Ductal carcinoma in situ in a 25-year-old man presenting with apparent unilateral gynecomastia

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ABSTRACT

Ductal carcinoma in situ (dcis) in a young man is rarely reported. Our patient, a 25-year-old man, presented with apparent symptomatic unilateral gynecomastia. He has a strong history of cancer on both the maternal and paternal sides of his family, including breast and lung (maternal) and melanoma, colon, and pancreatic (paternal). His mother tested negative for BRCA1 and BRCA2. There is no information on paternal genetic testing.

The patient was treated with left subcutaneous mastectomy. Upon histologic review of the sample, concurrent gynecomastia and dcis were discovered. To date, only 4 cases of gynecomastia and dcis have been described in younger male patients. Because only 30%–50% of patients with dcis eventually develop invasive cancer in the subsequent 10–20 years, dcis prevalence in the general population may be higher than predicted. 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 cancer in young men with gynecomastia.

KEY WORDS

Gynecomastia, ductal carcinoma in situ, male breast cancer

1. INTRODUCTION

Gynecomastia in men is a benign condition characterized by glandular tissue proliferation. It must be distinguished from pseudo gynecomastia and, more importantly, from breast carcinoma. Gynecomastia is most common during the neonatal, pubertal, and elderly periods, although it affects 33%–41% of men aged 25–45 years. Longstanding cases that are resistant to medical management or aesthetically displeasing are treated with surgical excision or without liposuction. With unilateral growth, alternative diagnoses beyond gynecomastia should be considered and fully investigated.

In contrast, cases of breast cancer in men are uncommon, occurring in 1 in 100,000 men and leading to fewer than 0.5% of male cancer deaths annually. Risk factors include testicular abnormality, estrogenic or androgenic imbalance (or both), Klinefelter syndrome, BRCA mutation, positive family history, obesity, radiation exposure, and liver disease.

Gynecomastia has been hypothesized to be associated with male breast cancer, but no increased risk has been found. Coexistence of the two conditions has only occasionally been identified. Even rarer are cases of ductal carcinoma in situ (dcis) with gynecomastia, especially in the young adult population. To date, only 4 cases of dcis in the setting of gynecomastia have been described in patients 25 years old or younger. Only one report describes unilateral gynecomastia similar to that seen in our patient.

2. CASE DESCRIPTION

A 25-year-old man reported new, localized discomfort in the periareolar region and growth of the left breast. Physical exam noted that the left breast was larger than the right, with swelling deep to the left nipple–areolar complex and no axillary lymphadenopathy. The right breast and the remainder of history and physical exam were unremarkable. Testicular exam was normal.

Family history of malignancy was significant, including the maternal grandmother (lung cancer metastatic to bone and bilateral breast cancer at ages 45 and 46 respectively), the maternal aunt (breast carcinoma), a second maternal aunt (breast carcinoma at age 60, relapse and bone metastases), maternal grandfather (pancreatic cancer), paternal grandfather (colon cancer), and paternal great-uncle and two paternal uncles (melanoma).

Ultrasound (Figure 1) reported 1.5 cm of mixed echogenic tissue in the left retroareolar region, consistent with benign changes and gynecomastia. A left subcutaneous mastectomy was planned and performed. The suspected gynecomastia (approximately 6.5×6.0×2.5 cm, 48 g) was completely excised. Pathology (Figure 2) reported gynecomastia with
abundant fibrous stroma separating ducts having columnar cells with inbudding. In addition, a cribriform pattern of cellular change was noted.

The pathology was consistent with nuclear grade I/III DCIS, the largest focus being 7 mm. Cribriform changes were absent in lines of resection, and no microinvasion was detected. Small granular matter was reported within the clear spaces; no necrosis and no calcification were noted. Supporting stroma was fibrous and hypocellular. Staining with P63 demonstrated basal nuclei in cribriform and noncribriform areas. Heavy-chain myosin was demonstrated to be...
not contributory. Estrogen receptor (ER) uptake was present in cribriform and noncribriform patterns equally with progesterone receptor (PR) staining (less on cribriform structures).

