtype that was estrogen receptor positive (ER)+, progesterone receptor positive (PR)+, and Her 2-neu negative. The patient remained in the hospital overnight and was discharged to home the following day.

Medical oncology was consulted and the patient was recommended to undergo adjuvant chemotherapy followed by adjuvant radiotherapy to the left chest wall and axilla, followed by adjuvant hormonal therapy with Tamoxifen. A PET/CT scan was negative for metastases and a MUGA scan was normal. The patient will receive a combination of Adriamycin and Cytosine given in a dose dense fashion every 2 weeks for 4 cycles. This will be followed by weekly Paclitaxel for 12 weeks, then Tamoxifen. Also recommended was post-mastectomy radiation therapy to the left chest wall, axilla and supraclavicular areas due to his lymph node positive disease. BRCA I and II testing was also ordered.

Discussion

Considering men possess breast tissue, albeit less than their female counterparts, it is not surprising that the male population is at risk for developing breast cancer. Male breast cancer (MBC) is rare, accounting for less than 1% of all breast cancers and less than 1% of all male cancers [1]. Similar to female breast cancer (FBC), the risk of MBC increases steadily with age and is associated and increased with the BRCA II mutation for early onset breast cancer. In a population based multinational study [2] of over 459,846 women and 2,665 men with breast cancer, the world standardized incidence rates were 66.7/10⁵ person-years in women but only 0.40/10⁵ person-years in men. Women were shown to be diagnosed at a younger median age (61.7 years) than men (69.6 years). Over the last 38 years, MBC

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Received: May 30, 2016 Accepted: July 27, 2016 Published: July 29, 2016



Figure 1: On physical exam there was a 2 cm mass present at 4:00 in the breast with a palpable 2.0 cm left axillary node.

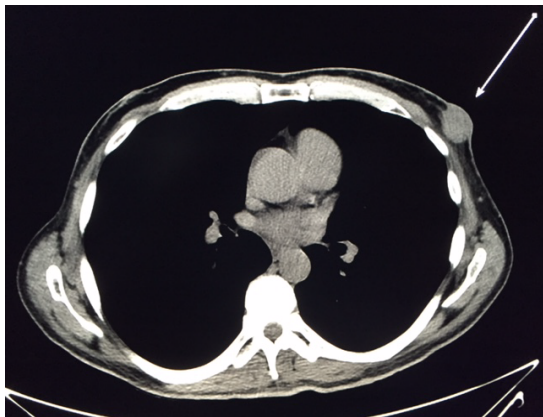


Figure 2: CT scan of the chest showed a mass in the left chest wall with a plane noted between the mass and the pectoralis major muscle.

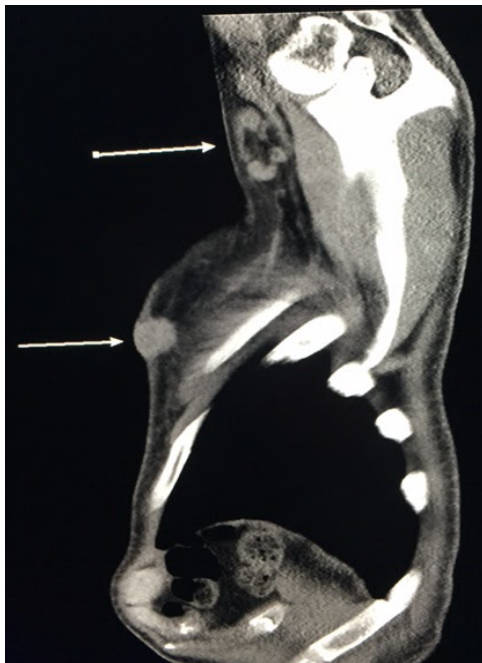


Figure 3: CT scan - Sagittal view showed the left chest wall mass and the suspicious left axillary lymph nodes (arrows).

