Invasive Pleomorphic Lobular Carcinoma of The Male Breast: A Rare Diagnosis with Radiologic-Pathologic Correlation

Carcinoma Lobular Pleomorfico Invasivo da Mama Masculina: Um Diagnóstico Raro com Correlação Radio-Patológica

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ABSTRACT

Male breast cancer is a rare disease, representing approximately 1% of all breast cancers, but its incidence appears to be increasing over the years. As normal male breast does not develop acini and lobules, lobular carcinoma is very rare, accounting for 1% - 2% of all cases of male breast cancer. Pleomorphic lobular carcinoma is an aggressive variant of invasive lobular carcinoma with only six cases of male breast reported in the literature until now, and none with associated Paget's disease. We report a case of an invasive pleomorphic lobular carcinoma with axillary lymph node involvement and associated Paget's disease in a high-risk man. Low awareness among men and a lack of a screening program often lead to a late diagnosis of male breast cancer, and consequently, at a later stages of disease, with lower survival rates compared to women. Early diagnosis is essential in order to improve patient outcomes and achieve better survival rates in men.

Keywords: Breast Neoplasms, Male; Carcinoma, Lobular; Magnetic Resonance Imaging; Mammography

RESUMO

O cancro da mama no homem é uma doença rara, representando aproximadamente 1% de todos os cancros da mama, embora a sua incidência pareça estar a aumentar. Como a mama masculina normal não é constituída por lóbulos, o carcinoma lobular é muito raro, representando 1% - 2% de todos os cancros da mama no homem. Apresentamos um caso clínico de um carcinoma lobular pleomórfico invasivo com envolvimento ganglionar axilar e doença de Paget do mamilo associada num homem de alto risco; trata-se de um caso extremamente raro, existindo apenas seis casos publicados na literatura até agora, e nenhum com doença de Paget associada. A falta de um programa de rastreio e a reduzida consciencialização da doença por parte da população masculina levam a diagnósticos tardios de cancro da mama no homem e consequentemente em estadios mais avançados da doença, com taxas de sobrevida baixas. A deteção precoce é essencial para melhorar alcançar melhores taxas de sobrevida nestes pacientes.

Palavras-chave: Carcinoma Lobular; Mamografia; Neoplasia da Mama Masculina; Ressonância Magnética

INTRODUCTION

Male breast cancer (MBC) is a rare disease, representing approximately 1% of all breast cancers, but its incidence appears to be rising over the years.[1,2] The most common histological subtype is invasive ductal carcinoma (IDC), usually of no special type. As normal male breast does not develop acini and lobules, lobular carcinoma is very rare, accounting 1% - 2% of all MBC.[3,4] Pleomorphic lobular carcinoma is an aggressive variant of invasive lobular carcinoma with only six cases of male breast reported in the literature until now, and none with associated Paget's disease. We report a case of an invasive pleomorphic lobular carcinoma with axillary lymph node involvement and associated Paget's disease in a high-risk man.

CASE REPORT

A 73-year-old male presented with a painless mass in the left breast that progressively increased in size for six months. He had known well-established risk factors for breast cancer (BC), namely, family history of BC (two nieces); 5 years ago, the patient was referred for genetic counseling and carried out genetic tests that confirmed the presence of the *BRCA 2* gene mutation; he was also included in a screening program, however, he refused it (missing medical appointments and radiologic screening tests).

His past medical history did not include any additional breast cancer risk factors, apart from obesity and treatment with finasteride for symptomatic benign prostatic hyperplasia.

Clinical examination revealed a painless and firm nodule, fixed to the nipple on the left breast without palpable axillary lymph nodes.

