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Oncology

Rare case of male breast intraductal papilloma progressing to invasive ductal carcinoma: A radiologic-pathologic correlation

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ABSTRACT

Although male breast cancer represents only 0.5%–1% of all breast cancer cases in the United States, the incidence of this disease is slowly rising [1]. Because of its extremely low prevalence, screening and treatment guidelines are not well established. Thus, analyzing cases of male breast cancer can accelerate this process. We present a case of a 52-year-old man, initially diagnosed with biopsy-confirmed intraductal papilloma without atypia, who presented 3 years later with progression of this benign lesion to ductal carcinoma in situ and development of de novo invasive ductal carcinoma. This report stresses the importance of symptom detection and risk factor modification with the goal of decreasing the incidence of this disease.

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Background

Because male breast cancer (MBC) is a rare disease, with less than 2500 new cases diagnosed each year, there is relatively little known about its etiology, risk factors, and prognosis compared with female breast cancer [2]. As a result, individual case reports are helpful in providing the epidemiologic data required to elucidate these important characteristics. This information is also useful to determine a diagnosis from a constellation of symptoms that seems to fit a certain disease but when laboratory results do not align.

We describe a case in a male patient of a benign breast mass that progressed to ductal carcinoma in situ and the

development of invasive ductal carcinoma (IDC) alongside this lesion. We also discuss risk factor modification and accepted treatments for MBC.

Case presentation

A 52-year-old African American man presented to his primary care physician in October 2014 due to nipple pain and discharge. The patient reported intermittent, expressible reddish brown discharge from the right nipple since 2011. Occasionally, a palpable lump was noticed with associated pain, but no erythema or dimpling was present. He denied trauma to the area and reported no recent weight loss.

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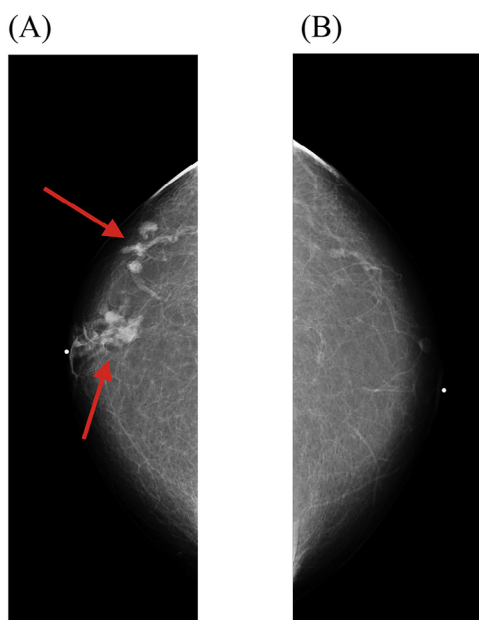


Fig. 1 – (A) Craniocaudal mammogram of the right breast demonstrating masses. (B) No suspicious abnormalities are noted in the left breast.

The patient's medical history included hypertension, hyperlipidemia, atrial fibrillation, and morbid obesity. His family history was significant because of a prolactinoma diagnosed in his sister. Serum thyroid stimulating hormone, free T4, and prolactin levels were normal, and liver and kidney functions were also normal.

Mammography and ultrasonography revealed areas of duct ectasia with 2 intraductal masses in the right breast and a mildly prominent right axillary node (Fig. 1). Several ultrasound-guided core needle biopsies were obtained from each lesion using an 18-gauge needle (Fig. 2). Pathologic examination of both masses revealed intraductal papillomas with microcalcifications. Same-day biopsy of the prominent lymph node showed reactive lymphoid tissue without malignancy.

His pain was managed conservatively with non-steroidal anti-inflammatory drugs (NSAIDs) and he was scheduled for routine follow-up appointments with our breast and primary care clinics.

Three years after this benign biopsy, the patient noticed enlargement of the palpable lumps and a change in color of the nipple discharge to dark brown. An ultrasound was ordered, which showed interval growth of the intraductal masses along with abnormal-appearing right axillary lymph nodes (Fig. 3). An excisional biopsy revealed estrogen receptor- and progesterone receptor-positive, human epidermal growth factor receptor 2-negative invasive ductal carcinoma (Figs. 4 and 5).

In November 2017, the patient underwent a right simple mastectomy, which revealed intermediate grade ductal carcinoma in situ. Biopsies of right axillary sentinel lymph nodes were negative for malignancy. The patient was referred to our hematology or oncology clinic, and hormonal therapy with tamoxifen was started.

Discussion

Invasive ductal carcinoma represents approximately 90% of new MBC diagnoses, whereas lobular carcinoma accounts for 1.5% of cases [3]. The most common presenting symptom is a palpable breast mass, which may be accompanied by nipple discharge, lymphadenopathy, or surrounding skin changes [4]. Imaging evaluation of MBC in men is identical to that in women, utilizing the breast imaging-reporting and data system (BI-RADS), and staging similarly using the Tumor, Node, Metastasis (TNM) staging system for breast cancer.

Careful examination was performed in both the IDC and ductal carcinoma in situ. Based on their histologic appearances, we believe the former malignant neoplasm developed de novo and the latter lesion developed from the original intraductal papilloma. Both intraductal masses found on the initial core biopsy were also adequately sampled and compared.

