MOH

Journal of Medical Case Reports

Invasive Cribriform Carcinoma of the Breast: Case Report and Review of the Literature

Madeleine Yeakle[1], Kyle Coombes[1], Kayvon Moin[1], Bishoy Mark Joseph[1], Joseph Varney[1], Sherif Nasr[2], Stephanie Bernik[3], and Mohamed Aziz[3]*

Abstract

Invasive cribriform carcinoma (ICC) is one of several known breast cancer variants. It is a rare form of invasive breast cancer with an incidence of approximately 0.3%-6% in primary breast carcinomas. ICC has a cribriform pattern resembling the histological structures of cribriform ductal carcinoma in situ (cribriform DCIS). Immunohistochemistry studies show a low-grade infiltrating carcinoma with an irregular cribriform growth pattern and absent myoepithelial cells. Distinguishing ICC from other types of breast cancer, particularly those with a cribriform pattern, can be challenging. This report presents a case of ICC in a 51-year-old woman with a brief review of current literature.

Introduction:

Invasive cribriform breast cancer is a rare type of breast cancer, and it is typically a low-grade, slow-growing cancer with a better prognosis than most other types. This type of breast carcinoma may be mixed with different types of breast cancer, mainly tubular carcinoma. This mixed pattern has an intermediate prognosis between invasive cribriform and invasive ductal carcinomas. Cribriform carcinoma is diagnosed as a pure form when seen in 90% of the tumor mass. Like tubular carcinoma, infiltrating cribriform carcinoma has an excellent prognosis. In cases with combined growth patterns of cribriform and tubular carcinoma, a well-differentiated mixed cribriform-tubular carcinoma designation is appropriate.[1,2]

With more than 2 million women diagnosed with breast cancer in 2020, and almost 700 thousand deaths worldwide, the World Health Organization Global Breast Cancer Initiative (WHO GBCI) has been working assiduously to reduce breast cancer mortality by 2.5% each year.[1] While several variants of breast cancer are known, our research focuses on one particular variant, invasive cribriform carcinoma (ICC) of the breast.

ICC was first described by Page et al.[2] in 1983 as a rare type of ductal carcinoma of the breast.[2,3] Histologically, it has similar features to cribriform ductal carcinoma in situ (cribriform DCIS).[4] It is considered a malignant neoplasm with a low metastatic potential, good prognosis, less lymph node invasion, higher frequency of well-differentiated tumors, and higher estrogen receptor (ER) and progesterone receptor (PR) positive rates.[3-5] This type of breast carcinoma may be mixed with other types of breast cancer, mainly tubular carcinoma. This paper presents a rare case of ICC in a 51-year-old woman, along with a brief literature review.

Case Presentation:

A 51-year-old woman presented to the clinic with a right breast lump in a few months. The mass was detected during routine mammography showing heterogeneously dense breast nodule. The patient had no family history of breast disease or any other type of tumor. On ultrasonography, an approximately 1.3 cm microlobulated isoechoic mass was detected in the upper outer quadrant of the right breast. Breast MRI imaging was performed to evaluate the consistency and extent of the mass. The growth showed an iso-signal intensity on a T1 weighted image and an iso- to slightly high signal intensity on a T2 weighted image. Radiological imaging was suspicious for malignancy, and a core biopsy of the mass was recommended for definitive diagnosis.

Microscopic examination of the core biopsy revealed an invasive tumor displaying nests and small islands of

Affiliations
[1]*American University of the Caribbean Medical School, USA*
[2]*Mount Sinai Medical Center, New York, NY, USA*
[3]*siParadigm Diagnostic Infirmatics, NJ, USA*

malignant cells exhibiting a cribriform pattern with well-differentiated nuclei and no mitotic activity with dense desmoplastic reaction. Uniform punched-out spaces punctuated the nests, and extensive secondary lumen formation with angular clusters of tumor cells was also noted. In addition, cribriform ductal carcinoma in situ was also present in about 10% of the tumor mass. The tumor cells displayed slightly enlarged uniform nuclei, inconspicuous nucleoli, uniform chromatin, and pleomorphism was minimal (Figure 1A-B).

