

Breast lobular carcinoma metastatic to the cervix: case report

Julia Wolff Barretto^{1*} , Maria Thereza Burko Rocha² ,
Miguel Mazorra Coelho Vieira² , Sérgio Ossamu Ioshii² , Júlia Costa Linhares² 

ABSTRACT

Breast cancer is the most common cancer among women, with 5 to 15% of these cases classified as invasive lobular carcinoma (ILC). Metastases can occur at any stage of the disease, with the most common sites being bones, lungs, lymph nodes, liver, and brain. However, extragenital metastasis to the uterus is rare. This study describes a case of a 52-year-old woman with breast pain for over a month. Mammography indicated a suspicious nodule (BIRADS 5). Physical examination revealed a breast nodule, *peau d'orange* skin, and axillary mass. Core biopsy diagnosed invasive lobular carcinoma. Tomographies suggested bone metastases. Additionally, she presented with abnormal uterine bleeding, and ultrasonography showed a suspicious uterine nodule, confirmed as a metastasis of ILC by immunohistochemical analysis. She had been treated with anastrozole since November 2023, with symptom reduction and clinical follow-up. It is known that ILC is the breast cancer most likely to metastasize to the genital tract. Previous reports mention difficulties in differentiation through imaging exams, with definitive differentiation achieved by biopsy of the cervix and/or later by surgery for tumor excision, with histopathological analysis and immunohistochemical profiling. There is limited scientific data on treatment options and prognosis in these cases. A study of approximately 1,650 patients with metastatic lobular carcinoma showed an overall survival of about 34 months. Thus, it is concluded that metastasis of invasive lobular carcinoma to the cervix is a rare entity, and this study aimed to contribute to the understanding of this condition and increase scientific evidence on the topic.

KEYWORDS: breast neoplasms; neoplasm metastasis; cervix uteri.

INTRODUCTION

Breast cancer is the most commonly diagnosed malignant disease in women (with an estimated 2.1 million new cases in 2018) and is the leading cause of cancer-related death in women in over 100 countries¹. The National Cancer Institute (INCA) projects approximately 73,000 new cases in Brazil for the 2023–2025 triennium, with an adjusted incidence rate of 41.89 cases per 100,000 women. The age-adjusted mortality rate from breast cancer in women in Brazil, based on the world population, was 11.71 deaths per 100 women, with higher rates observed in the Southeast and South regions and a progressive increase with age².

Invasive lobular carcinoma accounts for 5 to 15% of all breast carcinomas. While the incidence rates of invasive ductal carcinoma have remained stable, those of lobular carcinoma have been steadily increasing since 1980. This rise presents a significant clinical challenge, as lobular carcinoma is

more difficult to detect through both physical examination and mammography³.

Metastases can occur in both early-stage and locally advanced breast cancer, with the most common sites of dissemination being the bones, lungs, lymph nodes, liver, and brain^{4,5}. Metastases of extragenital origin to the uterus are rare, typically affecting the uterine body, while metastases to the uterine cervix represent an extremely rare site for this neoplasm^{4,6,7}.

Metastasis is the stage of cancer progression associated with the highest mortality, making knowledge of rare metastatic sites crucial for the early detection and interpretation of symptoms.

This study aims to report a case of lobular carcinoma in a 52-year-old female patient, presenting with metastases to the cervix and ovaries. Specifically, it focuses on a case of breast lobular carcinoma metastasizing to an exceptionally rare site, the cervix.

¹Faculdade Pequeno Príncipe – Curtitiba (PR), Brazil.

²Hospital Erasto Gaertner – Curtitiba (PR), Brazil.

*Corresponding author: juliacostalinhares@yahoo.com.br

Conflict of interests: nothing to declare. **Funding:** none.

Received on: 06/19/2024 — **Accepted on:** 08/16/2024

CASE REPORT

A 52-year-old female patient, previously healthy and in her reproductive years, G2C2, with menarche at 14 years, was referred to Hospital Erasto Gaertner (HEG) in May 2023, presenting with breast pain, changes in skin appearance, and a palpable nodule in the right breast. Symptoms began one month prior to her referral to this facility. Mammography revealed diffuse increased breast density, nipple retraction, diffuse architectural distortion, extensive radiodensity in the middle third of the breast, an ill-defined radiodensity in the right axillary region, and a slightly lobulated nodule, approximately 9 mm, in the right axillary region. These findings were classified as BIRADS 5.

