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Pathology Section

Co-existence of Multifocal Ductal Carcinoma in Situ with Microinvasion and Benign Phyllodes Tumour in the Same Breast: A Rare Case Report

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ABSTRACT

The presented case is a rare instance of multifocal Ductal Carcinoma In Situ (DCIS) with microinvasion in the presence of a benign phyllodes tumour in a 60-year-old postmenopausal woman. The patient reported that she had painless right breast lumps for four months and no previous trauma, hormonal treatment or family history of breast/ovarian carcinoma. A physical examination showed four discrete, mobile and non-tender masses without any skin changes or lymphadenopathy. Biochemical and haematological investigations were unremarkable. Mammography and targeted ultrasound imaging showed several heterogeneous nodules, one of which was lobulated fibroepithelial with the rest being segmental calcifications, which led to suspicion of multifocal DCIS with microinvasion. Wide local excision of all nodules was done. Histopathology also confirmed DCIS with microinvasion in three nodules and one benign phyllodes tumour, without having epithelial malignancy. This case underlines diagnostic challenge in coexisting DCIS and phyllodes tumours, emphasising the importance of proper imaging, surgical excision and histopathology for diagnosis and management of such rare cases.

Keywords: Adjuvant therapy, Breast neoplasm, Collision tumour, Fibroepithelial lesion, Histopathology

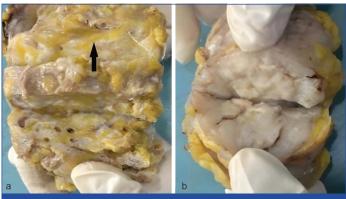
CASE REPORT

A 60-year-old postmenopausal woman presented to the surgical outpatient department in a tertiary healthcare centre with a four-month history of multiple painless lumps in her right breast, which she had first noticed during self-examination. There was no associated history of preceding trauma, fever, nipple discharge, or weight loss. The patient also denied the use of hormone replacement therapy. Also, there was no personal or family history of breast or ovarian carcinoma. She did not have any known history of metabolic disorder like diabetes mellitus, high blood pressure, thyroid dysfunction or obesity.

On her clinical examination, the right breast showed normal contour without any skin tethering, dimpling, peau d'orange, or nipple retraction. On palpation of the given right breast, four discrete, mobile, non-tender masses were identified, which were all localised. In the given patient, the overlying skin was free, and no local rise in temperature or erythema was noted. There was no evident axillary and supraclavicular lymphadenopathy. Also, systemic examination revealed no abnormal findings.

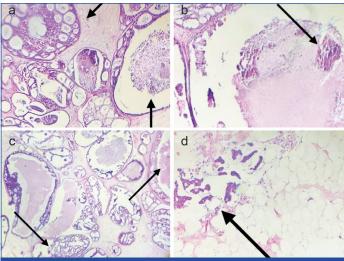
Haematological and biochemical tests, such as complete blood count, liver and renal function tests, fasting blood glucose, and serum electrolytes, were normal in the patient. Mammography with targeted ultrasound was done, which demonstrated multiple breast masses of varied morphology. The imaging was consistent with the presence of multiple right-breast nodules, with one showing a lobulated fibroepithelial pattern, while others revealed segmental calcifications, thus suggestive of ductal pathology. These findings were all categorised as suspicious, leading to the provisional diagnosis of multifocal DCIS with a possibility of microinvasion. The differential diagnosis at this point was multifocal invasive carcinoma, lobular carcinoma, and benign fibroepithelial lesions like phyllodes tumour, thereby warranting surgical excision. Following a multidisciplinary discussion, a wide local excision of all the nodules with orientation for margin assessment was planned.

Intraoperatively, four separate nodules were excised. Gross examination revealed a specimen that measured $15\times9\times3.5$ cm in aggregate. The nodules were labelled accordingly as A (largest), B (second largest), C (third largest), and D (smallest). Nodule A measured $9.5\times7\times2$ cm in size, while the smallest, nodule D, measured $5\times4\times4.2$ cm. Since the gross features of nodules C and D were similar to those of nodule A, only the representative image of nodule A has been provided in [Table/Fig-1a], whereas nodule B was well-defined, firm in consistency with cleft-like spaces as shown in [Table/Fig-1b].



