A Rare Presentation of Primary Breast Carcinoma in the Vulva: A Case Report and Literature Review

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Clinical Practice Points

- The embryological milk line extends from the medial thigh to the axillae and includes the vulva. Ectopic breast tissue can be found along this ridge, with an incidence of approximately 1% in the general population.
- Although ectopic breast tissue responds to the same physiological and pathologic processes as the mammary glands, the development of a mammary gland carcinoma in these tissues is an extremely rare event.
- Slightly more than 25 cases of mammary gland carcinoma of the vulva have been reported in the literature. Most cases present with aggressive tumors.
- These tumors should be treated as primary breast cancer, and adjuvant treatment can include chemotherapy, radiation, and hormonal therapy.
- We present a short literature review and discuss the clinical presentation, pathological findings, and adjuvant treatment.

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Introduction

The primitive embryonic milk line, which derives from the ectoderm, extends from the axilla to the groin, including the vulva. It appears during the fifth week of embryonic development and regresses in later stages.[1-4] The finding of ectopic mammary gland tissue along this line is unusual, with an estimated incidence of 1% in the general population, 0.22% to 0.6% in white individuals, and 3.5% in African American individuals.[5,6] There are reports describing it in up to 6% of the population.[5,6] Ectopic mammary gland tissue responds to hormonal stimulation and undergoes the same physiologic and pathologic processes found in the normal breast; however, the development of a mammary gland carcinoma (MGC) in this tissue is an extremely rare event. The most common location of ectopic breast tissue is in the axilla and ectopic MGC is also found most commonly in this site, comprising 91% of the total. Ectopic MGC in the vulva is even rarer, with approximately 28 cases of this carcinoma reported in the literature.[7-9]

Case Presentation

A 58-year-old multiparous, postmenopausal woman, with an 8-month history of a slowly growing vulvar nodule, was referred to our institution. Her previous medical history was unremarkable for breast cancer. Relevant family history includes a sister with pancreatic cancer and a brother with lung cancer. Physical examination revealed a 1.5-cm nodular lesion located on the transition between the right labia majora and minora, without clinical suspicion of enlarged lymph nodes in the inguinal region (Figure 1A). Both breasts and axillae were unremarkable on physical examination. Before referral to our institution, an incisional biopsy was performed, with an initial diagnosis of a basaloid carcinoma. However, on further pathology review, the diagnosis was revised as an adenocarcinoma, and again revised in our institution, as an undifferentiated carcinoma. On this third revision, an immunohistochemical profile (IHC) was performed, revealing positivity of

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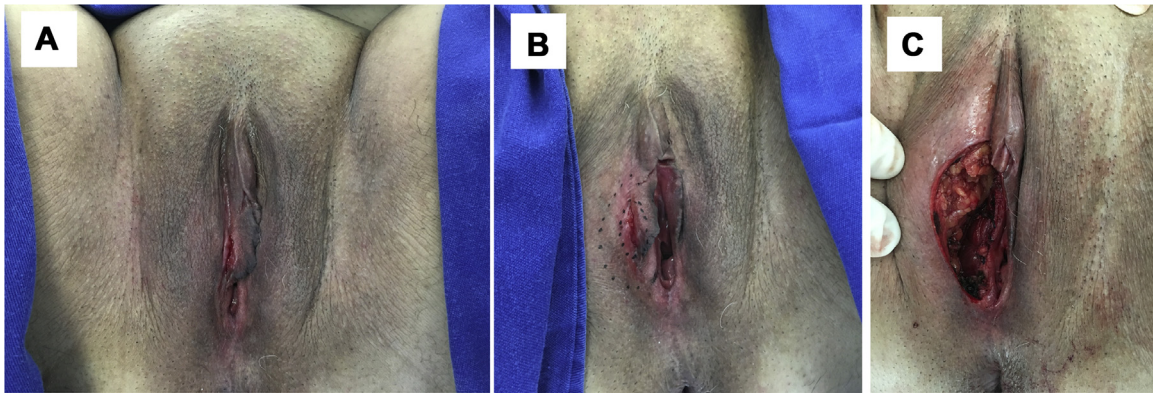
Figure 1 Pre- and Perioperative Photographs Documenting a Mammary Gland Carcinoma Arising From Ectopic Breast Tissue in the Vulva. (A) Preoperative State. (B) Delimitation of the Lesion and Surgical Margins for Resection. (C) After Local Wide Excision



AE1/AE3, GCDFP-15, mammaglobin, and estrogen receptor (ER), consistent with MGC.

After arrival at our institution, pelvic magnetic resonance imaging detected the small right vulvar lesion without enlarged lymph nodes. Bilateral mammography and breast ultrasound were unremarkable. Thorax, abdominal, and pelvic computed tomography scans found no evidence of disease or metastasis. A bone scan was performed and showed no evidence of disease.