During her first consultation with a breast specialist in July, physical examination revealed a locally advanced tumor in the right breast. The skin displayed a *peau d'orange* appearance and thickening throughout the breast, with firmer areas in the upper quadrants and retroareolar region, as well as nipple and skin retraction in the inferolateral quadrant. Additionally, a palpable mass was detected in the ipsilateral axilla, suggestive of lymph node involvement. A core biopsy was performed, and staging tests were ordered.

Core biopsy identified invasive lobular carcinoma, with additional immunohistochemical studies showing positivity for hormone receptors (estrogen and progesterone), negativity for HER2, and a proliferative index (Ki67) of 5%. Staging via computed tomography scans revealed predominantly sclerotic oval lesions scattered throughout the skeleton, which are suspicious for metastatic disease.

In addition to the breast complaint, the patient reported abnormal uterine bleeding, specifically menometrorrhagia. A transvaginal ultrasound was performed (Figure 1), which showed an anteroverted uterus with smooth contours and a uniform myometrial texture, except for a well-defined, hypochoic, heterogeneous



Figure 1. Transvaginal ultrasound showed increased uterine dimensions, along with the reported parity (11.1 x 5.5 x 8.2 cm. Volume: 250 cm³), a patulous uterine cavity of 14 mm, and heterogeneous content within it. Source: the authors.

nodular image on the posterior uterine wall, suggestive of an intramural myoma, measuring 19 x 18 x 20 mm. Uterine dimensions were increased, in addition to the reported parity (11.1 x 5.5 x 8.2 cm. Volume: 250 cm³). The uterine cavity was patent, measuring 14 mm, with heterogeneous contents inside, and no flow detected on Doppler, which may indicate blood content. The ovaries were of normal dimensions for the age group, and no free fluid was observed in the pelvic fundus or tubal collections. The cervix appeared normal, measuring 4.3 cm in its longitudinal axis.

Hysteroscopy was conducted, and the curetted material was sent for histological analysis. The results revealed atypical cell proliferation in the endocervical stroma. Immunohistochemical analysis identified metastasis of lobular breast carcinoma (Figure 2), with positive hormone receptors and negativity for HER2 (Figure 3).

The patient underwent laparotomy for salpingo-oophorectomy, aimed at achieving castration, along with peritoneal biopsy and peritoneal lavage cytology. Histological analysis of these samples also confirmed metastases of lobular breast carcinoma, with immunohistochemical findings consistent with those previously observed (cervix and breast).

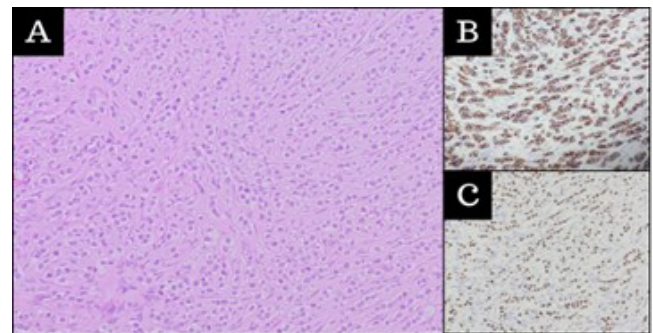


Figure 2. A: Neoplasia with cord-like distribution, featuring small cells with low nuclear grade (optical microscopy, hematoxylin and eosin, 400x); B: positivity for cytokeratin 7; and C: positivity for GATA3 (optical microscopy, immunohistochemistry, 200x).

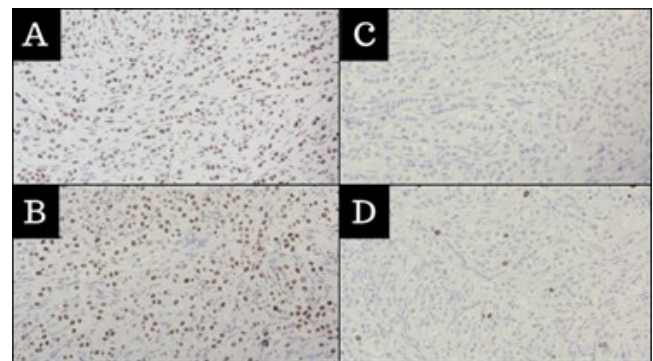


Figure 3. Immunohistochemical study showing positivity for hormonal receptors (estrogen (A) and progesterone (B)) and negativity for HER2 (C). The Ki67 proliferative index (D) was approximately 5% (optical microscopy, immunohistochemistry, 400x).