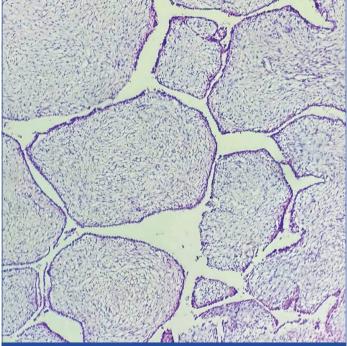
[Table/Fig-1]: a) Nodule A showing heterogeneous yellowish cheesy material (highlighted with black arrow); nodules C and D exhibited similar gross morphology; b) Nodule B was well-defined, firm in consistency with cleft-like spaces.

Histopathological examination of nodules A, C, and D revealed a few similar features as typical epithelial proliferation confined within ducts, showing cribriform architecture and central comedo-type necrosis. Areas of microinvasion, defined as foci of malignant cells breaching the basement membrane into the surrounding fibrous stroma with an invasive size of ≤ 1 mm, were also identified in the given nodules. These findings confirmed a diagnosis of intraductal carcinoma (DCIS, cribriform and comedo patterns) with microinvasion (IDC-MI) as shown in [Table/Fig-2].



[Table/Fig-2]: a) Histopathology slide (H&E, 10x) of nodule D, showing intraductal carcinoma with cribriform and comedo pattern shown with arrows; b) Histopathology slide of (H&E, 10x) of Nodule C, showing cribriform and comedo patterns; c) Histopathology slide of (H&E, 10x) of Nodule A, showing cribriform and comedo patterns; d) Histopathology slide of (H&E, 10x), showing stromal microinvasion.

In contrast, nodule B demonstrated a biphasic tumour which was composed of benign stromal overgrowth arranged in leaf-like fronds lined by benign ductal epithelium. There was no evidence as such of cytologic atypia, mitotic activity, or malignant stromal transformation, and no epithelial malignancy was identified within this lesion. These features of nodule B were diagnostic of a benign phyllodes tumour as shown in [Table/Fig-3].



[Table/Fig-3]: Nodule B features were diagnostic of a benign phyllodes tumour. Nodule B demonstrated a biphasic tumour composed of benign stromal overgrowth arranged in leaf-like fronds lined by benign ductal epithelium (40x).

The patient had an uneventful postoperative recovery. She tolerated oral feeds well, with the need for only minimal analgesia, along with no complications related to the wound. The surgical site healed primarily; thus, she was discharged by giving advice about wound care, physiotherapy for shoulder mobility, and regular follow-up. Immunohistochemical markers {Estrogen Receptor (ER), Progesterone Receptor (PR), HER2/neu, Ki-67} were not performed at our centre, and she was thereby subsequently referred to the oncology department for multidisciplinary evaluation.

The patient was then counselled for her diagnosis and management plan in the oncology department, including the importance of adjuvant radiotherapy, possible endocrine therapy, regular surveillance, and

lifestyle modifications. She was then reassured about the benign nature of the phyllodes tumour and educated about the signs of recurrence. At early follow-up, she was recovering well and good, wounds were healthy, and radiotherapy planning was in progress. The final diagnosis of the given case is multifocal DCIS (cribriform and comedo pattern) with microinvasion involving three nodules (A, C, and D) in the right breast, coexisting with a benign phyllodes tumour (Nodule B) also in the same breast, without any evidence of epithelial malignancy within the phyllodes tumour.

DISCUSSION

An intra-ductal epithelial neoplasm called as DCIS when one or more foci of microinvasions 1 mm and less in size can be detected, the lesion is classified as DCIS with microinvasion (DCIS-Mi), a rare transitional lesion between pure DCIS and frankly invasive carcinoma [1,2]. Phyllodes tumours are fibroepithelial breast neoplasms, which are less than 1% of total tumours of the breast [3]. Phyllodes tumours are morphologically categorised as benign, borderline and malignant, which clinically and radiologically resemble fibroadenomas; hence, proper histopathologic evaluation should be performed [3,4]. The cooccurrence of carcinoma (DCIS or invasive carcinoma) with a phyllodes tumour in the same breast, whether as carcinoma arising in the epithelial component of the phyllodes tumour, or as coexisting/collision lesions, is uncommon and is largely reported through isolated cases and small series [5]. The aim of the given article is to present the rare case of the coexistence of multifocal DCIS with microinvasion and a benign phyllodes tumour in the same breast by highlighting its clinicopathological features, diagnostic challenges, and implications for surgical and therapeutic management.