Bilateral mammography and breast ultrasound of the palpable area were performed. Mediolateral oblique and craniocaudal mammographic views demonstrated almost entirely fatty breasts with a 33 mm high-density opacity, with irregular margins, located in the subareolar region of the left breast, with associated nipple retraction and skin thickening (Fig. 1). Ultrasound confirmed a left breast mass in the same location, with a heterogeneous echo pattern (predominantly hypoechoic, with hyperechoic areas) and indistinct margins (Fig. 2). No suspicious axillary lymph nodes were observed. Ultrasound-guided core needle biopsy was

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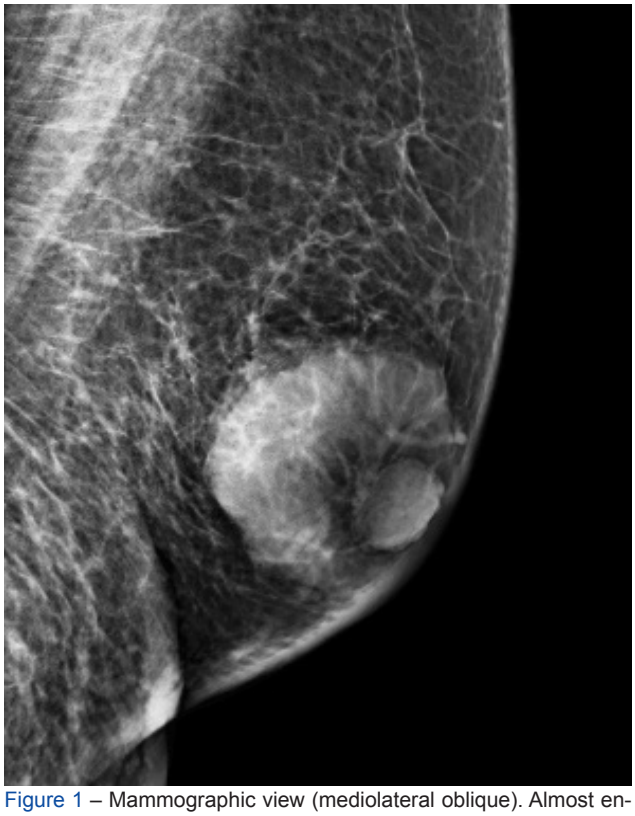

Figure 1 – Mammographic view (mediolateral oblique). Almost entirely fatty breast with a high-density opacity, with irregular margins, located in the subareolar region of the left breast, with associated nipple retraction and skin thickening.

undertaken, and the histologic diagnosis was suggestive of a grade 3 invasive pleomorphic lobular carcinoma (IPLC), that was estrogen receptor (ER) and progesterone receptor (PR) positive and human epidermal growth factor receptor (HER2) negative (SISH).

Breast magnetic resonance imaging (MRI) showed an intermediate signal intensity mass on T2-weighted (Fig 2.) with avidly enhancement and washout on T1W fat-suppressed after IV gadolinium administration (Fig. 3) and marked diffusion restriction, with high signal on diffusion-weighted imaging and low apparent diffusion coefficient value (ADC = 0.6 - 0.8 mm^2/s), strongly consistent with malignant disease. The lesion was located in the subareolar region and measured about 39 x 25 mm. Associated nipple retraction and skin thickening with enhancement were present. Pectoralis muscle and chest wall had no signals of invasion.

A multidisciplinary team decided to perform a left simple mastectomy with nipple excision and sentinel lymph node biopsy.

Gross histopathology (Fig.s 4 and 5) of the surgical specimen confirmed a 39 mm, grade 3 IPLC, that was ER and PR positive and HER2 negative (SISH); there was dermal invasion and focally associated Paget's disease. Macrometastases in axillary lymph nodes were also present.

The patient was evaluated in a multidisciplinary consultation one week after surgery and the team decided to perform a full axillary lymph node dissection based on