The patient is being monitored by professionals from the clinical oncology and mastology services; she developed anemia secondary to menometrorrhagia and is currently using ferrous sulfate, which has led to improvement in her hematimetric indices. For the treatment of breast neoplasia, anastrozole was prescribed and began in November 2023. The patient has tolerated the medication well, and during the last consultation (in December), she reported a significant reduction in right axillary lymph node enlargement, “softening” of the breast, and a decrease in right breast hyperemia.

DISCUSSION

Lobular carcinoma is the primary malignant breast neoplasm most commonly metastasizing to the genital tract, although extragenital metastases to the uterus are rarely observed⁷.

Histologically, lobular carcinoma is characterized by cells with minimal cohesion, either embedded in fibrous tissue or arranged in linear cords. These cells have rounded or oval nuclei with a rim of cytoplasm. Typically, mitoses are absent^{4,5}.

Immunohistochemical studies are conducted to distinguish metastatic lobular carcinoma from primary cervical neoplasms⁴. The panel for metastatic lobular carcinoma typically shows positive CK-7 and negative CK-20, with the breast-specific marker GCDFP-15 also positive. Lobular carcinoma is usually characterized by a loss of the adhesion protein E-cadherin. However, approximately 15% of lobular carcinomas do not exhibit this loss of expression^{4,5}.

Breast and gastrointestinal tumors are the most common extragenital cancers that metastasize to the uterus, with lobular carcinoma being the most prevalent histopathological type to do so^{6,7}. Uterine and vaginal metastases typically present with vaginal bleeding, while ovarian metastases often appear as asymptomatic ovarian masses⁸.

The ovaries are the most common sites of metastasis within the female genital tract, due to their extensive vascularization and lymphatic drainage⁹. In contrast, the cervix has limited vascular supply and only an afferent lymphatic drainage system, which may account for the relative rarity of metastases to the cervix compared to the ovaries⁶.

Lobular carcinomas exhibit a distinct pattern of metastasis distribution compared to non-special type carcinomas (ductal, not otherwise specified). They show a lower frequency of regional lymph node metastases and a higher incidence of metastases to distant sites, including the gastrointestinal tract, bones, skin, meninges, uterus, and ovaries³.

The clinical characteristics of uterine involvement are often nonspecific, typically presenting as vaginal bleeding and abdominal discomfort⁶. Anatomopathological findings from a previously published study reporting a case of lobular carcinoma with metastasis to the cervix indicated that the metastasis appeared as a

protruding mass with a whitish appearance on section, resembling the pattern found in leiomyomas¹⁰.

Differentiating metastatic tumors from primary reproductive system tumors is essential for accurate staging and treatment, though it can be challenging. Previous reports highlight difficulties in distinguishing these tumors through imaging tests, with some cases of metastatic lobular carcinoma presenting as lesions that mimic leiomyomas¹⁰.

Definitive differentiation can be achieved through cervical biopsy and/or post-surgical tumor removal, with histopathological analysis revealing the linear pattern characteristic of lobular carcinoma and an immunohistochemical profile consistent with this diagnosis^{3,10,11}.

Treatment options for cervical metastasis are influenced by individual factors such as the extent of the disease, the presence of other metastases, and the patient's performance status. Given the rarity of lobular carcinoma metastasizing to the cervix, there is limited well-established scientific data on treatment options and prognosis for these cases.

Previously published reports have documented the isolated use of adjuvant palliative therapy with anastrozole and S-1, as well as palliative chemotherapy with 5-fluorouracil, epirubicin, and cyclophosphamide, followed by hormone therapy. Additionally, the use of palliative radiotherapy for symptom management has been reported¹⁰⁻¹².

In a study involving approximately 1,650 patients with metastatic lobular carcinoma, the overall survival rate was approximately 34 months; there are no specific studies that address the survival of patients with this type of cancer metastasizing to the cervix¹³.