In a case reported by Sun L et al., a 30-year-old nulliparous Chinese woman presented with a small, firm breast nodule, which on imaging revealed a heterogeneous hypoechoic lesion without suspicious calcifications or architectural distortion [6]. Histopathological analysis of the excised specimen confirmed it as a benign phyllodes tumour having only mild stromal atypia, absence of stromal overgrowth, and low mitotic activity [6]. Interestingly, within the tumour, a 3.5 mm focus of intermediate-grade DCIS was identified, having rigid cribriform architecture, monotonous epithelial proliferation, and associated calcifications [6]. The DCIS was ER/PR positive, located 2 mm from the anterior margin, and clear by >5 mm from all other margins, whereas the phyllodes component approached <1 mm from anterior, posterior, and medial margins [6]. The patient underwent genetic counselling and BRCA 1/2 testing, which was negative [6]. Given her desire to start a family, she declined adjuvant radiation or tamoxifen therapy, and at one month of postsurgery, she considered a bilateral nipple-sparing mastectomy [6].

In a case reported by Ahmad A et al., a 35-year-old multiparous Pakistani woman with a long-standing history of bilateral breast lumps, initially stable and previously diagnosed as fibroadenomas, presented with a recent increase in size of right breast lumps associated with nipple discharge and pain [7]. Radiological evaluation showed multiple circumscribed, lobulated, solid-tocystic lesions, most of which were classified as BIRADS II-III [7]. A provisional diagnosis of fibroadenomas and a possible phyllodes tumour was thus suggested [7]. The biopsy of the right retro-areolar mass showed a fibroepithelial lesion that could be considered a lesion of phyllodes tumour, whereas the lump at the 2 o'clock position on the right breast and the lump in the left breast were characteristic of fibroadenomas [7]. All three lesions were excised surgically, and histopathological examination confirmed the retroareolar lesion as a benign phyllodes tumour [7]. The lesion on the left was a fibroadenoma and crucially, the lesion at the right 2 o'clock was an invasive carcinoma of No Special Type (NST), arising within a high-grade DCIS in the background of a complex fibroadenoma [7].

Author/Case	Patient demographics	Clinical presentation	Radiology findings	Histopathology	Management	Outcome/ Follow-up
Sun L et al., [6]	30-year-old nulliparous Chinese woman	Small, firm breast nodule	Heterogeneous hypoechoic lesion, no suspicious calcifications or distortion	Benign phyllodes tumour (mild stromal atypia, no overgrowth, low mitosis) with 3.5 mm focus of intermediate-grade DCIS (cribriform, calcifications)	Excision; BRCA1/2 negative; declined RT/tamoxifen; considered bilateral nipple-sparing mastectomy	At 1 month, planning risk- reducing surgery
Ahmad A et al., [7]	35-year-old multiparous Pakistani woman	Long-standing bilateral lumps, recent increase in size, nipple discharge, and pain	Multiple circumscribed, lobulated, solid-to-cystic lesions (BIRADS II-III)	Right retroareolar mass: benign phyllodes; Right 2 o'clock mass: invasive carcinoma NST with high-grade DCIS in background of complex fibroadenoma; Left breast mass: fibroadenoma	Surgical excision of all three lesions	Diagnosis clarified post-surgery; outcome not detailed
Jena S et al., [8]	42-year-old Indian woman	Large right breast lump for 6 years, progressively enlarged	Not specified	Borderline phyllodes tumour (stromal overgrowth, mild atypia, 3-5 mitoses/10 HPF) with high-grade DCIS (~10% lesion) and sclerosing adenosis	Wide local excision with round block oncoplasty; radiotherapy + tamoxifen	Good cosmetic result; disease-free at 3 years
Brahmachari S et al., [9]	36-year-old Indian woman, prior benign phyllodes excision	Recurrent left breast lump with pain	BI-RADS 4 lesion; irregular margins, skin thinning, axillary nodes	Recurrent benign phyllodes tumour (mild-moderate atypia, focal stromal overgrowth, <5 mitoses/10 HPF) with low-intermediate grade DCIS (luminal A, ER/PR+, HER2-, Ki-67 ~10%); no invasive carcinoma	Modified radical mastectomy (emergency due to bleeding); adjuvant tamoxifen	Disease-free on follow-up
Park HM et al., [10]	21-year-old Korean woman	A palpable mass in the upper outer quadrant of the right breast with an adjacent small mass	Oval heterogeneous mass on Ultrasound (US), mammography, MRI, PET/CT; no axillary lymphadenopathy or distant metastasis	Larger mass: invasive ductal carcinoma arising within borderline phyllodes tumour; Smaller mass: fibroadenoma; ER/PR positive, HER2 overexpression in carcinoma component	Breast-conserving surgery with sentinel lymph node biopsy; adjuvant radiotherapy and hormonal therapy	Disease-free at 38 months follow-up
Present case	60-year-old postmenopausal Indian woman	Multiple painless right breast lumps for 4 months, no trauma, discharge, or family history	Mammography & US: multiple nodules; one lobulated fibroepithelial lesion, others with segmental calcifications (suspicious)	Nodules A, C, D: multifocal DCIS (cribriform & comedo) with microinvasion (≤1 mm); Nodule B: benign phyllodes tumour (no atypia, no mitoses, no epithelial malignancy)	Wide local excision of all nodules; uneventful recovery; referred for adjuvant RT & endocrine therapy	Good early recovery; wounds healthy; radiotherapy planned.