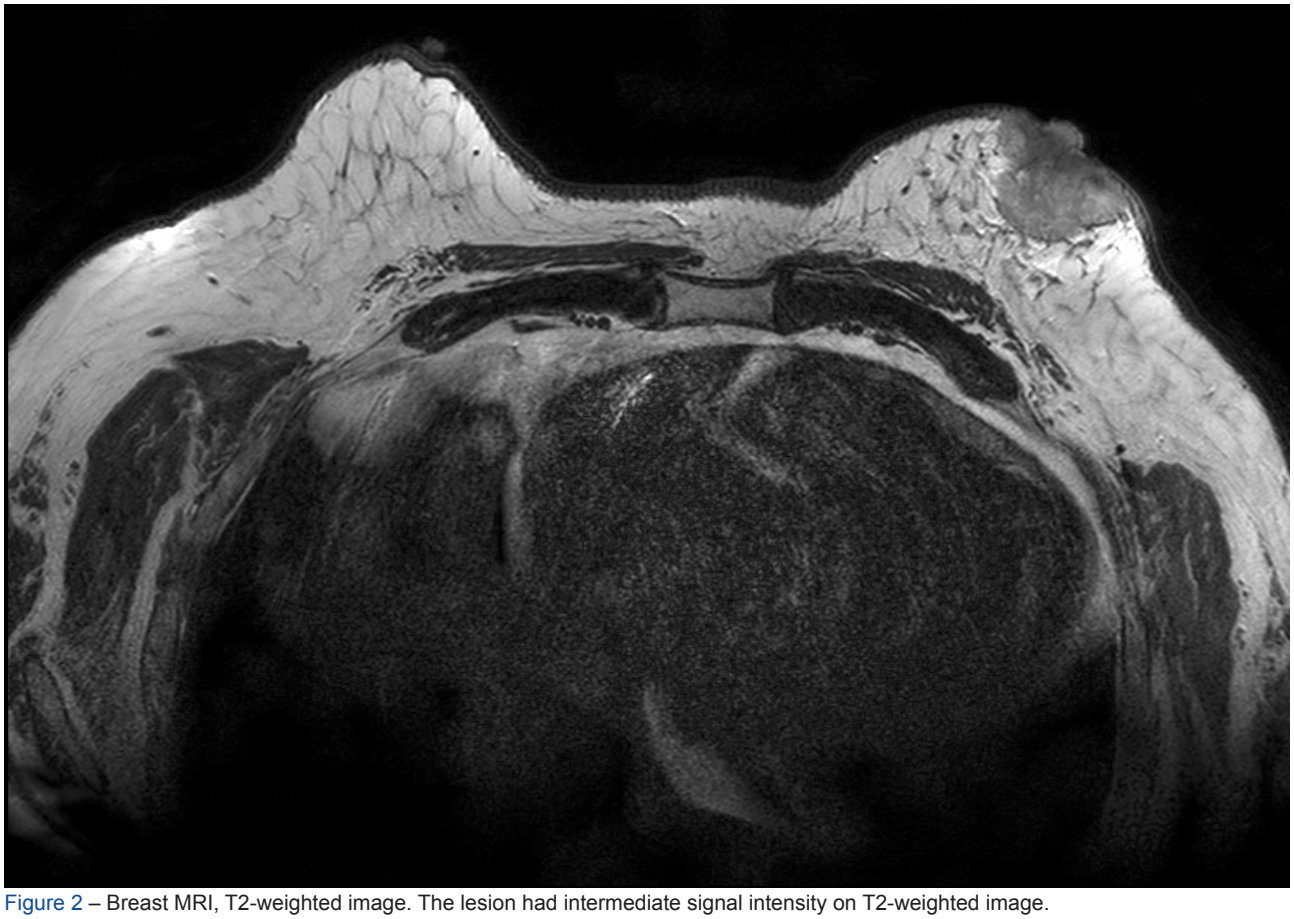

Figure 2 – Breast MRI, T2-weighted image. The lesion had intermediate signal intensity on T2-weighted image.

