# Invasive Cribriform Carcinoma of the Breast Detected Incidentally on Computed Tomography: A Case Report

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September 25, 2021

**Abstract**

Invasive cribriform carcinoma is a rare type of invasive breast carcinoma, and few cases have been reported. Its features are a cribriform pattern resembling the histological structures of cribriform ductal carcinoma in situ and an excellent prognosis. However, the extent of progress for intraductal extension must be carefully evaluated.

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**Abstruct**

Invasive cribriform carcinoma is a rare type of invasive breast carcinoma, and few cases have been reported. Its features are a cribriform pattern resembling the histological structures of cribriform ductal carcinoma in situ and an excellent prognosis. However, the extent of progress for intraductal extension must be carefully evaluated.

**Keywords:** Invasive ductal carcinoma, Invasive cribriform carcinoma, Breast cancer

## INTRODUCTION

Invasive cribriform carcinoma (ICC) is a rare type of invasive breast carcinoma that was first described by Page et al. in 1983[1], accounting for approximately 0.4% of all primary breast carcinomas[1-4]. Its main characteristic is a unique structure with most of its invasive component arranged in a cribriform pattern. The prognosis of patients with pure and classical ICC is excellent[1-3]. This case was incidentally discovered on CT as part of a preoperative examination for gynecological surgery. This quite rare case is reported along with a literature review.

## CASE REPORT

A 68-year-old woman was scheduled to undergo surgery for pelvic organ prolapse at the Department of Obstetrics and Gynecology of our institute. No family member of the patient had a history of breast or ovarian carcinoma. Contrast-enhanced CT performed as part of the preoperative examination showed a 1.4-cm-diameter tumor in the upper lateral quadrant of the left breast (Fig. 1a, b). The tumor shadow was suspected to be a breast carcinoma, and the patient was referred to our department. The patient had no complaints of nipple discharge or pain. On physical examination, there was a mobile, irregular mass of 1 cm in largest clinical diameter. In the preoperative diagnostic workup, the patient underwent a bilateral mammogram (MMG) which showed a high-density mass with no calcification in the breast parenchyma, highly suspicious for malignancy (Fig. 1c). Breast ultrasonography (US) showed a 1.3-cm, irregularly shaped, hypoechogenic mass (Fig. 1d). Serum tumor markers were within normal limits. A core needle biopsy of the mass demonstrated malignant cells proliferating in a cribriform or papillary pattern.

With a diagnosis of invasive ductal carcinoma, tubule forming type, in the upper lateral quadrant of the left breast, the patient underwent total mastectomy and sentinel lymph node biopsy. The patient chose total mastectomy to avoid postoperative radiotherapy. Intraoperative pathological examination confirmed that the two sentinel lymph nodes sampled in the axilla were negative for metastasis, and no axillary node dissection was performed.

The surgical specimen contained a hard, grayish, solid, and lobulated tumor with defined margins with a diameter of 1.5 cm (Fig. 2a). Microscopically, the tumor was composed entirely of packed epithelial islands with a cribriform appearance (Fig. 2b). The islands were irregularly shaped with an ovoid outline and separated by relatively thin fibrous connective tissue. Well-defined, rounded spaces (cribriform growth pattern) were formed within the islands, and proliferating tumor cells were columnar and rather uniform, having rounded to ovoid nuclei with nuclear pleomorphism grade of G1 (Fig. 2c). Cribriform ductal carcinoma in situ (DCIS) was seen around the tumor; on pathological examination, total tumor area was 2.7 cm x 1.5 cm and invasive area was 1.5 cm x 1.0cm. No lymphovascular invasion was identified, and the surgical margins were free of the tumor. On immunohistochemistry, the tumor islands had no positive cells for the myoepithelial marker CD10 (Fig. 3b), whereas myoepithelial cells were preserved around the DCIS (Fig. 3a). The tumor was classified as an invasive cribriform carcinoma of pure type. Nuclear immunoreactivity was strong for both estrogen receptor (ER) and progesterone receptor (PgR) and seen in 90% of the tumor cells (Fig. 3c, d). Human epidermal growth factor receptor 2 (HER2) expression was absent (Fig. 3e), and the Ki-67 labeling index was low (7%) (Fig. 3f). Two axillary sentinel lymph nodes were examined intraoperatively and showed no metastasis. In accordance with the 8$^{th}$ edition of the UICC TNM classification, the tumor was staged as pT1cN0.

The patient is presently free from local recurrence and metastasis 10 months after surgery on adjuvant hormone therapy.