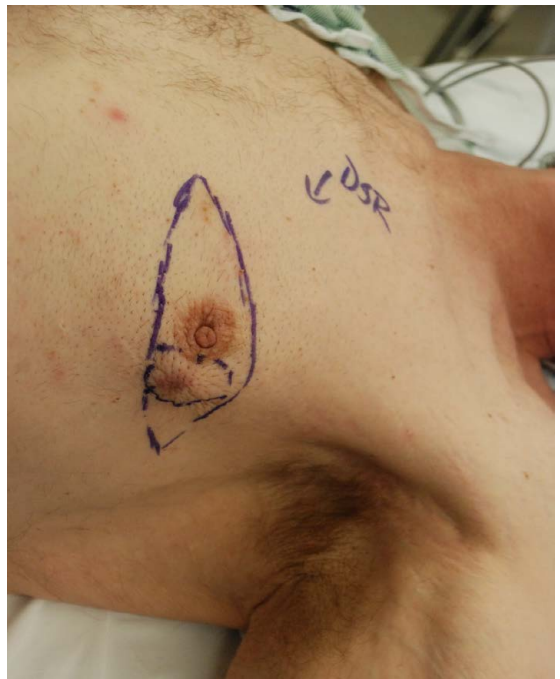


Figure 4: To make the diagnosis and for eventual surgical treatment the patient was taken to the OR and under LMA-general anesthesia an excisional biopsy was performed. Frozen section showed an infiltrating ductal carcinoma. The procedure was converted to a modified radical mastectomy. The palpable tumor and mastectomy incision is out-lined.



Figure 5: Gross examination in pathology showed a 2.0 cm tumor with apparent clear margins.



Figure 6: The left modified radical mastectomy with en bloc resection.

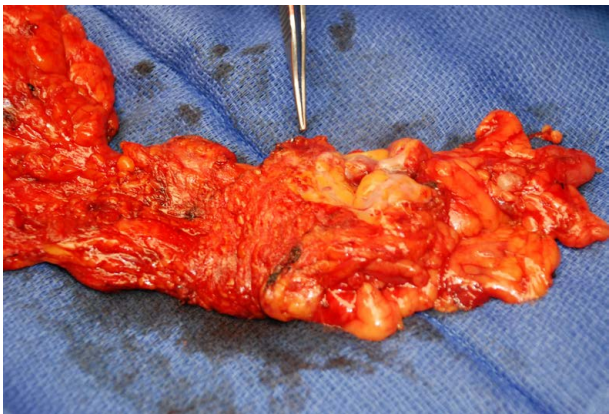


Figure 7: Gross examination of the axilla showed enlarged suspicious for metastases nodes.

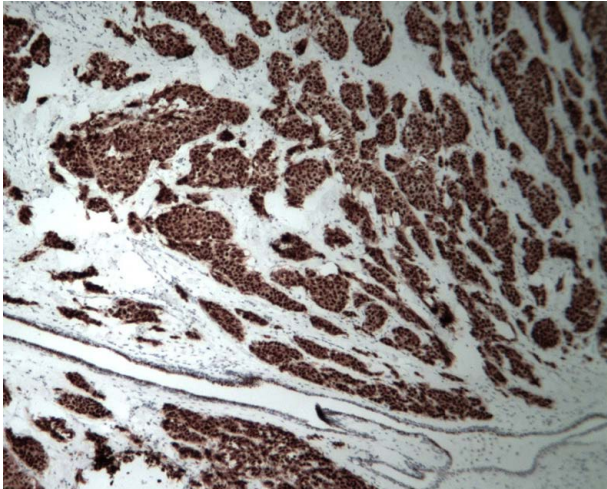


Figure 10: The primary tumor stained positive for the estrogen receptor.



Figure 8: Post-procedure - the mastectomy incision with a Jackson-Pratt drain in place.