Following the core biopsy, the histologic diagnosis of benign intraductal papilloma was discordant with radiology since the

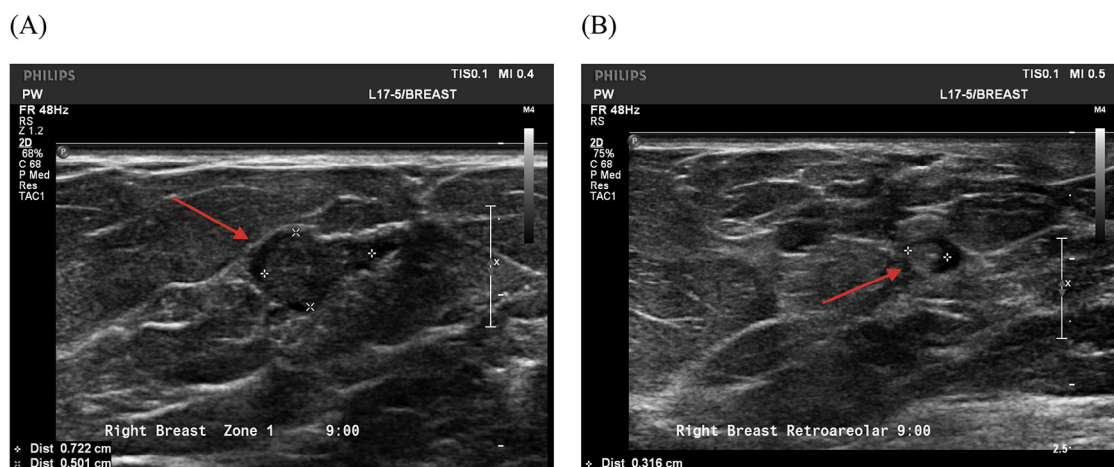


Fig. 2 – Right breast ultrasound images demonstrating (A) a 7 mm solid intraductal mass and (B) a 3 mm hyperechoic mass. Both lesions were located at the 9-o'clock position.

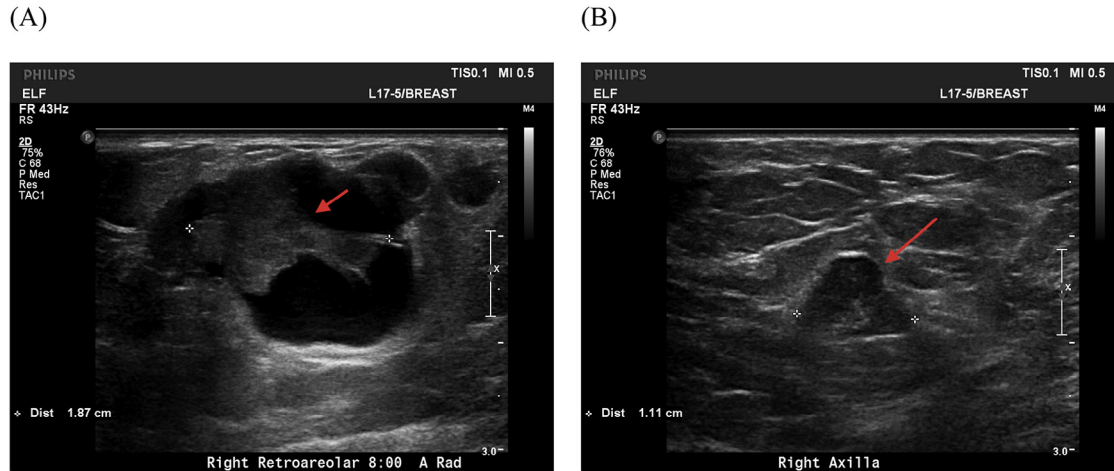


Fig. 3 – (A) Ultrasound image showing moderate to marked duct ectasia in the retroareolar region of the right breast, within which is a solid vascular isoechoic mass (arrow) at the 8-o'clock position measuring $1.7 \times 1.3 \times 1.9$ cm. (B) Eccentric cortical thickening is seen within a right axillary lymph node, which measures up to 1.1 cm.

BI-RADS score was 4 (suspicious for malignancy). The subsequent breast ultrasound (also BI-RADS 4) performed years later was concordant with the IDC demonstrated on excisional breast biopsy [5]. Suspicious features included increased mass size, moderate to marked breast duct ectasia, and cortical thickening within intramammary and axillary lymph nodes. Discordant features included small mass size and fibroglandular thickening.

Interestingly, IDC is associated with mutations of the BRCA1 and PT53 genes and has a higher frequency of unilaterality than lobular breast cancer [6,7]. Axillary lymph node involvement is the most important prognostic factor for MBC [8], with a 5-year survival rate of 90% in patients who are node-negative and a 5-year survival rate of 65% in patients who are node-positive [9]. Tumor size and hormonal status are also significant prognostic factors, with an 85% 5-year survival rate for tumors measuring less than 2 cm [8], and an improved rate for those that are hormone-receptor

positive [10]. This patient's axillary lymph node status, tumor size, and hormone receptor status confer an improvement to his prognosis. The patient denied experiencing any further discharge after the biopsy. This improvement, combined with the small mass sizes, prompted the decision to not excise these papillomas after initial biopsy.

