Ductal Carcinoma in situ in a 25-Year-Old Male with Unilateral Gynecomastia

Christopher J. Coroneos (Meds 2010)
Faculty Reviewer: Dr. Caroline Hamm

DCIS in a young male is rarely reported. Our patient is a 25 year old male who presented with symptomatic unilateral gynecomastia. He presented with a strong family history of cancer on both maternal and paternal sides of his family including breast, lung (maternal) and melanoma, colon and pancreatic (paternal). His mother tested negative for BRCA1 and BRCA2. There is no information on the paternal genetic testing. He was treated with left subcutaneous mastectomy. Upon histologic review of the sample, concurrent gynecomastia and ductal carcinoma in situ was discovered. To date, only four cases of gynecomastia and DCIS have been described in younger male patients. Since only 30 – 50% of patients with DCIS eventually develop invasive cancer in the subsequent 10 – 20 years, this figure in the general population may be higher. This case underscores the importance of family history in any patient presenting with a breast mass. Patients must be made aware of the risk, however small it may be, and physicians must remain cautious of malignancy in young males with gynecomastia.

Introduction

By definition, gynecomastia is a benign condition affecting males characterized on histology by glandular tissue proliferation.¹ It must be distinguished first from pseudogynecomastia, the deposition of fat with absence of glandular tissue proliferation seen in obese males and second, from breast carcinoma. The increasing size of the breast is due to parenchyma and/or fatty tissue. Gynecomastia is common and most prevalent in the neonatal, pubertal and elderly periods.² However, it is also present in 33-41% of adult males aged 25-45.² Long-standing cases that are resistant to medical management or aesthetically displeasing are treated with surgical excision with or without liposuction.³

In contrast, cases of male breast cancer (MBC) are uncommon, occurring in approximately 1 in 100 000 men⁴ and leading to under 0.5% of male cancer deaths annually.⁵ The age of incidence is typically 65-67 years.⁶-⁹ Risk factors include testicular abnormality, estrogenic/androgenic imbalance, Klinefelter syndrome, BRCA mutation, positive family history, obesity, radiation exposure and liver disease.⁸ While gynecomastia has been hypothesized to be associated with MBC, research indicates its incidence is not higher among MBC patients when compared to the general population.⁴,¹⁰,¹¹ The rare coexistence of the two conditions has been identified in the literature.¹²,¹³ Still more rare are cases of ductal carcinoma in situ (DCIS) with gynecomastia, especially in the young adult population. To date, only four cases of DCIS in the setting of gynecomastia have been described in patients that are 25 year old or less¹⁴-¹⁷ and only one of these describes unilateral gynecomastia as our patient does.¹⁶

Case Report

A 25 year old male presented in 2007 for cosmetic mastectomy. He reported a history of new onset localized discomfort in the periareolar region of the left breast and a growth in the left breast for one year, increasing in size. On presentation, both the size of the mass and the associated pain had decreased in magnitude.
Physical exam noted slight swelling deep to the left nipple areolar complex with no axillary lymphadenopathy. The right breast had no discernable changes. Family history was significant for malignancy including the maternal grandmother (metastatic lung cancer to bone and bilateral breast cancer at ages 45 and 46 respectively, death at 49), maternal great-aunt (breast cancer, death at 65), second maternal aunt (breast carcinoma at age 60, relapse and bone metastases, currently undergoing treatment), maternal grandfather (pancreatic cancer), paternal grandfather (colon cancer), paternal great-uncle and two paternal uncles (melanoma). He reported no other health concerns, and history was notable only for surgical hernia repair at age three. The remainder of the physical exam was unremarkable.

Ultrasound reported a small amount (1.5cm) of mixed echogenic tissue in the retroareolar region, consistent with benign changes and gynecomastia. Left subcutaneous mastectomy was performed. The suspected gynecomastia was completely excised, measuring approximately 6.5x6.0x2.5cm, weighing 48 grams. On microscopic examination, pathology reported gynecomastia having abundant fibrous stroma separating ducts having columnar cells with inbudding. In addition, a cribiform pattern of cellular change was present. Pathology was consistent with nuclear grade I/III DCIS, largest focus 7mm. The pathology report mentioned the relative rarity of intraductal carcinoma in the demographic group of our patient.

Further investigation included MR mammogram at three months post-operative, reporting increased signal intensity in the left retroareolar region consistent with post-surgical changes and no abnormal enhancement. CA 19-9 was normal at 13 kU/L. Ultrasound of the abdomen and bone scan demonstrated no abnormalities. Ultrasound of the right (unaffected) breast was unremarkable. The patient’s mother has tested BRCA1/2 negative. The patient underwent follow-up with medical and radiation oncologists and received genetic counselling. Given the negative surgical margins described on pathology, low grade malignancy, absence of axillary findings and potential toxicities of adjuvant treatment in this young age group, no further intervention was recommended.