No microcalcifications, lymphovascular invasion, or tumor necrosis were identified. Immunohistochemistry (IHC) studies indicated a strong positive finding for the estrogen receptors (ER), progesterone receptors (PR), and E- Cadherin (Figure 1C-D-E)., but negative for Her-2. Myoepithelial marker P63 was negative in the invasive component and positive in the in situ component.

A body imaging survey showed no evidence of metastatic disease. Breast-conserving surgery was performed; the entire tumor was removed with adequate safe surgical margins. There was no lymph node metastasis detected on the sentinel lymph node biopsy. The excised tumor showed pure cribriform architecture in more than 90% of the tumor mass, and there was no component of tubular carcinoma. The patient received postoperative hormonal treatment but no chemotherapy or radiation. The patient was followed up for four years with no recurrence or metastasis, after which she was lost to follow-up.

Discussion:

ICC has been recognized since 1983, when Page first described the lesion. His review of 1003 invasive breast carcinomas created the road map for the classification of these lesions, classical and mixed, while also pointing out the excellent prognosis these tumors exhibit.[2] He defined "classical" as lesions that were exclusively cribriform, like our case, or cribriform with a limited extent of invasive tubular elements only, and "mixed" as lesions that contained areas of less well-differentiated invasive carcinoma.[2]

With an incidence of 0.3-6%, ICC is typically diagnosed in older women, especially post-menopausal.[3-5] Clinically, ICC presents as a mass measuring on average 2 cm in diameter.[4,6] While it is frequently missed on mammography, this lesion may be identified on sonography.[4,6] Microcalcifications have been detected on radiography in only a few cases. Distinguishing ICC from other types of breast cancer, particularly those with a cribriform pattern (e.g., collagenous spherulosis, cribriform ductal carcinoma in situ "DCIS," adenoid cystic carcinoma), can be particularly challenging.[4,5]

Key radiographic and pathological characteristics can be helpful when evaluating breast lesions. Feel, shape, and location can also help formulate a differential. Cong et al.[5] assessed 9 cases of ICC using sonography and found that all masses exhibited a hypoechoic internal echo texture (9/9) and that some masses presented with an irregular shape (8/9), obscure boundary (5/9), partially microlobulated (5/9) or well-circumscribed (4/9) margins, and an inhomogeneous echo (8/9). Balci et al.[3] concluded that the irregular shape of the tumor, spiculated margins, angular margins, microlobulated margins, and nonparallel orientation are indications of a poorer prognosis. Our case displayed only a few of these reported features.

ICC is classified histologically as a specific subtype of invasive breast cancer, according to the WHO.[7] It is identified by the presence of atypical nests that display an island-like or angular distribution with no necrosis or adjacent small tubular carcinoma.[4,5] These glandular cavities are surrounded by a dense fibrous stroma, which gives rise to its cribriform structure.[4,5] ICC can also exhibit apocrine glands capable of secreting reddish mucus.[4] This histological pattern reveals low pleomorphism and grade, giving the tumor an overall favorable prognosis.[4] To differentiate ICC from another breast carcinoma with a cribriform pattern can be challenging. In almost all cases, the DCIS with a cribriform growth pattern can be identified by the presence of a myoepithelial cell layer. If in doubt, immunohistochemistry for myoepithelial cells can be helpful. Tubular carcinoma (TC) classic or pure TC does not have a significant cribriform growth pattern.