Figure 2 Histological Aspects of Vulvar Lesion. Histology Showed a Partially Well-Circumscribed Nodular Lesion, Superficially Disposed in Subcutaneous Vulvar Tissue, Immediately Underlying the Epidermal Folds, Partially Ulcerated (A, White Arrows), Composed of a Densely Packed Glandular-forming Neoplasia With Scant Intermixed Fibrous Stroma (B), Mainly Organized in a Solid Pattern, With Scattered Microcalcifications (C, Black Arrows), Analogous to Invasive Breast Carcinoma, Not Otherwise Specified Type, With High-Grade Nuclear Atypia Features, Such as a Convoluted and Pleomorphic Nucleus (D). Images Represent the Hematoxylin and Eosin (H&E) Stained Slides, at 25×, 40×, 100× and 400×

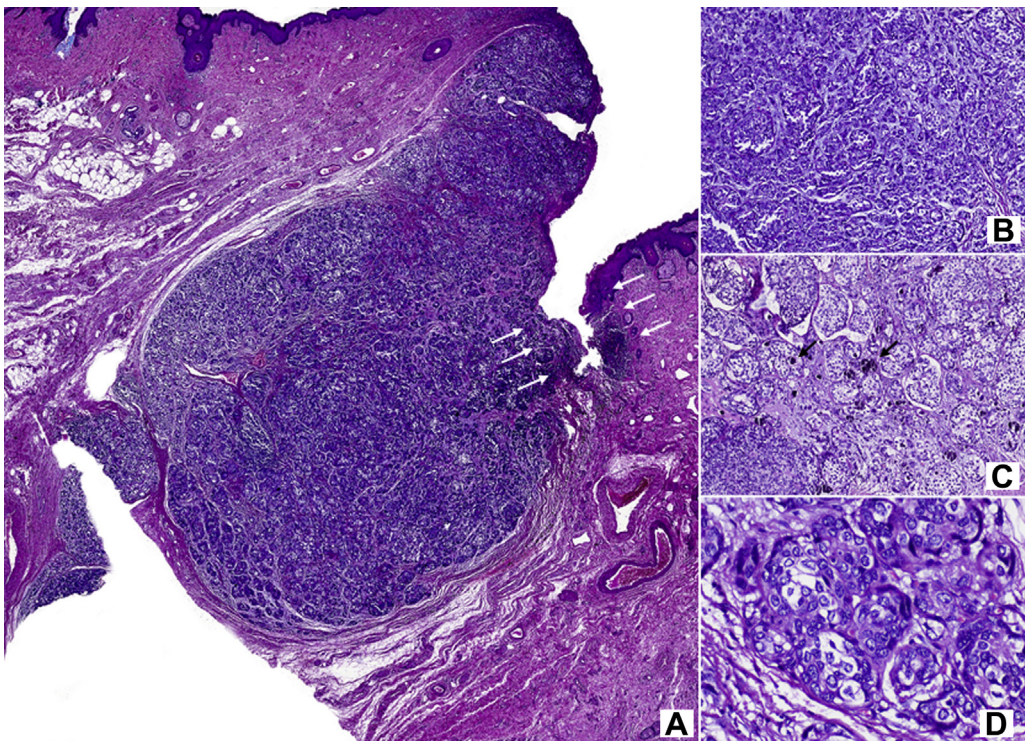
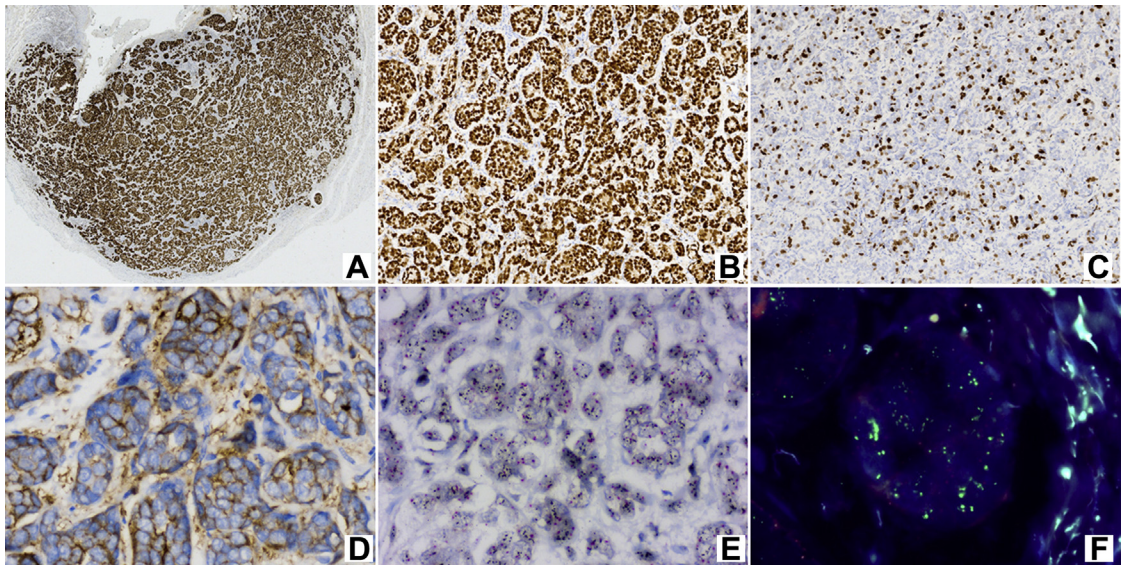