Because there are no established guidelines for the management of MBC, physicians refer to the treatment recommendations for female breast cancer, which include surgical and medical management. The agreed-upon treatment is modified radical mastectomy with sentinel node or axillary dissection depending on lymph node involvement [2]. Because the majority of MBC cases is hormone-receptor positive, tamoxifen has been shown to improve survival rates [11].

The underlying etiology of MBC provides insight into how this disease can be prevented and treated. Imbalances in estrogen and androgen levels increase the risk for MBC, and patients with testicular abnormalities, infertility, Klinefelter syndrome, and obesity are at greater risk. A positive family history of breast cancer (in either a male or female relative), radiation exposure, increasing age, and Jewish ancestry are also risk factors [3]. Our patient's long-standing morbid obesity is an important consideration in his cancer diagnosis, and although he was counseled on diet and exercise modification, met with our Registered Dietitian, and even started to show initial weight loss, these lifestyle changes would have had a greater impact had they been stressed much earlier. Thus, although a rare disease, the incidence of MBC can be attenuated by counseling patients on healthy lifestyle behaviors, which can mitigate the hormonal etiology of this disease.



Fig. 4 – Gross image of right breast mass fragments showing unoriented pale yellow soft tissue pieces measuring $3.5 \times 2.5 \times 2.0$ cm in aggregate and weighing 6.4 grams. (Color version available online.)

Conclusions

It is imperative physicians keep in mind that even men are at risk for breast cancer, and a risk factor as common as obesity can be avoided by simple lifestyle modifications.

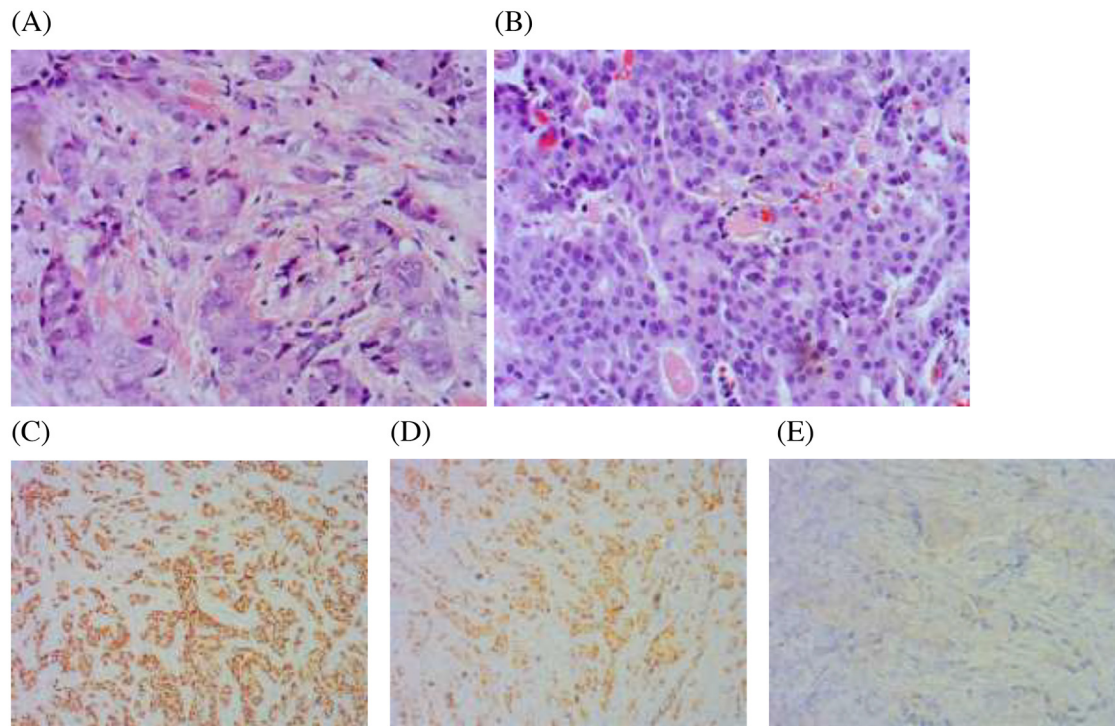


Fig. 5 – (A) Hematoxylin and eosin stain at 20× magnification showing infiltrating mammary carcinoma, ductal type (nuclear grade: 3, tubule formation: 3, mitotic index: 1, overall grade: 2/3). (B) Adjacent to the tumor is a papillary neoplasm diffusely involved by intermediate grade ductal carcinoma in situ. (C, D, E) Immunohistochemical stains for estrogen receptor (ER, Fig. 5C), progesterone receptor (PR, Fig. 5D), and human epidermal growth factor receptor 2 (HER2, Fig. 5E). Staining for ER shows 95% of tumor cells with strong or moderate nuclear positivity, staining for PR shows 60% of tumor cells with moderate or weak positivity, and staining for HER2 is negative with a score of 1+.

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