Mixed-type tubular carcinoma, however, often shows a cribriform component. Such well-differentiated tumors have been designated as either mixed-type tubular or mixed-type cribriform carcinomas. Adenoid cystic carcinoma can be identified by the presence of two or three cell populations (epithelial, myoepithelial/basaloid, squamous, or sebaceous cells) and hyaline bodies as well as thick basement membrane-like material. These features are absent in cribriform carcinoma.[8]

While metastases are rare in ICC, Zhang et al.[9] reported a case of a 59-year-old woman who presented with a large left breast mass she had noticed 13 years prior but had never sought treatment. Upon examination, her breast was ulcerated, and her nipple was fixed and invaginated. Two axillary lymph nodes were palpable. Emission computed tomography (ECT) demonstrated that the 10th and 11th thoracic vertebrae had metastatic lesions. Histological examination showed a pure invasive cribriform carcinoma.

ICC is most commonly found as an isolated lesion, but Choi et al.[10] reported a case of a 62-year-old woman who presented with an expanding, palpable left breast mass. Sonography revealed a 10-cm lobulated mass, and core biopsy revealed a fibroepithelial lesion diagnosed as a malignant phyllodes tumor. Once the lesion was removed, it was observed to have regions where epithelial components were replaced with tubular, cribriform structures showing low nuclear grade and low mitotic activity. The final diagnosis was invasive cribriform carcinoma arising within a malignant phyllodes tumor.

Although ICC is usually found in female patients, Katano et al.[11] described a case of a 70-year-old man who presented to the clinic with a painful palpable lump in his left breast. Examination by ultrasound revealed a hypoechoic mass measuring 12mm x 10mm x 8 mm. Fine-needle aspiration and core needle biopsy suggested malignancy, so surgery was scheduled for one month later. The clinicians could not feel or identify the mass with ultrasonography during a preoperative physical exam. The surgery was canceled. Eight months later, a mass was again identified on ultrasound and CT scan measuring 0.6 cm. A total mastectomy was performed, and a diagnosis of ICC without sentinel node metastases was made.

In addition to the histological classification of ICC, most patients have exhibited estrogen receptor (ER) and progesterone receptor (PR) positive tumors.[6] This corresponds to the favorable outcomes seen in patients with ICC. While the literature is unclear whether patients with ICC should receive chemotherapy, its smaller tumor size, less frequent axillary lymph node metastasis, a higher positive rate of ER and PR expression, no HER2 expression, and a lower proliferation index make it likely some patients may be suitable for no therapy, or endocrine therapy alone.[6] However, no standard treatment guidelines exist for ICC; thus, treatment is mainly based on invasive ductal carcinoma (IDC).[6,12]

Distinguishing ICC from other types of breast cancer, particularly those with a cribriform pattern, can be challenging. We hope that reporting this case will raise awareness of pathologists and clinicians to consider cribriform tumors with a good prognosis when benign radiographic characteristics are found. We also hope this paper will aid in what remains an unmet need in determining treatment guidelines specific to ICC.

Figures:

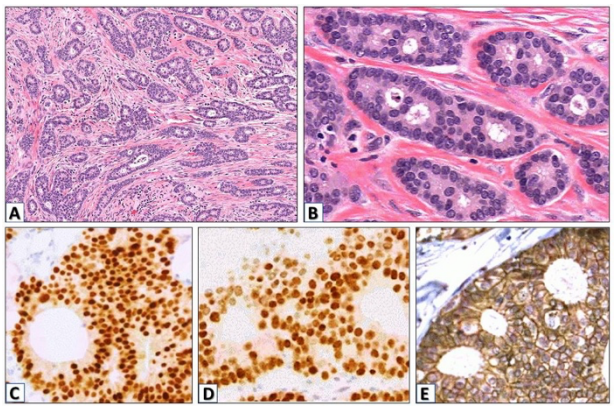

Figure-1: Pathological examination of the excised cribriform carcinoma

1A: Low power view showing invasive tumor displaying nests and small islands of malignant cells exhibiting a cribriform pattern with dense desmoplastic reaction (H&E stain X 20)
1B: High power view showing tumor cells displaying slightly enlarged uniform nuclei, inconspicuous nucleoli, uniform chromatin, and minimal pleomorphism (X 40)
1C: Tumor cells strongly positive for Estrogen receptors
1D: Tumor cells strongly positive for Progesterone receptors
1E: Tumor cells positive for E-Cadherin

