CASE REPORT

Invasive lobular carcinoma: a rare presentation in the male breast

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SUMMARY

Breast cancer in men is uncommon, accounting for <1% of all breast cancers. Even though lobular structures are quite infrequent in the male breast, rare cases of invasive lobular breast carcinoma have been described, representing 1–2% of all breast cancers in men. Risk factors include undescended testes, congenital inguinal hernia, orchiectomy, orchitis, testicular injury, infertility and Klinefelter's syndrome, previous thoracic radiotherapy, alterations of the oestrogen–testosterone ratio and familial history (BRCA 2 and 1). The authors present a case of a 52-year-old man with no relevant predisposing factors to breast cancer, who presented with a painless, firm nodule, fixed to the nipple on the left breast, associated with nipple retraction and ulceration, and fully characterised by mammogram and ultrasound. Histopathological and immunohistochemical analysis revealed the diagnosis of invasive lobular breast carcinoma and the patient underwent left radical mastectomy, followed by adjuvant chemotherapy, radiotherapy and hormone therapy. A brief review of the literature is presented.

BACKGROUND

Breast carcinoma in men is very rare, representing <1% of all breast cancers, and invasive lobular carcinoma (ILC) represents only 1–2% of them.¹ Since 1989, when the first case of ILC in a male patient without known oestrogen exposure was described, few cases have been reported in the literature.²

CASE PRESENTATION

A 52-year-old man, the father of two children, was referred to our institution, with a lump in his left breast. There was no history of predisposing factors to breast cancer such as medication use or relevant family history of cancer.

On physical examination, a painless, firm nodule, fixed to the nipple, was found in the transition of external quadrants of the left breast, associated with significant nipple retraction and ulceration. The axillary lymph nodes were not palpable.

INVESTIGATIONS

Bilateral craniocaudal (CC) and mediolateral oblique (MLO) mammographic projections showed an eccentric dense retroareolar nodule located in the transition of the external quadrants of the left breast, with spiculated and indistinct contour, infiltrating the nipple and retracting the skin, and highly suspicious for malignancy. A few microcalcifications were seen (figures 1 and 2).

Complementary ultrasound revealed an irregular, solid, 3 cm hypoechoic and inhomogeneous nodule with indistinct borders, connected to and retracting the nipple, corresponding in size and location to the lesion seen on the left mammogram (figure 3). Axillary ultrasound did not reveal suspicious lymph nodes. The left breast was then categorised according to American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) as BI-RADS 5, and an ultrasound-guided core biopsy was performed using an automated 14-gauge needle. The histopathological and immunohistochemical analysis which showed monomorphic cells arranged in sheets and in single file, negative for e-cadherin, revealed the ultimate rare diagnosis of ILC, confirmed in the analysis of the radical mastectomy specimen (figures 4 and 5).

Systemic evaluation (thoracic X-ray, abdominal ultrasound and bone scintigraphy) excluded signals of metastatic involvement.

DIFFERENTIAL DIAGNOSIS

Invasive ductal carcinoma (IDC) of no special type is the most common histological type of male breast carcinoma. As the imaging appearance of IDC of no special type and ILC may overlap each

Figure 1 Craniocaudal and mediolateral oblique projections of the left breast showing a palpable solitary irregular mass, with spiculated borders and high density, located in the transition of the external quadrants. A few microcalcifications are seen. Note the nipple and skin retraction.

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Figure 2 Craniocaudal and mediolateral oblique projections of the right breast do not reveal signs of malignancy.

other, it is considered the main diagnostic hypothesis when physical examination and imaging findings suggest malignancy. Although rare, metastases from another primary cancer can present as a breast mass. In both cases, biopsy and histopathological analysis are mandatory to identify the correct diagnosis.

On the other hand, patients and physicians might be concerned by the presence of a breast mass related to gynecomastia, particularly when it is asymmetric. Related risk factors and the typical mammographic appearance of an irregularly marginated subareolar density allow a confident diagnosis of this common presentation.³ Imaging patterns of gynecomastia include nodular, dendritic and diffuse patterns.⁴

Other benign conditions, such as granular cell tumour, can mimic breast carcinoma not only in physical examination also in imaging studies. Biopsy is required to establish the correct diagnosis and avoid non-proper treatment.⁵

Figure 3 Ultrasound of the area that corresponds to the mammographic abnormality showing an irregular mass, hypoechoic and heterogeneous, which does not reveal posterior acoustic features, and contacts the nipple. Colour Doppler ultrasound showing some flow.

Figure 4 The 3 cm tumour caused nipple retraction and was adjacent to the deep surgical margin. Its limits were quite discernible macroscopically.

TREATMENT

The patient underwent left radical mastectomy with sentinel lymph node (SLN) biopsy. Postoperatively, he received three cycles of adjuvant chemotherapy with 5-fluorouracil, epirubicin and cyclophosphamide, followed by three cycles of docetaxel. After chemotherapy, radiation therapy was initiated, a total dose of 50 Gy and 66 Gy was applied to the chest wall and to the surgical site, respectively. After completion of radiotherapy, the patient began a 5-year course of tamoxifen.

OUTCOME AND FOLLOW-UP

Gross examination of the left radical mastectomy specimen revealed an eccentric 3 cm tumour located in the subareolar region, invading the pectoralis major muscle (figure 4).

Microscopically, the tumour was composed of discohesive cells individually dispersed or arranged in sheets. Lymphovascular invasions were absent (figure 5).

The sentinel node biopsy was negative, and the tumour was pathologically staged as pT4a pN0 pM0 according to the tumor, node, and metastases (TNM) staging system developed and updated by the American Joint Committee on Cancer (AJCC), and the Union for International Cancer Control (UICC).

