

From Benign To Malignant: A Case Report of Male Breast Cancer Mimicking Gynecomastia

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Abstract: Male breast carcinoma is a very rare malignancy, accounting for less than 1% of all breast cancer cases. Non-specific clinical presentations and low medical suspicion often lead to delayed diagnosis and poor outcomes. This report presents a rare case of male breast cancer that was initially diagnosed as gynecomastia. A 40-year-old man comes in with progressively enlarged right breast mass, initially appearing in childhood and developing significantly in the last two years. Physical examination showed a hard, immovable, and painful mass of 7 × 10 cm with no discharge from the nipple or enlargement of axillary lymph nodes. Histopathology confirms mixed carcinoma: invasive carcinoma of non-specific type and invasive lobular carcinoma. No metastases were found on imaging. Immunohistochemistry showed ER(+), PR(+), HER2(-), and Ki-67 by 20%. The patient underwent a modified radical mastectomy, chemotherapy, and tamoxifen therapy, with six months of recurrence-free results. This case highlights the importance of distinguishing gynecomastia from malignancy, especially in young men without risk factors. Early diagnosis through imaging and biopsy is essential for proper treatment and better clinical outcomes.

Keywords: Breast Cancer; Diagnosis Dini; Male Gynecomastia; Mature Male; Terapi Tamoxifen

1. Introduction

Accounting for just 1% of all breast cancer cases, male breast cancer is a rare malignancy often hiding in plain sight. In 2020, around 2,620 new cases were expected in the United States, up from 900 in 1991. Men are typically diagnosed later than women due to the low incidence and lack of early signs and symptoms. The risk is higher in certain populations: non-Hispanic Whites (1.3 per 100,000), Asians (0.7 per 100,000), and Hispanics (0.8 per 100,000). The risk increases with age, rising significantly at age 50 (1.7 per 100,000) and peaking at age 80 and above (8.3 per 100,000) ¹.

About 15-20% of men with breast cancer have a first-degree relative that suffers from the disease. Men with high estrogen levels due to obesity or alcohol dependence are at greater risk. Certain jobs involving heat, radiation, or chemicals also increase the risk. Other risk factors include age, diseases associated with high estrogen levels, radiation exposure, hormonal replacement, black race, and obesity. A positive family history of breast cancer is the most significant risk factor, the risk is increased by twofold if the first degree is affected, and increased by fivefold with multiple affected first degree relatives.^{1,2}

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Mutations in the BRCA1 and BRCA2 genes, which are associated with breast cancer in women, also increase the risk of breast cancer in men. Approximately 4% to 33% of men with breast cancer have a BRCA2 gene mutation, and 0% to 6% have a BRCA1 gene mutation. About 75% of men with breast cancer will find a painless lump, usually located near the nipple. Men usually notice the first symptoms themselves, generally a lump or nipple retraction. Other symptoms may include nipple discharge, swollen armpit lymph nodes, and skin lesions. The most common differential diagnosis is gynecomastia. Gynecomastia, which is the excessive growth of breast tissue in men, is caused by an imbalance of estrogen and androgen, which can be caused by various factors. For example, it can occur as part of normal puberty due to being overweight, endocrine disorders, side effects of medications (e.g., certain antipsychotics, anabolic steroids, and exogenous hormones), and kidney or liver dysfunction³. Often, men have more confined tumors but have a higher chance of lymph node involvement and a higher probability of metastasis during the diagnosis. Axillary involvement, which is present in approximately half of the male breast cancer cases, is the primary predictor of recurrence and metastasis probability². Between 0.1% and 0.2% of all breast cancers are located in men, the most common of which is the infiltrating ductal carcinoma, not otherwise specified (IDC-NOS), followed by ductal carcinoma in situ (DCIS)³.

Because there are no screening guidelines for men, diagnosis is often delayed, with an average of 21 months from symptom onset to diagnosis. As a result, about 46.7% of cases involve at least one lymph node by the time they are diagnosed. Mammograms are effective in detecting male breast cancer, with high sensitivity and specificity, but there is no evidence supporting routine screening for men without symptoms^{1,2}.