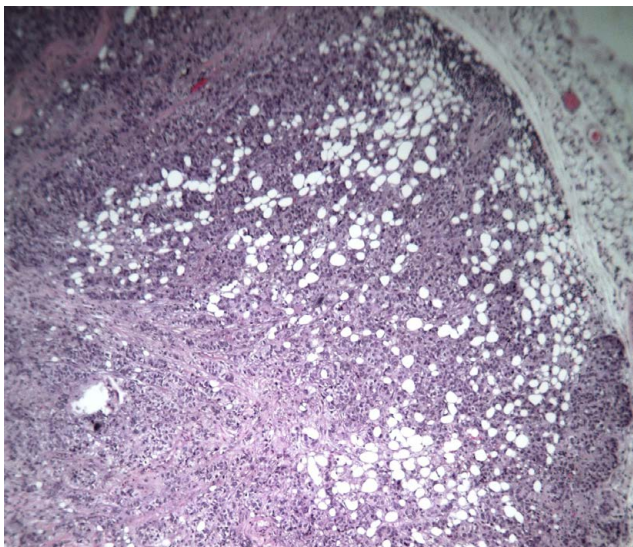


Figure 9: Photomicrograph of the primary tumor - 40 × - the tumor was an infiltrating ductal carcinoma - Hematoxylin and Eosin Stain.

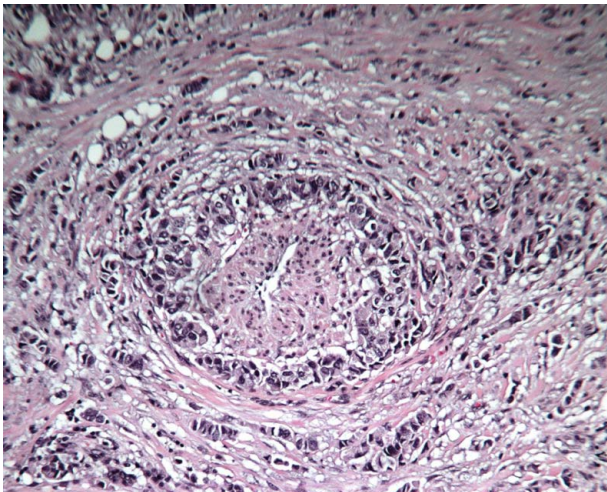


Figure 11: In the primary tumor peri-arteriole stranding of the malignant cells was noted.

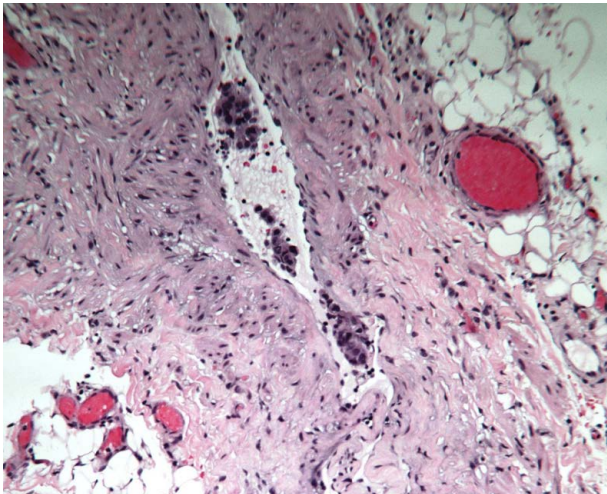


Figure 12: The primary tumor exhibited lymphovascular invasion.