## DISCUSSION

ICC is a unique type of invasive breast carcinoma that was first described by Page et al. in 1983[1]. ICC consists of invasive epithelial islands containing well-defined, rounded spaces similar in appearance to cribriform-type ductal carcinoma *in situ*(DCIS). The islands have an ovoid or angular outline and are set within a desmoplastic stroma. They consist of multilayered epithelial cells of small to intermediate size forming

secondary glandular structures lined by cuboidal to columnar cells. The World Health Organization (WHO) classification (5$^{th}$ edition) required an invasive breast carcinoma to have > 90% of the tumor composed of cribriform islands of epithelial cells with low-grade nuclei and sparse mitoses. ICCs are typically ER-positive (95-100%), PR-positive (69-89%) and HER2-negative[5,6]. The present case showed that most of the tumor showed a cribriform pattern and was classified as pure ICC. Pure ICC tends to have a smaller tumor size and a lower rate of lymph node metastasis than mixed ICC[4]. However, there is no report yet whether there is a difference in prognosis between the two types.

Adenoid cystic carcinoma (ACC) may also exhibit cribriform patterns. However, the cribriform spaces in ACC lesions contain basaloid cells (myoepithelial-like cells) and basement membrane material, and they are negative for ER, PgR, and HER2[7].

The radiological features of ICC are indistinguishable from those of other breast carcinomas[8]. The imaging findings of the present case showed no diagnostic features.

The mortality rate of patients with ICC is reported to be lower than that of those with non-specific types of invasive ductal carcinoma (IDC), and the 5-year survival rate is reported to be over 95%[2,3,9,10]. The reasons for the excellent prognosis of ICC seem to be related to its characteristics. First, tumor size tends to be small, less than 2 cm, 75% of which are T1a to T1c. Next, ICC has less nodal metastasis. Finally, ICC has higher rates of positive ER and PR staining, which means that it is hormone-sensitive, and negative HER2 expression.

In fact, ICC pathologically has smaller tumor diameters than IDC, and has a higher rate of Lumpectomy in the previous study by Liu et al [9]. However, in this case, the tumor diameter of the invasive cancer was 1.5x1.0 cm, but the pathological tumor size was 2.7x1.5 cm, which was 1.2 cm larger. Although ICC is a tumor type with a good prognosis, we must consider the intraductal growth of the tumor and measure the exact size of the tumor in ICC cases. ICC requires rapid intraoperative pathological diagnosis and postoperative radiation therapy, and if not, ICC is a tumor type that should be considered for total mastectomy.

There is no consensus on ICC drug therapy yet. Colleoni recommended that favorable luminal special type tumors may be suitable for no therapy or endocrine therapy alone[11]. However, it must be cautious to make the decision. The case of pure ICC could still have distant metastases (bones) if left untreated for a long period of time (13 years)[12].

The patient is doing well and remains disease-free 10 months after surgery on adjuvant hormone therapy.

## Conclusion

A case of pure ICC of the breast with a good prognosis was presented. Further studies of more patients with longer follow-up are needed.

## DECLARATIONS

### Abbreviations

ACC: Adenoid cystic carcinoma, CT: Computed tomography, DCIS: Ductal carcinoma in situ, ER: Estrogen receptor, HER2: Human epidermal growth factor receptor 2, ICC: Invasive cribriform carcinoma, IDC: Invasive ductal carcinoma; MMG: mammogram, PgR: progesterone receptor, UICC: Union for International Cancer Control, US: Ultrasonography, WHO: World Health Organization.

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

The patient provided written, informed consent to publish this case report and any accompanying images.

### Availability of data and materials

The data are not available for public access because of patient privacy concerns but are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

**Funding**

No funding was received for this study.

**Authors' contributions**

Author 1: Yasuhiro Adachi drafted the manuscript.

Author 2: Takefumi Katsuki drafted and proofed the manuscript.

Author 3: Takakazu Sasaguri proofed the manuscript.

Author 4: Keiji Hirata proofed the manuscript.

Author 5: Naoki Nagata had given final approval of the version to be published.

All authors read and approved the final manuscript.

**Acknowledgements**

None.

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**FIGURE LEGENDS**

Figure. 1: Preoperative examination (Plain CT, MMG, US)

a and b: Plain CT shows an irregularly shaped tumor (arrow) with a diameter of 14 mm in the upper-outer region of the left mammary gland. No left axillary lymphadenopathy is observed.

c: MMG in the medio-lateral oblique view, a tumor shadow (arrow heads) is seen in the upper region of the left mammary gland.

d: US shows a 1.3-cm, irregularly shaped, hypoechogenic mass in the upper-outer region of the left mammary gland.

Figure. 2: Findings of the resected specimen,

a: Grayish white, solid, and lobulated tumor (arrow) in the mammary gland.

b: HE staining shows tumor cells growing in a cribriform, partly papillary pattern in a low-power field.

c: Most of the tumor shows a cribriform pattern in the high-power field.

Figure. 3: Immunohistological findings

a: The tumor islands have no positive cells for CD10, whereas myoepithelial cells are preserved around the DCIS.

b: No CD10-positive cells were found in the invasive cribriform cancer area.

c: ER is strongly stained

d: PgR is strongly stained.

e: HER2 expression is judged as score 0.

f: Ki67 staining is observed in 7% of all cells.