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Male Breast Carcinoma in a Relatively Young Patient

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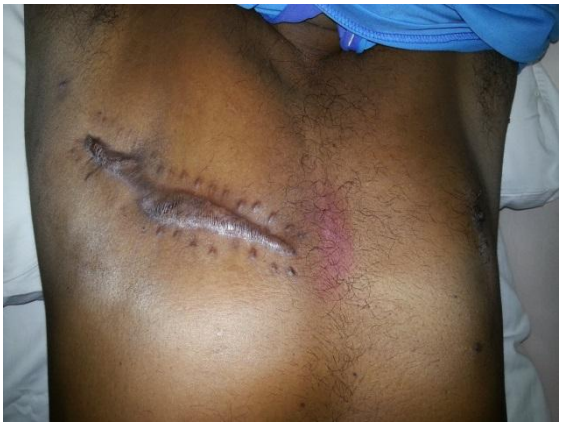
Abstract: *Cancer of the breast among men is rare, accounting for less than one percent of cancer incidence and mortality in this sex group.It accounts for 0.2% of all cancers, and 1% of all breast cancers. The peak age of onset is 67-71 years old which is much later compared to women. Several risk factors have been identified, such as genetic and hormonal abnormalities.Diagnosis and treatment of male breast carcinoma (MBC) is similar to that of female patients, but men tend to be treated with mastectomy rather than breastconserving surgery. We present a case of male breast carcinoma in a 48 year old man with no obvious risk factors and who underwent a modified radical mastectomy and subsequent chemotherapy.*

I. Introduction

Breast cancer in men is rare, and it accounts for about 1% of all malignant breast neoplasm cases. The estimated incidence is 1 case for each 100,000 men (1). When compared with females, male patients tend to be older at the time of diagnosis and have a higher-stage disease and greater lymph node involvement(4).Infiltrating ductal carcinoma is the predominant histologicaltype(8).As in women, prognostic factors that have been evaluated include tumour size and the presence or absence of lymph node involvement, both of which correlate well with prognosis(2).Although the outlook for men is the same as stage-matched women, overall the prognosis is worse because of delayed presentation—on average 6–10 months from symptom onset to diagnosis (10).

II. Case Report

A 48 years old man presented to surgical outpatient clinic with a right breast lump. He noticed the lump 3 years ago and it has been slowly increasing in size. It is a painless lump at the retroareolar region. On further questioning, he has no nipple discharge, retraction, ulceration or constitutional symptoms. Past medical and drug history were unremarkable but he has family history of malignancy as his brother passed away due to an unknown malignancy. Physical examination revealed a retroareolar lump at the right breast measuring about 3 by 2cm. It is a hard and non tender mass which fixed to underlying pectoralis muscle. There was no nipple retraction or any skin changes. The contralateral breast was normal and no axillary or supraclavicular lymph nodes were felt. An ultrasound of the breast was reported as highly suspicious right breast mass. A FNAC done then showed malignant cells. Proceeded with a CT scan of the thorax/abdomen/pelvis which showed no distant metastasis and patient subsequently underwent a modified radical mastectomy with Level II axillary clearance. Histopathological examination was reported as infiltrating ductal carcinoma, Bloom Richardson grade 2 with clear surgical margin, no involvement of the axillary nodes, absent of lymphovascular invasion and estrogen/progesterone receptor was positive and C-erb-B2 negative.TNM staging for this patient was T2N0M0. Patient was referred to oncologist for further treatment. He completed 4 cycle of chemotherapy comprise of IV Doxorubicin and IV cyclophosphamide on Day 1 every 3 weeks. He is currently awaiting for adjuvant radiotherapy.