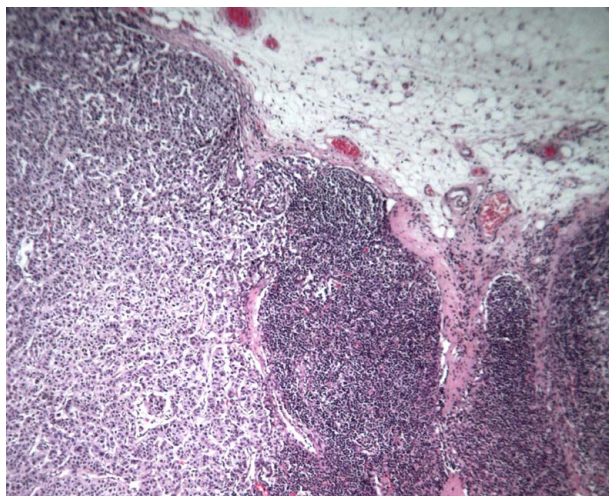


Figure 13: Photomicrograph of a axillary node showing a deposit of metastatic breast cancer. 10-12 left axillary nodes were positive for metastases with extranodal disease noted.

incidence has remained relatively stable, whereas FBC has become increasingly common due to the use of mammography screening and hormone replacement therapy beginning in the 1980's. Since there is no screening mammography use in men and the duration of symptoms before diagnosis is reported to be longer, men will present with greater stage of disease.

The differential diagnosis [3] includes pseudogynecomastia which is just the benign proliferation of fatty tissue with no glandular tissue under the areolar. It usually occurs in obese patients and is bilateral and was unlikely in this thin patient with a unilateral mass. True gynecomastia may be physiologic or pathologic and occurs in males when the ratio of testosterone to estrogen decreases. Pathologic causes include exposure to certain drugs or herbal agents, decreased testosterone secretion or increased estrogen production. It is also usually bilateral and located sub areolar and is described as a rubbery, mobile, tender mass and again unlikely in this patient with a unilateral mass that was located lateral to the sub areolar area. Benign breast lesions including breast abscesses, cysts, papillomas, fibroadenomas and phyllodes tumors should be considered, along with metastases from primary cancers at other sites. In this particular patient a malignancy was at the top of the differential due to the physical exam findings of a hard mass with apparent axillary adenopathy. The fact that the mass was movable would suggest that there was not any muscle invasion and clear margins could be obtained with a mastectomy. To make the diagnosis a fine needle aspiration (FNA) could be performed if supplies and an experienced cytologist is available. This was not the case and thus an open excisional biopsy was performed.

The treatment for MBC has traditionally followed guidelines for the treatment of breast cancer in the female population. Due to the rarity of the cancer, the fact that the tumors are usually large in comparison to the size of the breast, and the fact that many of the tumors arise beneath the nipple or involve the nipple-areolar complex, mastectomy has been the standard treatment. A complete axillary node dissection is routinely included to provide the nodal staging information, since the regional nodes are the most common site of metastases. However, during the past 10 years, the surgery for breast cancer in women has become more conservative, with breast