Most treatment modalities for male breast cancer are extrapolated from the current standard of care for female breast cancer because of the relative rarity of male cases^{1,4}. A treatment algorithm available right now is illustrated in Figure 1.

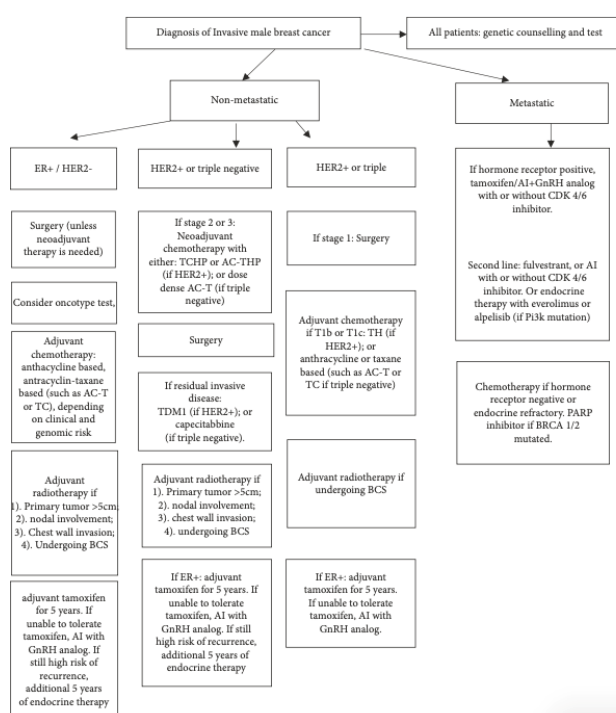


Figure 1. Treatment algorithm for male breast cancer.

Generally, the prognosis for male breast cancer is worse compared to that for female breast cancer. Because it is relatively rare, treatments are often based on those used in females, whereas male breast cancer has some peculiar characteristics that need particular consideration. The worst prognosis has been reported to be due to delayed diagnosis and increased age. Possibly the older age found in males is due to delay in diagnosis³.

2. Objective

This case report represents a rare case of male breast cancer which was initially mistaken for gynecomastia and points out the clinical and diagnostic dilemma in distinguishing these two conditions. By discussing the atypical presentation, diagnosis, histopathology, and therapeutic response of the patient, this case report tries to make clinicians aware that even without classical risk factors, malignant breast disease can occur in males. Early identification and diagnosis are important for better prognosis and prevention of delayed treatment.

3. Case Illustration

This 40-year-old male patient was referred to the Surgical Oncology Department from the General Surgery Department for a suspected case of breast cancer. The patient was initially diagnosed with gynecomastia. He related having a small, coin-sized lump on the right side of the chest since the age of 10, which had progressively increased in size over the past two years. Initially, the mass was nontender and did not raise clinical suspicion. There was no significant past medical or family history of malignancy. The patient denied any consumption of alcohol, anabolic steroids, or other medications. He also had no history regarding hormone therapy. At presentation, his body mass index (BMI) was 27.9 (overweight), and he had experienced an unexplained weight loss of approximately 10 kgs over the last six months.

On physical examination, the patient was hemodynamically stable with normal vital signs. On inspection and palpation, a firm, immobile, tender mass measuring 7 × 10 cm was found to be located in the right breast region. The overlying skin was thickened with slight erythema but without any evidence of nipple inversion, abnormal discharge, peau d'orange, or skin ulceration. No axillary lymphadenopathy was found by palpation.

