Cribriform carcinoma arising in a benign phyllodes tumor

Dear Editor,

Phyllodes tumor is a rare biphasic neoplasm of the breast exhibiting proliferation of epithelial and stromal components that can be further categorized into benign, borderline, and malignant according to a few histopathological parameters.[1] The epithelial component within phyllodes tumor may show proliferative changes with rare occurrences of malignant transformation.[2,3] These carcinomas were reported to occur either within or adjacent to phyllodes tumors in the ipsilateral or contralateral breast. They can occur in conjunction with benign, borderline, or malignant phyllodes.[2-5] In many instances, the carcinomatous components were identified incidentally on histopathological evaluation.

A 60-year-old woman presented with a 2-year history of left breast lump, which was increasing in size. Mammogram showed an irregular hypoechoic lesion with a cystic component and increased vascularity at the left upper outer quadrant of the left breast. The initial impression was left breast phyllodes tumor, and classified as BIRADS category 4a that suggest a low probability of malignancy. However, biopsy of the lesion showed tubular and cribriform glands with loss of myoepithelial cells suspicious of invasive carcinoma. Wide local excision (WLE) revealed a well-circumscribed solid whitish lesion measuring 65 mm × 35 mm × 50 mm composed of malignant glands arranged in tubular and cribriform pattern embedded within a benign phyllodes tumor [Figure 1]. The malignant glands are lined by cells exhibiting monomorphic, round, hyperchromatic nuclei, inconspicuous nucleoli, moderate amount of cytoplasm with cytoplasmic blebbing, and apical snouts. The phyllodes tumor exhibit clefts, ducts, and a leaf-like arrangement of benign two-tiered epithelium with fibromyxoid stroma. The stromal cells showed no cytological atypia, increased in mitosis, or stromal overgrowth.

Immunohistochemically, the malignant glands showed the absence of myoepithelial markers and were positive for estrogen receptor (ER) and progesterone receptor with equivocal (2+) human epidermal growth factor receptor 2 (HER2) expression [Figure 2]. Dual-colour dual-hapten *In-Situ* hybridization (DDISH) showed no amplification of HER2 gene. A diagnosis of invasive cribriform carcinoma in the background of benign phyllodes tumor, pT3 was rendered. She underwent a sentinel lymph node biopsy 3 months' post-WLE, which was negative for malignancy. She has completed radiotherapy and is currently on tamoxifen. She has remain recurrence-free 15 months after the diagnosis.

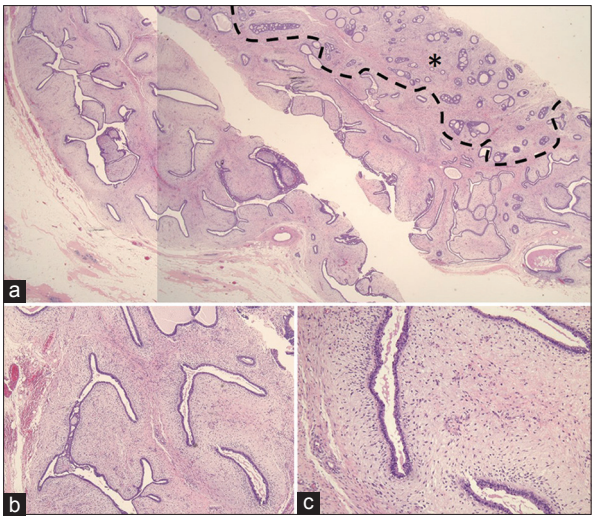

Figure 1: Cribriform carcinoma (asterisk, demarcated by dashed line) arising within a benign phyllodes tumor (a: H and E, ×12.5). Benign ductal epithelium with fibromyxoid stroma forms clefts (b: H and E, ×40). The stroma showed proliferation of spindle cells with increased cellularity and mitosis of 3–4 per 10 high-power field (c: H and E, ×100). There was no stromal overgrowth present