preservation and lumpectomy replacing mastectomy in up to 66% of the patient population. The axillary surgery has also become more conservative with intraoperative lymphatic mapping and sentinel lymph node biopsy replacing radical node dissections. Alterations in treatment strategies for men have lagged behind those in women. This being said, conservative treatment is possible and becoming much more likely for cases of MBC, despite the larger tumor/normal breast tissue ratios in men. Preservation of the nipple-areolar complex and hair-bearing ability of the chest, symmetry of breast size and shape, and maintaining a positive self-image is reasons given for men to choose breast preservation [4]. In a recent series [5] reported from the Surveillance, Epidemiology and End Results (SEER) database by Stanford University clinicians, 4,707 male patients with breast cancer were identified from the years 1983-2009. 86.6% of the men underwent mastectomy and 13.2% underwent lumpectomy and radiation therapy. A greater proportion of the population had breast conserving surgery in the later years, 10.6% from 1983-1986 compared to 15.1% from 2007-2009. After lumpectomy, most women undergo adjuvant radiation therapy to treat the remainder of the breast, but only 35.4% of the men were treated with this adjuvant therapy. This series suggests that men with breast cancer may not be receiving standard of care treatment since only 35% of the men treated with lumpectomy had adjuvant radiation therapy and only 34% had their axilla evaluated with a nodal staging procedure. Despite these findings, 10-year breast cancer-specific survival for MBC was 82.8% and overall survival was 46.9% in the lumpectomy patients compared to 77.3% and 46.4% respectively in the mastectomy patients. Decreasing survival was associated with increasing age of the patient, the African/American race, and increasing grade and stage of the tumor. Treatment, however, was not a factor. In another series [2], male patients had a significantly improved relative survival from breast cancer than their female counterparts after correcting for age, year of diagnosis, stage and treatment. Female patients with breast cancer have experienced incremental improvements in survival over the past 30 years, but the improvement in MBC is not as pronounced. Comparing the years 1976-1985 and 1996-2005, the hazard ratios for breast cancer death declined by 42% among women but only 28% in men [6]. Since MBC is a rare entity, when diagnosed it should be treated with similar guidelines used to treat FBC. Patients should be given the choice between mastectomy and breast preservation. Nodal staging should also be performed with the lymphatic mapping technique [7,8], adjuvant radiation therapy after lumpectomy and adjuvant chemotherapy should be offered where appropriate. An overarching lack of treatment guidelines and differences in compliance can explain some of the difficulties in treating MBC. Local-regional treatments (primary site and nodal surgery and radiation therapy) and adjuvant treatments have not been evaluated in clinical trials and guidelines for care are lacking.

For the medical oncologist, the adjuvant management of male breast cancer is similar to that used in female breast cancer. Adjuvant chemotherapy is used to treat male breast cancer patients who have a substantial risk or recurrence and death from breast cancer. Unfortunately, prospective trials evaluating the benefits of adjuvant systemic chemotherapy in men have not been performed. Retrospective series have suggested that adjuvant chemotherapy lowers the risk for recurrence in male patients [9-11]. Given the established benefit of chemotherapy in women and the suggestive evidence in men, most clinicians use similar guidelines for adjuvant chemotherapy in male and female patients. Men with HER-2/neu negative breast cancer are recommended combination systemic

chemotherapy, usually with an anthracycline. The preferred regimens per the National Comprehensive Cancer Network (NCCN) include dose dense doxorubicin and cyclophosphamide (AC) followed by either dose dense paclitaxel or weekly paclitaxel. HER-2/neu positive breast cancer is treated with trastuzumab based systemic chemotherapy. The preferred regimens per the NCCN include AC followed by paclitaxel and trastuzumab or a combination of docetaxel, carboplatin, and trastuzumab (TCH). The role of adjuvant endocrine therapy in male breast cancer is supported by retrospective studies with tamoxifen. One report demonstrated an improvement in survival of 61 vs 44 percent in men who received tamoxifen in addition to mastectomy as compared to mastectomy alone [12]. There is insufficient data at this time to support the use of an aromatase inhibitor (AI) in the adjuvant setting in men. A retrospective analysis evaluated the use of an AI or tamoxifen in 257 men with stage I to III breast cancer. At a median follow up of 42 months, treatment with an AI was associated with a higher risk of death compared to tamoxifen (32 vs 18 percent) [13,14]. The Adjuvant Tamoxifen: Longer Against Shorter (ATLAS) trial supports 10 years of adjuvant tamoxifen rather than 5 years in women. Data from this study is extrapolated and applied in male breast cancer.

International efforts have been undertaken to better understand breast cancer in men. The EORTC, the Breast International Group and the North American Breast Cancer Group [8] are collaborating on a large prospective study of male breast cancer that involves clinical data and tissue collection to evaluate patterns of care, clinical outcomes, and biologic determinants. Having already registered 1,000 male patients, this International cooperation will provide statistical power to allow meaningful advances in the comprehension and treatment of male breast cancer. This case report is particularly important for both patients and physicians, as it may raise awareness related to the disease presentation. Although there are several case reports in the literature detailing unique MBC occurrences, this particular case was thought to illustrate a more standardized presentation of breast cancer in men.

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