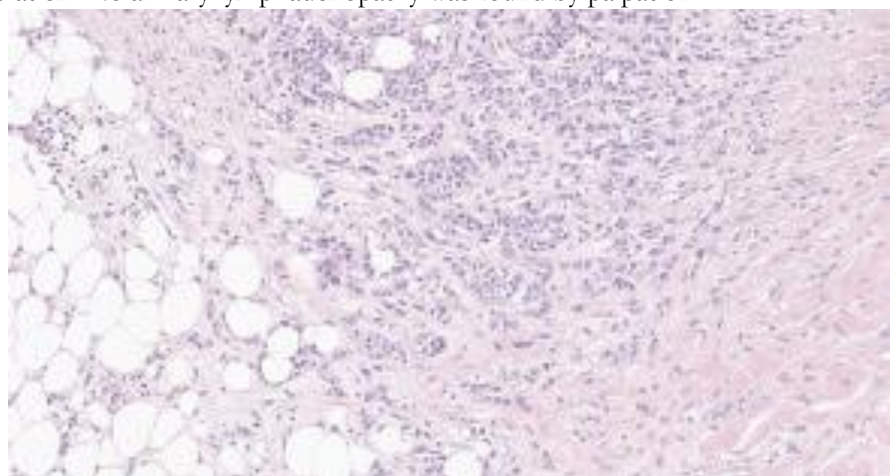


Figure 2. Histopathological findings of invasive carcinoma NST mixed with invasive lobular carcinoma

A core needle biopsy was performed, and a histopathological examination confirmed that it was a case of mixed carcinoma, made of invasive carcinoma of no special type and invasive lobular carcinoma. Imaging studies, including chest radiography and abdominal ultrasonography, were conducted to evaluate for metastasis; both were unremarkable. Immunohistochemical staining revealed strong positivity for estrogen (ER) and progesterone (PR) receptors (90% each), HER2-negative status, and a Ki-67 proliferation index of 20%.



Figure 3. Clinical presentation of the patient at the six-month postoperative follow-up.

The patient subsequently underwent a modified radical mastectomy. Adjuvant therapy consisted of six cycles of cyclophosphamide-doxorubicin chemotherapy followed by tamoxifen. Postoperative follow-up included routine imaging with chest X-ray and abdominal ultrasound every three months during the first year and biannually during the second year. No signs of local recurrence or distant metastases were detected during follow-up evaluations.

4. Discussion

The mammary glands in men are disc-shaped, similar in diameter to the areola, and approximately 3 to 4 millimeters thick. These glands consist of fatty tissue, several excretory ducts, and connective tissue, but do not have acini or lobules⁶. This breast tissue can respond to hormonal stimuli, leading to the growth of connective tissue and ducts (gynecomastia), and it can also develop cancer^{1,6}. Gynecomastia and breast cancer are the most common breast pathologies in men. Male breast cancer is significantly less prevalent than in women, it often carries a poorer prognosis due to delayed detection, typically occurring at more advanced stages. The average age at diagnosis in males is around 60, approximately a decade later than in females^{7,8}. Notably, the patient in this case was diagnosed at just 40 years old, without any prior medical conditions or familial history of malignancy, making the presentation both atypical and clinically significant.

In the early stages, breast cancer in men is typically asymptomatic and painless, with most patients seeking medical attention only when symptoms appear, indicating advanced disease. The most common clinical presentation is a unilateral retro-areolar or para-areolar nodule, usually eccentric to the nipple, averaging 20 mm at the time of diagnosis⁹. Pain is associated with the mass in only 5 to 10% of cases. Skin or chest wall involvement is frequent,

leading to fixation of the mass, sometimes accompanied by axillary adenopathy. Nipple alterations are rare, with retraction observed in 5 to 10% of cases, ulceration in 6%, and secretion in 9%. Notably, 57-75% of men with bloody nipple discharge have cancer, making this symptom an important indicator of potentially non-invasive disease^{2,3}. In this case, the patient did not have nipple alterations or discharge, however he presented with a unilateral sub-areolar nodule that is immobile, with hard and painful to palpate. This may explain his previous diagnosis of gynecomastia, as the early stages of the condition often present with similar clinical features.