Types of carcinoma component arising within a phyllodes tumor that has been reported include ductal carcinoma *in situ* (DCIS), mixed DCIS and invasive carcinoma, invasive carcinoma, lobular carcinoma *in situ*, invasive lobular carcinoma, and neuroendocrine carcinoma.[3,4] Two previous cases of invasive cribriform carcinoma were reported to arise within a malignant and borderline phyllodes tumor, respectively.[3,5] Our case showed invasive cribriform carcinoma arising within a benign phyllodes tumor, which would be the first case report to date. Cribriform carcinoma of the breast is a rare low-grade invasive carcinoma where more than 90% of the tumor shows well-defined cribriform spaces. It accounts for only 0.4% of invasive breast carcinomas and presents at a median age of 63 years.[1] The cribriform islands are ovoid to angulated and set within a desmoplastic stroma. The cells display low-grade nuclear features, and mitosis is sparse. Cribriform carcinoma usually expresses ER and shows no HER2 gene amplification. Cribriform carcinoma can be differentiated from cribriform DCIS by the absence of myoepithelial cells, as demonstrated in our case.

Adequate margin is essential in preventing recurrence in phyllodes tumour. Thus, WLE with 1-2 cm margins

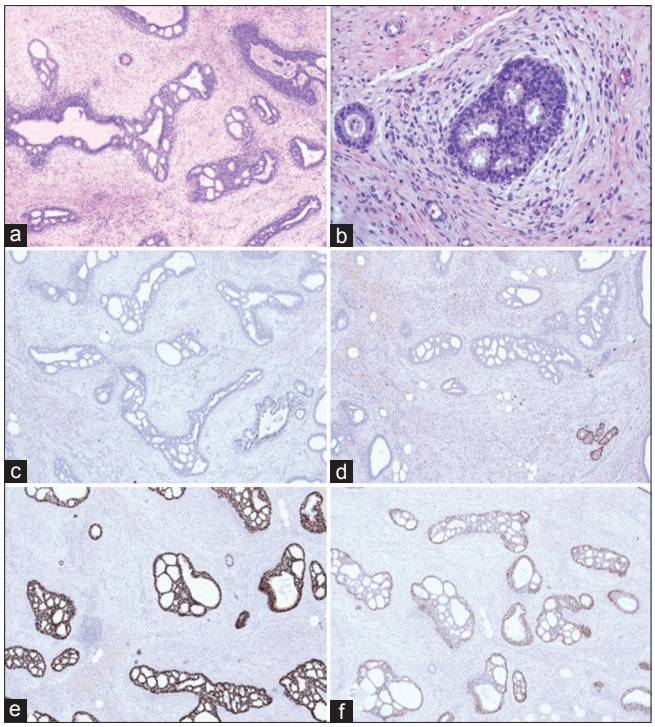

Figure 2: Numerous malignant glands are arranged in tubular and cribriform patterns surrounded by cellular fibromyxoid stroma. The glands are lined by single to multilayered glandular cells (a: H and E, ×40; b: H and E, ×100). The malignant glands display the absence of myoepithelial cells (c: p63, ×40; d: S100, ×40) with positivity toward ER (e: ER, ×40) and PR (f: PR, ×40). ER: Estrogen receptor (ER), PR: Progesterone receptor

or mastectomy is recommended.[3,4] Axillary lymph node dissection is not indicated for malignant phyllodes involving only the stromal component.[4] The presence of carcinomatous components consequently changes the management despite no current standard adjuvant therapy for this disease. Axillary lymph node evaluation is deemed required with the possibility of further resection and adjuvant therapy to treat the invasive carcinoma. A review by Wu *et al*. of invasive carcinoma arising within malignant phyllodes tumor showed cases exhibiting axillary lymph node metastasis. His analysis also discovered despite these cases receiving either combination of surgery, chemotherapy or radiotherapy, a few developed distance metastases and succumbed to the disease.[5] Awareness of potential invasive carcinoma arising within a phyllodes tumor is crucial for careful evaluation of an otherwise benign tumor. The presence of carcinomatous components can alter the management, whereby axillary lymph node evaluation and adjuvant therapy may be required to allow a better survival rate for the patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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