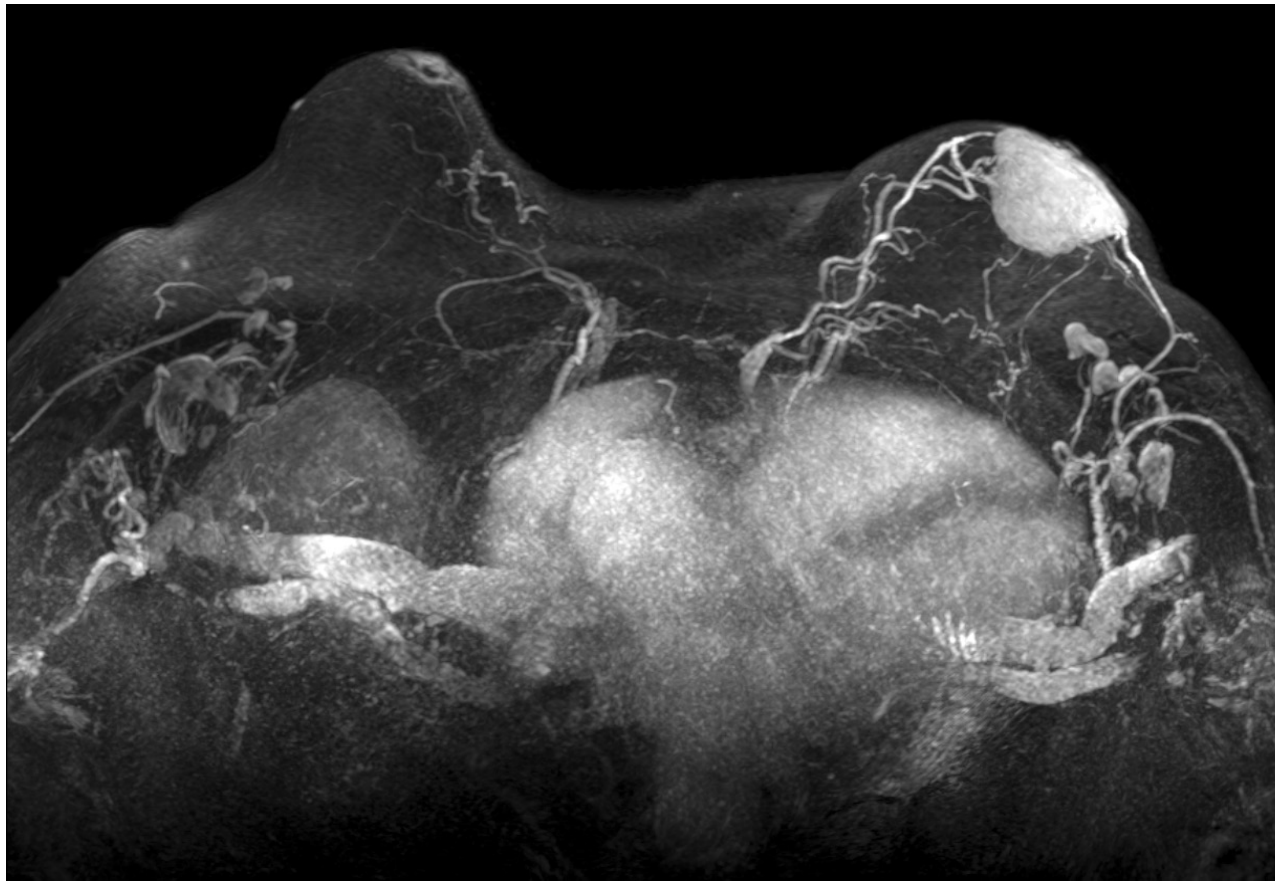

Figure 3 – Breast MRI, axial maximum intensity projections (MIP). Axial MIP demonstrated a mass enhancement on T1W FS after IV gadolinium administration.

histopathology results. Full axillary lymph node dissection was performed three weeks after mastectomy. This was the time needed to have the definitive histopathology report and new discussion by a multidisciplinary team, according to the institutional protocol. As adjuvant therapy, chemotherapy and radiation therapy were also proposed and accepted by patient.

DISCUSSION

Male breast cancer is rare, and invasive pleomorphic lobular carcinoma (IPLC) is even more rare, so its natural history and treatment management is yet poorly understood.

The loss of e-cadherin is the histopathological hallmark of IPLC (differentiating it from invasive ductal carcinoma - IDC).[4,5] Pleomorphic lobular carcinoma is an aggressive variant of ILC with higher pleomorphism, atypia and elevated proliferative index.[4,5] Most IPLC had positive estrogen and progesterone receptors.[2,4,5] As expected, conditions associated with an abnormal estrogen-to-androgen ratio levels (Klinefelter syndrome, estrogen treatment for prostate cancer, exogenous estrogen or testosterone use, obesity, orchitis/epididymitis) are relevant risk factors in this cancer subtype; furthermore, elevated concentrations of estrogen can stimulate the development of acini and lobule. Other important risk factors include advanced age, family history, gene mutations (notably *BRCA 1* and *2*) and chest wall irradiation.[2]

MBC most commonly presents as a palpable painless breast lump, usually located in the subareolar region or the upper outer quadrant; it is typically unliteral and slightly more frequent in the left breast. It also may be associated with skin changes and bloody nipple discharge or retraction. Axillary adenopathy is typically palpable in advanced cases.