Magnetic resonance imaging at 3 months post surgery reported increased signal intensity in the left retroareolar region consistent with postsurgical changes and no abnormal enhancement. Cancer antigen 19-9 was normal at 13 kU/L. A bone scan and ultrasonography of the right breast and abdomen were unremarkable. The patient’s mother has tested negative for BRCA1/2. Follow-up with medical and radiation oncologists and genetic counselling were completed. The patient declined genetic testing.

Given the negative surgical margins described on pathology, the diagnosis of DCIS, an absence of axillary findings, and the potential toxicities of adjuvant treatment in the young age group to which this patient belonged, no further intervention was recommended. He is well, and no recurrence was detected at 2 years’ follow-up.

3. DISCUSSION

Male breast cancer is uncommon. As with the incidence in women, the incidence of breast cancer in men has increased (to 1.08 in 100,000 in 1998 from 0.86 in 100,000 in 1973)2. Overexpression of the human epidermal growth factor receptor 2 (HER2), a negative prognostic factor in women, is found less often in men7. Men are more frequently ER and PR positive, perhaps indicating increased proliferative activity8.

Ductal carcinoma in situ accounts for approximately 5%–7%5 of male breast cancer. The papillary form of DCIS is most common, but all subtypes that present in women also occur in men9. Pure DCIS occurs in only 5% of cases because the pathology is often associated with invasive cancer elsewhere9. The condition is more common in women, representing 20% of breast cancer cases, with fewer high-grade intraductal papillary cases than are seen in men10. Of all male and female patients with DCIS, 30%–50% eventually develop invasive cancer in the subsequent 10–20 years, and so the actual prevalence in the general population may be higher11. The causes of DCIS in men are unknown, because men lack the terminal duct lobular unit (TDLU) in which DCIS frequently originates in women9. Not all cases are associated with the TDLU, however; and it is hypothesized that cases in men originate from duct epithelium9.

Breast cancer, whether invasive or noninvasive, is exceptionally rare in young men. At the time of our patient’s presentation, only 6 cases had been described in males under the age of 252,4,12–15. Only 4 males of any age have had breast cancer revealed on pathology examination after surgical intervention for gynecomastia2,4,12,16.

Although bilateral gynecomastia is more common, there is no evidence that either unilateral or bilateral disease increases the risk for male breast cancer5. However, rapid growth in one breast necessitates consideration of diagnoses beyond gynecomastia and should be further investigated1. Obesity is an independent risk factor and may confound the association with gynecomastia2. Gynecomastia in adults can be a result of persistence from puberty or of drugs, cirrhosis, hypogonadism, testicular tumour, and hyperthyroidism1.

Beyond the enlarged breast, our patient had an otherwise normal physical exam and associated investigations. Given the patient’s history and examination, Klinefelter syndrome was not suspected. Of note are comments on the surgical pathology of putative anabolic steroid use. Use of anabolic steroids or similar substances is not mentioned anywhere else in the patient’s medical record.

The literature indicates that gynecomastia should be biopsied if presenting with the possibility of Klinefelter syndrome, with bloody discharge, or with firm, irregular, or unilateral mass1. Other sources endorse mammography to recognize mass, because mammography distinguishes between glandular tissue and fat, although it is not universally supported for small and dense male breasts6. Mammography for male breast cancer has been reported to be successful, with 92% sensitivity and 91% specificity17.

Our patient underwent ultrasonography, which demonstrated findings consistent with gynecomastia with no mention of the masses or microcalcifications typical of DCIS6. The possible increased risk of squamous cell carcinoma and testicular cancer later in life18 is considered before surgery is undertaken in a younger patient, and annual screening is suggested for cases of gynecomastia5.