[Table/Fig-4]: Comparative table of present case and previously published similar cases [6-10].

In a case reported by Jena S et al., a 42-year-old Indian woman presented with a slow-growing right breast lump of six years' duration, which had progressively enlarged to occupy almost the entire breast [8]. Although initially advised mastectomy at another centre, she sought breast-conserving treatment and was managed with wide local excision and round block oncoplasty [8]. Histopathological examination revealed a borderline phyllodes tumour, which was characterised by stromal overgrowth, mild atypia, and 3-5 mitoses per 10 HPF. In addition, there was coexistent sclerosing adenosis and a high-grade DCIS component comprising approximately 10% of the lesion [8]. Immunohistochemistry results also confirmed ER positivity [8]. All surgical margins were negative [8]. The patient thereafter received radiotherapy and endocrine therapy with tamoxifen [8]. Mainly, oncoplastic reconstruction produced good cosmetic results with conservation of the breast [8]. She has no recurrence after three years of follow-up, which highlights the importance of a personalised multimodal treatment in these rare and complicated cases [8].

A 36-year-old Indian woman with a history of excised benign phyllodes tumour in the past presented in a case reported by Brahmachari S et al., with a recurrent left breast lump and pain [9]. Imaging results indicated a BI-RADS 4 lesion with suspicious characteristics like irregular margins, skin thinning, and ipsilateral axillary lymphadenopathy [9]. FNAC raised suspicion of ductal carcinoma and an attempted core biopsy was complicated by tumour bleeding, which required emergency modified radical mastectomy [9]. Histopathological analysis revealed a benign phyllodes tumour with focal stromal overgrowth, mild to moderate atypia, and minimal mitosis, less than 5/10 HPF, as is characteristic of recurrent benign phyllodes tumour [9]. Notably, the epithelial component exhibited low- to intermediate-grade luminal type A (ER/PR positive, HER2 negative, Ki-67 510 percent) DCIS, without invasive carcinoma [9]. There were no nodal metastases present, and surgical margins were clear [9]. Accordingly, adjuvant hormonal therapy with tamoxifen was initiated, and she remained disease-free on follow-up [9].

In a case reported by Park HM et al., a 21-year-old female from Korea presented with a palpable mass in the upper outer quadrant of her right breast along with a small mass adjacent to it [10]. An oval heterogeneous mass was seen on imaging {ultrasound, mammography, Magnetic Resonance Imaging (MRI) and Positron Emission Tomography/Computed Tomography (PET/CT)} without any signs of axillary lymphadenopathy or distant metastasis [10]. The bigger mass was an invasive ductal carcinoma, which was arising within a borderline phyllodes tumour, whereas the smaller mass was a fibroadenoma [10]. The patient has gone through breast-conserving surgery with sentinel lymph node biopsy, and histopathology revealed that there is ER/PR Positivity and HER2 overexpression in the carcinoma component [10]. She was treated with adjuvant radiotherapy and simultaneous hormonal therapy and remained disease-free at 38 months of follow-up [10]. A comparative table of the present case and previously published similar cases is described in [Table/Fig-4] [6-10].

CONCLUSION(S)

The prevalence of coexistence of multifocal DCIS with microinvasion and benign phyllodes tumour in the same breast is extremely low, making its diagnosis and treatment difficult. The case highlights the significance of meticulous histopathological investigation of all abnormal lesions that are excised in the breast, since radiological data can be deceptive. It requires a multidisciplinary approach to be sure of the accurate diagnosis, proper surgical intervention and adjuvant treatment. Follow-ups are essential in the long term to check recurrence and direct treatment and enhance outcomes in these rare clinicopathological situations.

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