According to the American College of Radiology's appropriateness criteria for diagnostic evaluation of the symptomatic male breast, mammography and/or ultrasound should be performed in men with unexplained or suspicious unilateral breast enlargement.[5] IPLC in men typically presents with an irregular mass, with spiculated or indistinct borders, subareolar or eccentricity of the nipple.

Tissue sampling must be obtained by core needle biopsy in patients with uncertain or suspicious radiological findings.[6]

Therapeutic strategies for MBC are not well established. According to the National Comprehensive Cancer Network, mastectomy with sentinel lymph node biopsy or axillary lymph node dissection remains the mainstay of surgical treatment in men. In the adjuvant setting, chemotherapy and hormone therapy may be applied, according to tumor characteristics and stage.[2]

Following a primary breast cancer, the risk of a second is significantly compared to the general male population. Ipsilateral annual mammographic surveillance should be

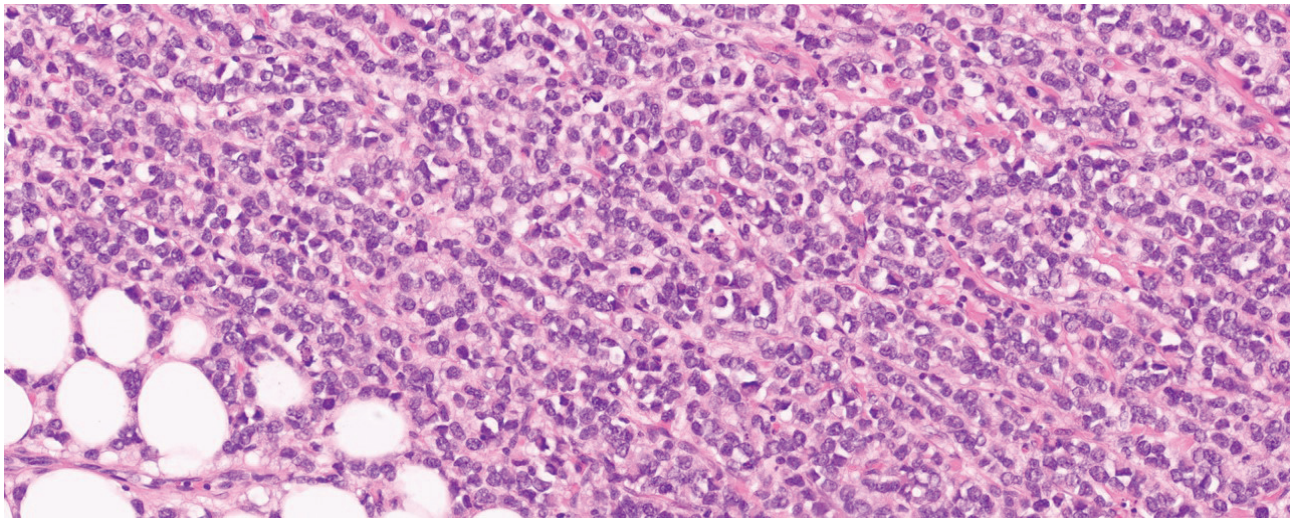

Figure 4 – Histological features of invasive lobular carcinoma of the breast, pleomorphic subtype. The image of histologic section shows neoplastic cells arranged in single file linear cords.