III. Discussion

Male breast cancer is relatively rare and has an incidence of 1 in 100,000 men, accounting for less than 1% of breast carcinoma cases and of all malignancies in men (4). While the aetiology of male breast cancer is uncertain, risk factors include genetic predisposition, prior radiation exposure, alterations of the estrogen-testosterone ratio and occupational hazards(5).Specifically to men, however, risks also include old age, high socio-economic status, exposure to female hormone (patients with prostatic cancers on oestrogen treatment) and patients with reduced testicular function (Klinefelter's Syndrome, mumps orchitis, and undescended testicles(9).Of note is a very strong relationship for male breast cancer (50-fold increase) that has been observed with Klinefelter syndrome, a condition associated with increased gonadotropin and decreased androgen levels, normal estrogen levels, and therefore a high ratio of estrogen to androgen (7).In terms of lifestyle factors, it was found that body mass index was statistically significantly associated with male breast cancer. Familial breast carcinoma, positive BRCA-gene, liver diseases causing a hyper-oestrogenic status were also associated with increased risk of developing male breast carcinoma(2).In populationbased series of men with breast cancer unselected by family history, BRCA1 mutations are much less common; 0%–4% of men with breast cancer harbour this mutation.Mutations in the BRCA2 gene are more frequent in males with breast cancer, with 4%–16% of men with breast cancerreported to be mutation carriers in population-based series(12).

Male breast cancers are predominantly of ductal origin due to the lack of terminal lobules within the male breast. As a result, lobular carcinoma in situ (LCIS) and infiltrating lobular carcinoma are extremely unusual in male patients (5).Other types of cancers occurring in the male breast include papillary (2.6%), mucinous (1.8%), and medullary (0.5%). (6). It is reported that 90% of MBC express ER (estrogen receptors), whereas 81-96% express PR (progesterone receptors (10).

About 42% of breast cancer cases in men are diagnosed in stage III or IV. This is probably because men do not seek medical attention for breast masses as quickly as women. In addition, the tumor is usually closer to the skin in males, which increases the likelihood of infiltration into the dermis (1).The most common presenting symptoms in male breast cancer patients are a painless subareolar lump, nipple retraction, and bleeding from the nipple (12).Because the male breast is rudimentary and most tumours are central, nipple involvement is seen in up to 50% of cases at presentation (11).Changes in the nipple-areola complex occur in up to one third of patients in the form of nipple fixation or retraction, inversion, oedema or eczema. Bloody discharge is associated in 75% of cases with malignancies whereby ulceration of the skin is reported in approximately 27% of patients (10).Usually the primary consideration in the differential diagnosis is gynecomastia, which affects approximately 30% of healthy men (12).

As with symptomatic female patients, the diagnosis is made by triple assessment, with both mammography and ultrasound scanning having high sensitivity and specificity for male patients (11). The core needle biopsy is important because it enables a definitive diagnosis of invasive breast cancer and the evaluation of estrogen receptors, progesterone receptors, and Her-2 status (1).Mammographic characteristics of male breast cancer are sub-areola and eccentric to the nipple. According to Appelbaum et al, "Margins of the lesions are well defined; calcifications are rarer and coarser than those occurring in female breast cancer (9).The sensitivity and specificity of mammography for the diagnosis of male breast cancer have been reported to be 92% and 90%, respectively. Ultrasonography can also be a useful adjunct and provide information regarding nodal involvement(12).

The principles of treatment of MBC are similar to those used for females with breast cancer. Men are less likely to have breast conserving surgery, radiotherapy or receive chemotherapy compared with stage-matched female cases (10). The mainstay of breast cancer surgery for men is modified radical mastectomy. This procedure involves removal of the ipsilateral breast tissue, the nipple-areolar complex, and levels I and II of the axillary contents(11). The fascia of the greater pectoral muscle should be removed as well.Axillary lymph node dissection is clearly an important component of therapy, because men who have nodal dissection omitted tend to have poorer outcomes (12).

Adjuvant chemotherapy with cytotoxic agents has been shown to favourably influence survival in men with lymph node-positive cancer(11). A series of 24 male patients with stage II breast cancer was treated at the National Cancer Institute with adjuvant CMF (cyclophosphamide, methotrexate, and fluorouracil). The projected 5-year survival rate was >80%, which was significantly higher than a similar cohort of historical controls. Retrospective series have also suggested that adjuvant chemotherapy lowers the risk for recurrence in male patients (12). Some studies have demonstrated an improved disease-free and overall survival using adjuvant anthracycline-based therapies (1). Because of the high probability of an indefinite period of infertility following chemotherapy, sperm cryopreservation should be recommended for all young patients with cancer prior to the start of chemotherapy.

