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## Case Report

Rare case of invasive lobular carcinoma in a male <sup>☆</sup>

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## ABSTRACT

Invasive lobular carcinoma (ILC) in the male breast is a rare subtype of a rare disease in men, accounting for approximately 1%-2% of all male breast cancers [1,2]. Only a few cases have been reported in the literature. The pathophysiology is uncommon due to a paucity of lobular development seen in men. We present a rare case of ILC in the male breast, highlighting imaging, pathology findings, and clinical management.

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## Introduction

Male breast cancer is rare, accounting for approximately 1%-2% of all breast cancer diagnoses [1,2]. The vast majority of male breast cancers are of the invasive ductal carcinoma (IDC), not otherwise specified subtype. Invasive lobular carcinoma (ILC) is extremely rare in the male breast, accounting for an estimated 1-2% of all breast cancers in men compared to 10%-15% in women, with very few cases reported in the literature [2,3]. This is due to a paucity of lobular proliferation seen in men, which is stimulated by estrogen. We present a case of male ILC, highlighting imaging features, pathological characteristics, and clinical management.

## Case report

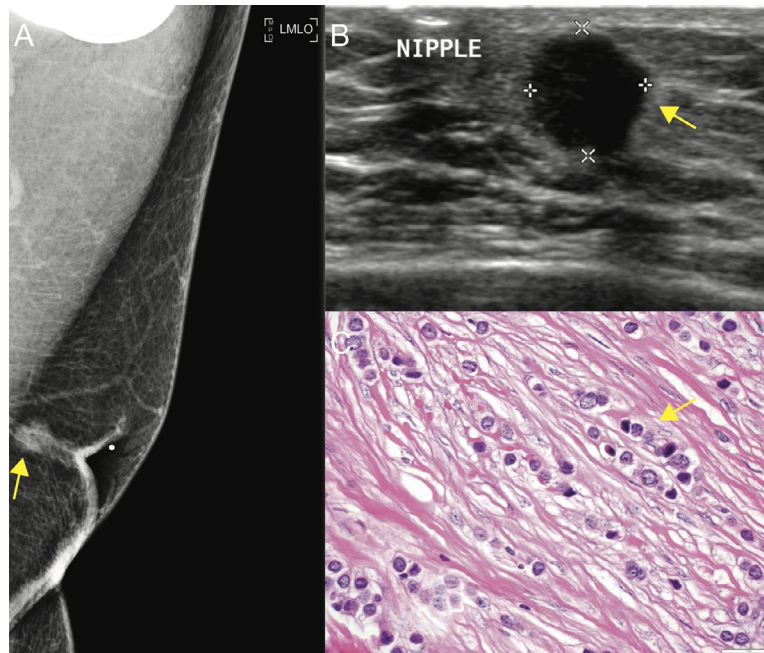
A 73-year-old male with a family history of postmenopausal breast cancer in his mother presented to the breast clinic with a 2-month history of a left breast lump. Outside of family history and an elevated body mass index of 27 kg/m<sup>2</sup>, the patient had no known additional breast cancer risk factors. Bilateral 2D mammogram and targeted left breast ultrasound of the palpable area was performed. The left mammogram and targeted left subareolar ultrasound demonstrated a 10 mm irregular mass with spiculated margins eccentric to the nipple with associated left nipple retraction (Fig. 1). Notably, no associated gynecomastia was visible mammographically. The mass was

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**Figure 1 – (A) Mediolateral oblique (MLO) mammographic view on presentation demonstrates an irregular retroareolar left breast mass with associated nipple retraction. (B) Targeted left breast ultrasound demonstrates an irregular hypoechoic mass with spiculated margins located eccentric to the nipple. (C) Histopathology with hematoxylin and eosin staining on high-power magnification (400x) show the classic invasive lobular carcinoma growth pattern of linear files of dyscohesive cells (yellow arrow).**

sampled by the referring provider under palpation-guided fine needle aspiration (FNA); however, the sample was inadequate for diagnosis.

Given the high clinical suspicion for breast cancer, the patient proceeded directly to excisional biopsy with intraoperative frozen section to guide further management. During the excisional biopsy, the frozen section was positive for ILC. A left mastectomy with nipple excision and sentinel lymph node biopsy was subsequently performed during the same operation. All 3 excised lymph nodes were negative for malignancy.

Final pathology revealed a 15 mm Grade 2 ILC with lobular carcinoma in situ. The invasive carcinoma was estrogen receptor positive, progesterone receptor positive, and human epidermal growth factor receptor (HER2-neu) negative. Epithelial cadherin (CDH1) was also tested, demonstrating a loss of expression that is characteristic of lobular carcinoma. The patient subsequently underwent negative genetic testing for BRCA 1 and 2. The patient took Tamoxifen as adjuvant hormone therapy for 5 years following surgery. No recurrence has been identified in over 7 years of follow-up.