Submitted: June 14th, 2022 | **Accepted:** July 19th, 2022 | **Published:** July 29th, 2022

***Corresponding author:** Madeleine Yeakle*, Department of Pathology, American University of the Caribbean School of Medicine, Email: madeleineyeakle@students.aucmed.edu

Citation: Yeakle M, Coombes K, Moin K, Joseph BM, Varney J, Nasr S, Bernik S, and Aziz M, (2022) Invasive Cribriform Carcinoma of the Breast: Case Report and Review of the Literature, 1(1), 15-18.

Acknowledgements:

Special thanks to Jiangchuan Tao, MD siParadigm Diagnostic Informatics, and Mary Morse, MD candidates, American University of the Caribbean, for their assistance in preparing manuscript images and reviewing the final manuscript.

References:

1. World Health Organization. Breast Cancer. Available from: https://www.who.int/news-room/fact-sheets/detail/breast-cancer; cited 2021 Mar 26.
2. Page DL, Dixon JM, Anderson TJ, Lee D, Stewart HJ. Invasive cribriform carcinoma of the breast. Histopathology. 1983 Jul;7(4):525-36.
3. Balci P, AKIN IB, Köremezli N, Durak MG, Altay C, Gezer NS, Sevinç Aİ. Evaluation and comparison of radiologic-pathologic findings in invasive cribriform carcinoma of the breast. Turkish Journal of Medical Sciences. 2017;47(3):738-47.
4. Mo CH, Ackbarkhan Z, Gu YY, Chen G, Pang YY, Dang YW, Feng ZB. Invasive cribriform carcinoma of the breast: a clinicopathological analysis of 12 cases with review of literature. International Journal of Clinical and Experimental Pathology. 2017;10(9):9917.
5. Liu J, Zheng X, Han Z, Lin S, Han H, Xu C. Clinical characteristics and overall survival prognostic nomogram for invasive cribriform carcinoma of breast: a SEER population-based analysis. BMC cancer. 2021 Dec;21(1):1-1.
6. Cong Y, Qiao G, Zou H, Lin J, Wang X, Li X, Li Y, Zhu S. Invasive cribriform carcinoma of the breast: a report of nine cases and a review of the literature. Oncology Letters. 2015 Apr 1;9(4):1753-8.
7. Rakha E, Pinder SE, Shin SJ, Tsuda H. Tubular carcinoma and cribriform carcinoma. In: Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ, editors. WHO classification of tumours of the breast. 4th edition. Lyon: IARC Press; 2012. pp. 43–45.
8. Farid Moinfar F. Essentials of diagnostic breast pathology: a practical approach. Springer Science & Business Media.
9. Zhang W, Lin Z, Zhang T, Liu F, Niu Y. A pure invasive cribriform carcinoma of the breast with bone metastasis if untreated for thirteen years: a case report and literature review. World Journal of Surgical Oncology. 2012 Dec;10(1):1-6.
10. Choi Y, Lee KY, Jang MH, Seol H, Kim SW, Park SY. Invasive cribriform carcinoma arising in malignant phyllodes tumor of breast: A case report. Korean Journal of Pathology. 2012 Apr;46(2):205.
11. Katano K, Yoshimitsu Y, Kyuno T, Haba Y, Maeda T, Kitamura S. Temporary spontaneous regression of male breast cancer: a case report. Surgical Case Reports. 2020 Dec;6(1):1-7.
12. Zhang W, Zhang T, Lin Z, Zhang X, Liu F, Wang Y, Liu H, Yang Y, Niu Y. Invasive cribriform carcinoma in a Chinese population: comparison with low-grade invasive ductal carcinoma-not otherwise specified. International Journal of Clinical and Experimental Pathology. 2013;6(3):445.