Figure 3 Immunohistochemical Features. The Neoplasia Evidenced Diffuse and Strong GATA-3 Nuclear Expression, a Transcription Factor Expressed in Breast Epithelia Differentiation (A). The Neoplasia Also Expressed Strong Positive and Ubiquitous Estrogen Receptor (B), With High Proliferative Index, and Approximately 50% Nuclear Positivity of Ki-67 (MIB-1) (C). Equivocal Human Epidermal Growth Factor Receptor 2/neu Gene Expression (Immunohistochemistry, D) Was Further Classified as Amplification by Silver In Situ Hybridization and Fluorescence In Situ Hybridization (E, F). Images Were Photographed at (A) 25×, (B-D) 400×, (E) 630×, (F) 1000×



After multidisciplinary discussion and exclusion of disease in the breast, it was decided to proceed with a surgical resection and sentinel lymph node evaluation of the vulvar lesion. In an attempt to locate the sentinel lymph node, a lymphoscintigraphy with an injection of 0.8mci phytate technetium 99m was performed on the same day of the surgical procedure. The lymphatic mapping was considered unsatisfactory, and consequently the patient underwent a right inguinal lymphadenectomy associated with the previously planned wide vulvar excision (Figure 1B).

The final pathology report revealed a 1.2-cm invasive carcinoma with mammary features, mainly organized in a solid and well-circumscribed fashion, composed of densely packed glandular structures with high-grade nuclear features (grade 3) and high mitotic index (Figure 2). Lymphovascular and perineural invasion was not detected and the final surgical margins were free of disease. All lymph nodes in the right groin were negative for metastatic disease. The IHC was consistent with MGC, being positive for GATA-3 and ER (100%), with a high proliferative index (Ki-67/Mib-1 of 50%). Dubious human epidermal growth factor receptor 2 (HER2) expression (score 2) was further confirmed as amplified status on silver in situ hybridization and fluorescence in situ hybridization (Figure 3).

After a multidisciplinary tumor board videoconference with the Global Cancer Institute, it was decided to treat the tumor as a primary breast carcinoma due to its pathological characteristics. The patient will receive adjuvant chemotherapy (4 cycles of doxorubicin with cyclophosphamide, followed by 12 weeks of paclitaxel with trastuzumab, to be carried out for 18 cycles), and hormonal therapy with an aromatase inhibitor.[10-12]

Discussion

Given the rarity of a breast carcinoma in the vulva, these cases have historically been difficult to diagnose. As illustrated in our case, 3 pathology reports determined alternative diagnoses. Ductal carcinoma is the most common histology for this rare clinical scenario; ductal carcinoma is also the most common histology for primary carcinomas of the breast. Lobular, mucinous, and mixed ductal-lobular histologies also have been reported.[2,3] The age of the patients ranged from 45 to 82 years, compatible with the age of presentation of breast cancer. As in our case, the most common clinical presentation is a painless nodule arising most often in the labia majora. Some cases have reported aggressive presentations of advanced carcinomas with a poor prognosis.[3,13,14]

The surgical procedures for the cited cases included a radical vulvectomy or wide local excision with lymph node dissection and adjuvant treatment with radiation, chemotherapy, or hormonal therapy. In the literature, the treatment for these cases has been extrapolated from breast cancer. A tailored therapy should be chosen depending on the tumor's histological and molecular characteristics.[13,14]

With regard to local treatment of our patient, we assumed that all ectopic breast tissue was removed during the wide vulvar excision. The right inguinal lymph nodes were all negative, so we elected to omit radiation therapy, especially considering the risk of increased morbidity and lower limb lymphedema. The patient has a good performance status. Given the possible aggressive behavior of this tumor, we decided to include adjuvant chemotherapy with an anthracycline-taxane regimen and trastuzumab,

followed by hormonal therapy with an aromatase inhibitor due to the positive ER of the tumor and postmenopausal status of the patient.[10-12]

Conclusion

In these cases, it is crucial to exclude primary MGC of the breasts, as some cases of metastatic, synchronous, or metachronous breast tumors in the vulva have been reported.[14] Bartholin gland carcinoma, invasive Paget disease, primary carcinoma of the major and minor vestibular glands, carcinoma originating from the sweat gland, and metastatic breast carcinoma should be considered in the differential diagnoses.[15] The presence of estrogen and progesterone receptors and positivity for other breast markers can support a diagnosis of mammary gland origin.[16] In our case, the pathologic and molecular findings and the absence of abnormal breast findings confirmed the diagnosis of MGC in the vulva arising from ectopic breast tissue.

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Disclosure

The authors declare that they have no competing interests.

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