## Discussion

ILC in the male breast is a rare subtype of a rare disease. Male and female breast development is similar until puberty, at which time female exposure to estrogen stimulates lobular proliferation with the formation of terminal ductal lobular units [4]. Breast lobules do not proliferate in men without the

exposure of estrogen; therefore, lobular-related pathologies such as fibrocystic change, fibroadenomas, lobular carcinoma in situ, and ILC are rare [5]. Factors that increase the risk for all types of male breast cancer include older age, family history, genetic risk factors (BRCA2>BRCA1 mutations, Klinefelter syndrome), hormone status (increased circulating estrogen due to obesity, medications or disease states), and radiation exposure [6]. While the exact pathogenesis of lobular carcinoma in men remains uncertain, it is possible that sex hormone dysregulation outside the pubertal period may support lobular development in men given that increased estrogen states are risk factors for male breast cancer.

The American College of Radiology's appropriateness criteria for evaluation of the symptomatic male breast state that imaging with a combination of mammography and ultrasound is indicated if benign breast disease cannot be differentiated from breast cancer on the basis of clinical findings [7]. Gynecomastia, the most common benign breast finding in men, tends to present as dense tissue centered in the subareolar region in a nodular, dendritic, or diffuse pattern [8].

In a literature review of male breast ILC case reports, Senger et al. notes that the majority of patients clinically presented with a palpable mass [2]. Additional presentations included skin thickening, nipple retraction, and lymphadenopathy [2]. Whereas gynecomastia is often bilateral and centered in the subareolar region, breast cancer in males is often unilateral and located eccentric to the nipple [6]. The imaging characteristics of our ILC case could not necessarily be differentiated from IDC, presenting as an irregular mass with spiculated margins on both mammogram and ultrasound.

Breast cancer often presents at a later stage in men compared to women, likely due to a lower clinical suspicion of the disease. In a retrospective study of 5494 men and 835,805 women with all types of breast cancer, Anderson et al found that men had larger tumor size (2.4 cm versus 2.2 cm) and were more likely to have positive axillary lymph nodes (incidence rate ratio of 0.73 versus 0.50) compared to women [9]. In another retrospective study of 88 men and 96,609 women with ILC, Senger et al. found that a larger proportion of men had stage IV disease compared to women (13.6% versus 5.9% of reported cases) [2]. The majority of male ILC tumors in this study were estrogen and PR positive (95% and 73%, respectively), similar to the female ILC population (95% and 78%, respectively) [2]. Therefore, risk factors that increase circulating estrogen levels may be particularly relevant for male ILC development. A pathological hallmark of ILC that distinguishes it from IDC is the loss of e-cadherin (CDH1), a cell adhesion protein, resulting in the dyscohesive appearance of the tumor cells on histopathology [10].

Tissue sampling may be obtained by FNA or core needle biopsy (CNB). It should be noted that FNA cannot determine hormone receptor status and may lead to false negative results. In a review of FNA versus CNB of the breast, Willems et al. concluded that CNB has a greater sensitivity, specificity, and ability to perform additional diagnostic tests than FNA, reporting average success rates of 99% for CNB compared to 60%-75% for FNA [11]. Thus, CNB under ultrasound guidance is preferred.

Perioperative frozen section is not as reliable as permanent section surgical pathology due to significant frozen section artifact. False positive and false negative results are rare but do occur. Specifically regarding ILC, Lester notes that identification on frozen section can be particularly difficult; tumor cells may be mistaken for lymphocytes or histiocytes, therefore preoperative diagnosis is preferred [12]. In a retrospective review of 2110 specimens of palpable breast tumors evaluated with frozen section, Cserni notes that false negative and false positive diagnostic errors were due to several factors including misinterpretation, poor specimen quality, and sampling error [13].

Treatment guidelines for male breast cancer are not well established. However, the National Comprehensive Cancer Network states that mastectomy with sentinel lymph node biopsy or axillary lymph node dissection remains the mainstay of surgical treatment in men, preferable to breast conservation with radiation. Chemotherapy and hormone therapy may be used in the adjuvant setting depending on tumor characteristics. All men with breast cancer are also recommended to consider undergoing genetic testing [14].

Anderson et al. suggest that the tumor biology of male breast cancer is more similar to that of postmenopausal women rather than premenopausal women [15]. In their retrospective study, breast cancers in men and postmenopausal women were more likely to demonstrate lower histological grade and positive hormone expression compared to those in premenopausal women [15]. Several key differences between breast cancer in men and women exist, including later presentation, increased tumor size, positive nodal status, and decreased incidence of certain pathology subtypes such as ILC in men [9,15,16].

While male breast cancer is a rare disease, it is imperative that clinicians consider this diagnosis when men present with suspicious findings. Specific findings that should warrant further work-up include palpable lumps in the breasts or axillary regions, nipple discharge, or other skin changes including nipple retraction or discoloration. Additionally, breast cancer risk should be assessed in men with strong family history or other breast cancer risk factors. Breast cancers remains a largely treatable disease in both men and women, but early detection remains a critical factor in curative treatment.

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