CONCLUSIONS

Lobular carcinoma of the breast presents diagnostic and therapeutic challenges, particularly when it metastasizes to uncommon distant organs. This case report underscores the importance of meticulous clinical follow-up and interdisciplinary collaboration for the effective management of patients with this neoplasm and cervix metastases. Further studies are required to develop specific therapeutic approaches and enhance patient outcomes.

AUTHORS' CONTRIBUTION

JWB: writing – original draft, writing – review & editing. MTBR: data curation, investigation, writing – original draft, writing – review & editing. MMCV: data curation, investigation, writing – original draft, writing – review & editing. SOI: conceptualization. JCL: conceptualization, data curation, investigation, supervision, project administration, writing – original draft, writing – review & editing.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394-424. <https://doi.org/10.3322/caac.21492>
2. Instituto Nacional de Câncer. Coordenação de Prevenção e Vigilância. Divisão de Detecção Precoce e Apoio à Organização de Rede. Dados e números sobre câncer de mama: relatório anual 2023 [Internet]. [cited on 2024 May 15]. Available from: https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/relatorio_dados-e-numeros-ca-mama-2023.pdf
3. World Health Organization. WHO classification of tumours of the breast. Lyon: International Agency for Research on Cancer; 2019.
4. Fontinele DRS, Vieira SC, Silva Júnior RG, Rodrigues TS. Lobular carcinoma of the breast with metastasis to the uterine cervix. *J Cancer Res Ther.* 2019;15(6):1411-4. https://doi.org/10.4103/jcrt.JCRT_469_18
5. Cerkauskaite D, Zilinskas K, Varnelis P, Oreibi ME, Asejev V, Dulskas A. Ovarian metastases from breast cancer: a report of 24 cases. *J Gynecol Obstet Hum Reprod.* 2021;50(6):102075. <https://doi.org/10.1016/j.jogoh.2021.102075>
6. Bogliolo S, Morotti M, Valenzano-Menada M, Fulcheri E, Musizzano Y, Casabona F. Breast cancer with synchronous massive metastasis in the uterine cervix: a case report and review of the literature. *Arch Gynecol Obstet.* 2010;281(4):769-73. <https://doi.org/10.1007/s00404-009-1264-0>
7. Ustaalioglu BB, Bilici A, Seker M, Salman T, Gumus M, Barisik NO, et al. Metastasis of lobular breast carcinoma to the uterus in a patient under anastrozole therapy. *Onkologie.* 2009;32(7):424-6. <https://doi.org/10.1159/000218367>
8. Di Micco R, Santurro L, Gasparri ML, Zuber V, Fiacco E, Gazzetta G, et al. Rare sites of breast cancer metastasis: a review. *Transl Cancer Res.* 2019;8(Suppl 5):S518-S552. <https://doi.org/10.21037/tcr.2019.07.24>
9. Perisić D, Jancić S, Kalinović D, Cekerevac M. Metastasis of lobular breast carcinoma to the cervix. *J Obstet Gynaecol Res.* 2007;33(4):578-80. <https://doi.org/10.1111/j.1447-0756.2007.00554.x>
10. Horikawa M, Mori Y, Nagai S, Tanaka S, Saito S, Okamoto T. Metastatic breast cancer to the uterine cervix mimicking a giant cervical leiomyoma. *Nagoya J Med Sci.* 2012;74(3-4):347-51. PMID: 23092107.
11. Munjal P, Sivasuriam A. 144 metastasis to cervix from breast cancer: a rare presentation. *Eur J Obstet Gynecol Reprod Biol.* 2022;270:e10. <https://doi.org/10.1016/j.ejogrb.2021.11.051>
12. Lokadasan R, Ratheesan K, Sukumaran R, Nair SP. Metastatic lobular carcinoma of breast mimics primary cervix carcinoma: two case reports and a review of the literature. *Ecancermedicalscience.* 2015;9:571. PMID: 26435744.
13. Sun MS, Yan HC, Gao M, Liu HJ, Xu L. De novo metastatic lobular breast carcinoma: a population-based study from SEER database. *Asian J Surg.* 2022;45(12):2608-17. <https://doi.org/10.1016/j.asjsur.2021.12.036>