Immunohistochemistry showed negativity for e-cadherin, expression of oestrogen receptors in 100% of the tumour cells and no expression (0) of epidermal growth factor receptor 2 (ERBB2) (figure 5). The final diagnosis of ILC was thus reached.

The evaluation for mutations of the breast cancer genes was negative for BRCA 1 and BRCA 2.

The postoperative course was uneventful except for mild seroma formation at the surgical site.

The patient has been evaluated annually at our Institution, revealing normal physical examination, without elevation of tumour markers. No signs of recurrence on mammogram or ultrasound were found during 3 years of follow-up.

DISCUSSION

Breast carcinoma in men is very rare, representing <1% of all breast cancers, and ILC is uncommon among them.⁶

Male breast cancer is typically diagnosed at an age ~5–10 years older than the age at which it is diagnosed in women, with a mean age at diagnosis of ~67 years.⁷

The risk of breast carcinoma in men is increased in patients with undescended testes, congenital inguinal hernia,

Figure 5 The tumour is composed of monomorphic cells arranged in sheets and in single file, and is negative for e-cadherin, making it an invasive lobular carcinoma (H&E, $\times 4$, $\times 10$ and $\times 40$, respectively). Oestrogen receptors were positive in all cells and epidermal growth factor receptor 2 was negative (0).a

orchiectomy, orchitis, testicular injury, infertility and Klinefelter's syndrome, previous thoracic radiotherapy, alterations of the oestrogen–testosterone ratio and familial history (BRCA 2 and 1), among other controversial risk factors.¹ To date, there has been no evidence linking gynecomastia with male breast cancer.⁸

BRCA 1 or 2 mutations are thought to be found in 4–40% of cases, with the BRCA 2 mutation being more common. Therefore, all men diagnosed with breast cancer should be referred for genetic counselling and BRCA testing.^{2,9}

The most common invasive subtypes of breast cancer in men are IDC of no special type (85% of all tumours) and papillary carcinoma (5% of all tumours).¹ ILC is an extremely rare subtype (representing only 1% of all tumours in men) because lobules and acini are usually not found in normal male breast tissue. Therefore, lobular carcinoma makes up for a smaller percentage of breast carcinoma cases in men than in women (10–15% of all tumours).²

Characteristic histological appearance of discohesive cells infiltrating breast parenchyma, either individually dispersed or arranged in linear cords, and negativity for e-cadherin, are reliable diagnostic criteria. As in postmenopausal women, breast cancer in men is most commonly positive for hormone receptors.¹⁰

Screening mammography for male breast cancer is not feasible due to the low incidence of this disease entity.⁷ Most men with breast cancer usually present with a painless, firm, usually subareolar mass, with cases of nipple involvement ranging between 40% and 50%. There may be associated skin changes, including nipple retraction, ulceration, or fixation of the mass to the skin or underlying tissue. The left breast is involved slightly more often than the right, and <1% are bilateral.¹¹ Axillary adenopathy is typically palpable in advanced cases. It has been reported that ~50% of affected men have axillary nodal metastasis at initial evaluation.⁷

Mammography is the initial imaging modality for a clinically suspicious mass, followed by ultrasound and other techniques, as needed, including MRI. Bilateral CC and MLO mammographic views should be obtained.⁷ Mammographic features often include a spiculated mass or area of architectural distortion, with a minority of tumours displaying an asymmetric density or normal mammographic findings. Features suggestive

of malignancy also include eccentricity to the nipple, spiculation and microcalcifications.⁴ On the other hand, ultrasound may show an irregular mass with a hypoechoic or heterogeneous echotexture. In a minority of cases, the tumour may appear as a well-circumscribed mass or an isolated shadowing without a mass, or may even be sonographically occult.⁴

Any suspicious mass requires biopsy to confirm the diagnosis and to assay for hormone receptor content, as well as ERBB2 status.^{7,8}

Treatment of male breast cancer depends on the stage of disease at the time of diagnosis and the hormone receptor status of the tumour. Radical mastectomy with SLN biopsy in men with clinically and imaging node-negative breast cancer or modified radical mastectomy when axillary lymph node metastasis is present, are the optimum local therapies. Unlike in female breast cancer, lumpectomy does not play an important role in the treatment of breast carcinoma in men, because of the small volume of male breast tissue.¹²

Although there are limited data regarding the indications for adjuvant radiotherapy in men treated for breast cancer, most

Learning points

- ▶ Invasive lobular carcinoma (ILC) of the breast is extremely rare in men, because lobules and acini are usually not found in normal male breast tissue.
- ▶ The major risk factors of ILC include undescended testes, congenital inguinal hernia, orchiectomy, orchitis, testicular injury, infertility and Klinefelter's syndrome, previous thoracic radiotherapy, alterations of the oestrogen–testosterone ratio and BRCA 2 or 1 mutation.
- ▶ The characteristic histological appearance of discohesive cells infiltrating breast parenchyma, either individually dispersed or arranged in linear cords, and negativity for e-cadherin, are reliable diagnostic criteria of ILC.
- ▶ The longer interval between first symptom and diagnosis observed in men contributes to presentation of more advanced stages at the time of initial diagnosis, with poorer prognosis.

studies support the benefit of adjuvant chemotherapy according to the stage of the disease. For men with hormone receptor-positive breast cancer, endocrine therapy is also recommended following surgery.¹³

Finally, although the small size of the male breast favours early detection, the interval between first symptom and diagnosis appears to be longer in men. As a result, the tumour may be advanced at the time of diagnosis, which may contribute to the poorer survival seen in men.^{2 14} Most contemporary reports of both male and female breast cancer that were carefully matched for age at diagnosis, stage and grade, do not substantiate a significantly worse survival in men.^{14 15}

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