**Discussion**

Breast cancer in males is far less common than in females. On average, the typical age of onset is up to ten years older than in females. Similar to female cases, incidence of MBC has increased from 0.86 per 100 000 in 1973 to 1.08 in 1998. HER2 overexpression, a negative prognostic factor in women, is found less often in males. Male cases are more frequently ER and PR positive, perhaps indicating increased proliferative activity.

DCIS accounts for approximately 7% of MBC and is far less common than invasive ductal (90% of cases), though lobular malignancy is still more rare with only 1.5% of cases. Median age of incidence is 65 years. Pure DCIS occurs only in 5% of cases as the pathology is often present in association with infiltrating malignancy elsewhere. DCIS is more common in females, representing 20% of cases. Only 30 – 50% of all male and female patients with DCIS eventually develop invasive cancer in the subsequent 10 – 20 years, so actual prevalence in the general population may be higher. Compared to males, fewer intraductal papillary cases with higher grade and younger age are seen in females. The etiology of DCIS is unknown for males since they lack the terminal duct lobular unit (TDLU) where the malignancy has frequently been found to originate in females. However, not all cases are associated with the TDLU and it is hypothesized cases in males originate from epithelium of ducts. Only a limited number of large studies pertaining to male DCIS are available.

Breast cancer of any form in young men is exceptionally rare. At the time of our patient’s presentation, only six cases had been described in males under age 25, and only four cases of males of any age with breast cancer revealed on pathological examination following surgical
intervention for gynecomastia.\textsuperscript{14,15,29,33} To our knowledge, among males 25 years of age or younger, a case of unilateral gynecomastia and DCIS has only been described once in the literature with Chang’s account of a 16 year old male.\textsuperscript{16}

Our patient originally presented with unilateral gynecomastia, though bilateral cases are more common.\textsuperscript{34} There is no evidence that either unilateral or bilateral gynecomastia increase risk for MBC.\textsuperscript{35} Obesity is an independent risk factor, and may confound the association with gynecomastia.\textsuperscript{15} Gynecomastia in adults is most often due to persistence from puberty, drugs, cirrhosis, hypogonadism, testicular tumor, hyperthyroidism and idiopathic.\textsuperscript{36} Beyond his breast, our patient had an otherwise normal physical exam and investigations. Of note however, is the comment in the surgical pathology report of putative anabolic steroid use. Use of anabolic steroids is not mentioned anywhere else in the patient’s medical record. Some state that cases of gynecomastia should be biopsied if presentation includes query Klinefelter’s syndrome, bloody discharge, firm, irregular or unilateral mass.\textsuperscript{37,38} Others endorse mammography to recognize mass since it distinguishes between glandular tissue and fat,\textsuperscript{39,40} though it is not universally supported since male breasts are small and dense.\textsuperscript{41,42} Mammography for MBC has been reported as successful as 92% sensitive, 91% specific.\textsuperscript{43} Our patient received an ultrasound which demonstrated findings consistent with gynecomastia but made no mention of possible malignancy. It did not report microcalcifications typical of DCIS.\textsuperscript{17} The patient was seen again in follow-up with no improvement and surgical intervention of gynecomastia for comesis was planned. The possible increased risk of squamous cell carcinoma and testicular cancer later in life\textsuperscript{44} is considered prior to surgery in a younger patient and annual screening is suggested for cases of gynecomastia.\textsuperscript{16}

DCIS will most often present with bloody nipple discharge and a mass\textsuperscript{21}, though mild symptoms, concurrent gynecomastia and the scarcity of its incidence result in frequent mis-
gynecomastia, subcutaneous mastectomy was performed. The patient was well and no recurrence was detected on follow-up at three months.

There is no indication in the literature that samples from gynecomastia procedures should be routinely sent for pathological examination. Given the unilateral nature in our patient, samples were sent for examination to rule out the rare occurrence of malignancy. Liao et al. recognize the routine histological examination of samples in female cases of reduction mammaplasty. It is further suggested that the same procedure be following for gynecomastia samples when possible, noting suction lipectomy may make it difficult because of large volume and destruction of cells. Perhaps surgical mastectomy should be applied to more cases, allowing for better review of not only the sample itself, but also the surgical margins.

Our patient had a significant family history of breast cancer, though his mother had tested negative for BRCA 1 and 2. Fifteen to twenty percent of all MBC patients have a family history of breast cancer. Just as our patient was, all MBC cases are routinely offered genetic counselling. Beyond BRCA, MBC has been associated with PTEN mutation in Cowden’s syndrome as well as MLH1, a mismatch repair gene related to hereditary nonpolyposis colorectal cancer syndrome. Our patient did not undergo genetic testing since his mother had tested negative.

References
6. Anderson W, Althius MD, Brinton LA, Devesa SS. Is male breast cancer similar or different than female breast cancer? Breast cancer research and treatment 2004;83:77-86.
45. Joshi A, Kapila K, Verma K. Fine needle aspiration cytology in the management of male