The cause of male breast cancer is unknown. Many subjects have no risk factors, but genetic, hormonal, and environmental factors have been documented. Recognized risk factors for male breast cancer include a history of breast cancer in a first-degree relative, previous benign conditions, or chest radiation. The probability of male breast cancer is increased by hormonal effects that lead to an excess of estrogen, this is manifested as a lack of testicular descent, congenital hernia, orchiectomy, orchitis, infertility, and Klinefelter syndrome¹. Klinefelter syndrome in men carries an increased risk of breast cancer, ranging from 20 to 50 times higher compared to the general population. It is also associated with obesity due to hormonal imbalance; hence, a man with a body mass index greater than 30 kg/m² has a greater risk of experiencing the disorder¹⁰. Risk factors have been classified into three categories which predispose men to breast cancer. High-risk factors include hormonal imbalances, radiation exposure, Klinefelter syndrome, BRCA2 gene mutation, and family history of cancer. Low or moderate risk factors include occupational heat exposure, obesity, and BRCA1 or CHEK2 gene mutation¹⁰. In this patient, the risk factors of breast cancer is unclear. He had no prior hormonal imbalances, no genetic mutations, and was only overweight. His occupation was a day-to-day laborer with no known exposure to intense heat.

Imaging studies play a key role in the differential of malignant breast disease from benign conditions of the breast, including gynecomastia, unilateral hypertrophy, epidermal inclusion cysts, lipomas, fibromas, acute and tuberculous mastitis, lymphoma, sarcoma, hemangioma, metastatic tumors, myofibroblastoma, adenopathies, bruises, abscesses, and papillomas. Diagnosis is based on clinical examination, mammography, ultrasound, and biopsy. Mammography helps in differentiating malignancy from gynecomastia, as most carcinomas present eccentrically outside the subareolar area while gynecomastia presents as a density centered on the nipple extending fan-like to the rear. The normal male breast consists mainly of fat tissue with few duct structures lining a prominent pectoral muscle in the subareolar area. The echographic findings in male breast carcinoma are similar to those in females, with the lesions presenting as hypoechoic with irregular, spiculated, or lobed borders¹¹. This patient lives in a rural area, where hospitals are scarce diagnostic facility is limited. This explains the delayed diagnosis of breast cancer, as referral takes more time and out-of-pocket expenses than in urban areas.

All of the different subtypes of breast cancer that have been described in women can be found in men, with 80%-90% of them being invasive and 80% of them being ductal carcinomas. Ductal carcinoma in situ is uncommon, but its prevalence, especially the papillary variety, is 5% and has increased as a result of earlier detection. Since the male breast has only ductal tissue, ductal carcinoma is the most common form of histology. About 90% of these tumors have receptors for estrogen and progesterone, therefore, Tamoxifen is commonly used

as a treatment^{1,4}. Due to the underdeveloped lobular structures in the male breast, Invasive Lobular Carcinoma (ILC) is rare, though sporadic cases have been documented in the literature. This subtype comprises of just 1% of all male breast malignancies. Our patient presented with a mixed carcinoma, specifically invasive carcinoma NST mixed with invasive lobular carcinoma, a rare subtype occurring in male breast cancer. Although it is not as rare as ILC, this mixed type is also uncommon^{12,13}.

Biopsy is the sole method of diagnosing breast cancer that is definitive, and should be performed on all patients with irregular or asymmetric masses, nipple discharge, axillary adenopathy, or masses that are attached to the skin. The small size of the male breast's cells allows the tumor to reach the chest wall prior to the appendage. However, in ductal carcinoma in situ, the cancer cells remain in the ducts without invading the fatty tissue; in the invasive lobular carcinoma, the cancer cells originate from the mammary glands and invade the fat cells; in the invasive ductal carcinoma, the cancer cells are derived from the ducts and can spread to other parts of the body⁹. In this case, the malignancy was accurately diagnosed prior to significant disease progression, allowing for timely intervention. With timely diagnosis and appropriate management, the patient is likely to achieve a favorable outcome and an improved overall survival rate.

5. Conclusion

This case accentuates the need to maintain a high index of suspicion for malignancy in males presenting with breast enlargement, even when the clinical features may suggest gynecomastia. Though rare, carcinoma in males can present with symptoms similar to those of benign conditions and may be diagnosed late if not followed properly. Early detection, proper imaging, and histopathological confirmation are necessary for timely intervention and a better prognosis. The physician should consider male breast cancer among the differential diagnoses, especially if the patient presents with persistent or asymmetric changes in the breast, regardless of the patient's age or risk factors.

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