MBC patients should be offered postoperative radiotherapy according to the guidelines drawn up for females. Those few men who have breast-conserving surgery should be offered post-operative radiotherapy.

Men with large tumours, locally advanced disease, extensive axillary nodal involvement or poor prognostic factors such as high histological grade and vascular invasion should all be offered post-mastectomy radiotherapy(10).Patient with high risk of locoregional recurrence appears to benefit from radiotherapy where the predictor of locoregional recurrence includetumorsize, involved axillary lymph nodes and margin status.

Breast cancer is more often hormone receptor-positive in men than in women, and approximately 80% of breast cancers in men have hormone receptors (11).Tamoxifen in the adjuvant setting have shown a reduced riskof breast cancer recurrence and death (12).Aromatase inhibitors are not usually used as they only block peripheral oestrogen production that accounts for 80% of oestrogen production in men (11). As for now, there are insufficient data to recommend an aromatase inhibitor in the adjuvant setting for male patients.

Given that the vast majority of men have estrogen receptor–positive tumors, hormonal therapy is often the first approach in metastatic disease.Tamoxifen has established efficacy in metastatic male breast cancer, with an approximate 50% response rate, and is considered the preferred first-line approach. Luteinizing hormone–releasing hormone agonists, with or without antiandrogens, have also been reported to be effective in male breast cancer (12).Ablation treatment has been successful in some cases. Orchidectomy is the initial procedure in this option. If this is not successful, adrenalectomy and hypophysectomy show comparable results although these are rarely done nowadays (9).

There is no difference in prognosis between male and female breast carcinoma when compared at similar stages and thus, it is important to recognize male breast carcinoma in its earlier stages (3). Mbc is thought to have a worse prognosis than in women. If corrected for stage of development this is obviously not true. This might be caused by delayed diagnosis, increased age of onset, increased comorbidity and a more progressive stage at initial presentation (2).Hill et al, reported an overall five year and ten year survival rate in patients with localized disease to 86% and 64% respectively. With positive lymph nodes, the five and ten year survival rate decreased to 73% and 50% respectively (9).Prognosis depends upon tumour size, histological grade, nodal status and hormone receptor status. The most important prognostic factor is the lymph node status. Those who are node negativecan expect a five-year survival rate of 90%, compared with 65% five-year survival rate for node positive cases.MBC patients tend to fare worse because of late presentation associated with more advanced disease. Since MBC cases tend to be older than female patients there is an increased incidence of co-morbidities, which could adversely affect their prognosis (10). Men with breast carcinoma have a poor prognosis, especially in the younger age group, because most breast enlargements in young men are dismissed as gynecomastia. This potential misdiagnosis can result in an unnecessary delay in treatment(1). Median survival from the time of presentation with metastatic disease is approximately 26.5 months (11).

IV. Conclusion

Male breast cancer remains a rare disease, although the incidence is increasing. Risk factors for male breast cancer include genetic factors and hormonal abnormalities particularly Klinefeltersyndrome, family history of breast cancer and radiation exposure.BRCA 2 gene is more strongly linked to MBC compared to BRCA 1.Men tend to be diagnosed at an older age than women and with later stage disease. Most of the histologic subtypes that are seen in women are also present in men, except that lobular histology is much rarer.As in women, retraction or bloody discharge from the nipple, enlargement of axillary nodes or ulceration of the skin of the nipple is serious clinical signs, in which the diagnosis of breast cancer should be considered. The investigation must be a combination of a clinical exam, mammography, cytologyand percutaneous biopsies. Estrogen receptors and progesterone receptors are present in most cases of breast cancers in males. Modified radical mastectomy with axillary clearance is the treatment of choice and adjuvant chemoradiation should be offered to patients. Hormonal therapy plays an important role and adjuvant Tamoxifen is currently the gold standard. There is no difference in prognosis between male and female breast carcinoma when compared at similar stages and thus, it is important to recognize male breast carcinoma in its earlier stages. The key is early detection and prompt treatment.

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