Ductal carcinoma in situ most often presents with bloody nipple discharge and a mass19. The rare incidence of DCIS and the presence of concurrent gynecomastia can frequently result in misdiagnoses4. Our patient’s DCIS was diagnosed on routine postoperative pathology investigation without preoperative diagnostic evaluation and staging. Fine-needle aspiration cytology is accurate in men when sufficient tissue is obtained, although in up to 25% of cases, samples are insufficient20. Profiles for ER, PR, and HER2 are obtained. The remainder of the diagnostic work-up mirrors that for cancer in women.

The prognosis in male DCIS is uncertain. It may be worse than it is in women, but this suggestion is disputed because of small sample sizes10. At 8 years of follow-up in women, the frequency of ipsilateral tumours is 13% with lumpectomy and breast irradiation; mortality is 1.6%21. Cutuli et al. observed 4 recurrences in follow-up of 27 male DCIS patients: 3 after lumpectomy, and 1 after modified radical mastectomy22. Among all cases of male breast cancer, 0.7% will suffer contralateral disease with a standardized incidence ratio of 30 overall and 110 for patients younger than 50 years of age at onset23. Recurrence
risk can be determined in men as it is in women, using the updated University of Southern California/Van Nuys Prognostic Index\(^4\), which is based on age, histologic grading, surgical margins, and size of the lesion. The score is graded to indicate treatment with excision alone, adjuvant radiation, or mastectomy\(^24\).

Treatment of male DCIS does not have an established benchmark; it is guided by experiences reported in the literature\(^4\). Total mastectomy has been suggested, and a recurrence following this procedure has yet to be described\(^19\). The National Surgical Adjuvant Breast and Bowel Project B-17 study illustrated the benefit of radiotherapy for DCIS in women\(^21\). Research pertaining to lumpectomy and adjuvant radiotherapy for men is sparse. Simple excision alone is often endorsed\(^19,22\), although some authorities maintain that total mastectomy be performed because nipple excision is usually necessary\(^4\). Excision of the nipple is done because the small size of the male breast typically leads to subareolar involvement\(^4\). There is no evidence for the use of axillary lymph node dissection, tamoxifen, or adjuvant radiation with or without chemotherapy\(^19\). Because our patient received treatment for what was thought to be gynecomastia, subcutaneous mastectomy was performed. Subcutaneous mastectomy is not indicated for breast cancer with subareolar involvement among women\(^25\).

Significant discussion occurred regarding local therapy for this patient, and the decision was made to continue with subcutaneous mastectomy alone. That decision is supported in a review from the American Society of Clinical Oncology\(^26\). Those authors concluded that the admonitions against skin-sparing mastectomies by surgical oncologists—although seeming reasonable—are supported only by anecdotal experience. In the patient with an inheritable predisposition to breast cancer, prophylactic mastectomies may be performed using the skin-sparing technique.

The literature does not indicate that samples from gynecomastia procedures undergo pathology examination. Given the unilateral presentation in our patient, samples were examined to rule out cancer. Liao et al.\(^2\) endorsed routine histology examination of samples in female cases of reduction mammaplasty and suggested the same for males when possible. Suction lipectomy may make a histology exam difficult because of a large volume and destruction of cells\(^2\). Surgical mastectomy may allow for a better review both of the sample itself and of the surgical margins.

Our patient has a significant family history of breast cancer, although his mother is BRCA1- and BRCA2-negative. Family history is present in 15%–20% of male breast cancer, and genetic counselling is routine. Beyond BRCA, male breast cancer has been associated with PTEN mutation in Cowden syndrome and with mutations in androgen receptor, CHEK2, and CYP17\(^1\). Given that his mother had tested negative, our patient declined genetic testing.

4. CONCLUSIONS

Here, we described a rare case of concurrent gynecomastia and DCIS in a young adult male. While the literature reports a few experiences with similar cases, very few supported recommendations for treatment can be found. The potential sequelae of radiation in our patient’s demographic were felt to outweigh benefit. Our case underscores the importance of ruling out cancer in patients with a positive family history.

5. REFERENCES


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