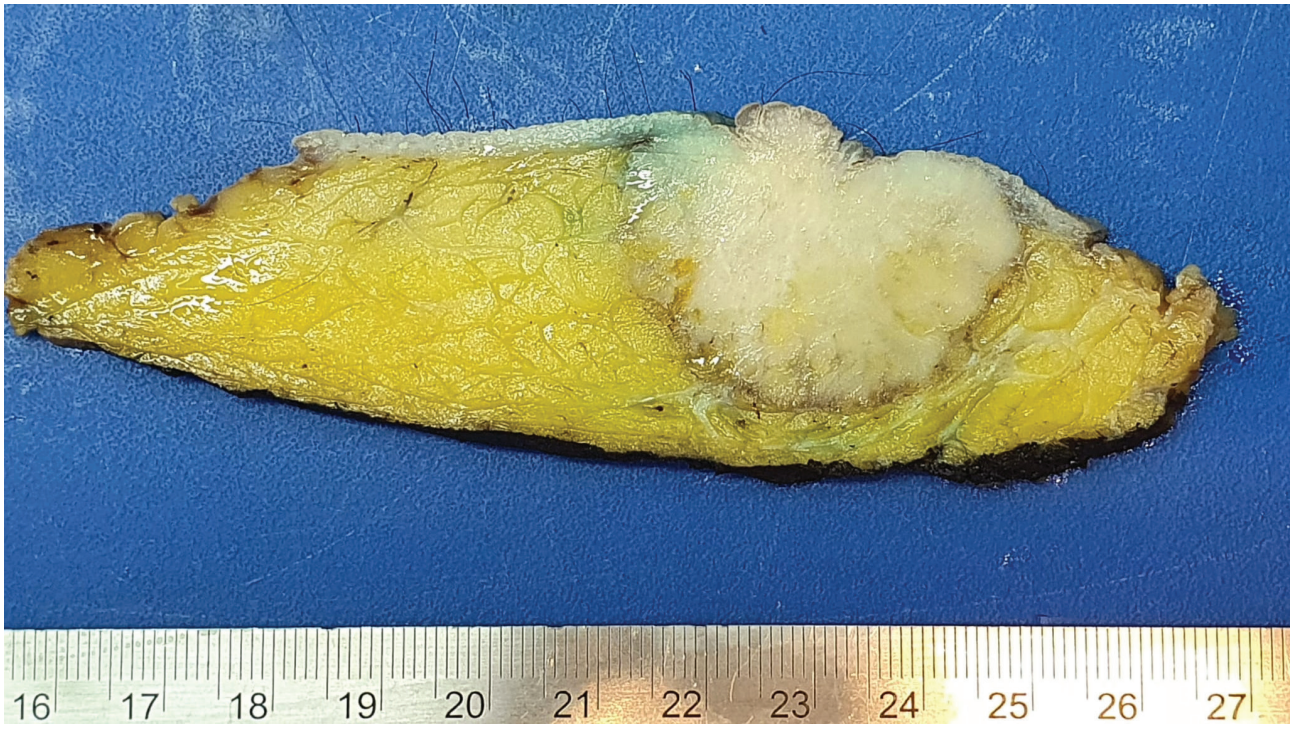

Figure 5 – Surgical specimen: left mastectomy. Circumscribed white, firm and spiculated tumor, with ill-defined margins, measuring 39 mm, located in the subareolar region. There was extension to the nipple and nipple-areola complex without skin ulcers and/or nodules.

offered to men with residual breast tissue and contralateral annual mammography may be offered in the presence of a history of breast cancer and a genetic predisposing mutation. Men who develop suspicious symptoms after treatment should be evaluated for recurrence with mammography, ultrasound, and core needle biopsy; MRI should be performed if conventional triple assessment is not enlightening.[7,8] Patients with strong family history or other risk factors for BC should referred for genetic counseling and genetic molecular evaluation.[3]

The main differential diagnosis is made with invasive ductal carcinoma, the most common histological subtype of MBC, but its imaging features may overlap with the radiologic appearance of IPLC. Only the histopathologic examination can differentiate these identities.[4,5] Benign hypotheses, such as unilateral gynecomastia, would be unlikely; it should be central and concentric to the nipple, without skin or nipple changes.[3]

Low awareness among men and a lack of a screening program, often lead to a late diagnosis of MBC, and consequently, later stages of disease, with lower survival rates compared to women. Early diagnosis is crucial in order to improve patient outcomes and achieve better survival rates in men.

AUTHORS CONTRIBUTION

MC: Concept of the word, draft of the manuscript.

BC: Significant contribution for the draft and critical review of the manuscript.

RF: Pathology images. Contributed for the draft and critical review of the manuscript.

JCM: Radiology images. Contributed for the draft and critical review of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

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