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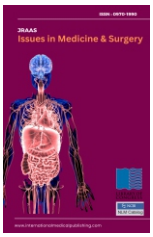

Case Report

Section: Pathology

Spectrum of Fibroepithelial Breast Lesions in a Single Patient: From to Fibroadenoma Malignant Phyllodes Tumor

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HIGHLIGHTS

- Rare tumor coexistence
- Phyllodes spectrum identified
- Imaging overlap observed
- Histology confirmed diagnosis
- Early detection essential

Key Words:
Fibroepithelial lesion
Fibroadenoma
Phyllodes tumor
Malignant phyllodes
Breast lump
Histopathology

ABSTRACT

Introduction: Fibroepithelial lesions of the breast comprise a diverse group of biphasic tumors ranging from benign fibroadenomas to phyllodes tumors, which are further categorized as benign, borderline, and malignant. Although fibroadenomas are common benign breast lesions, phyllodes tumors are relatively rare and may clinically and radiologically mimic fibroadenomas, making accurate diagnosis challenging. The coexistence of multiple fibroepithelial tumor types in a single patient is exceptionally uncommon and highlights the complexity of these lesions. **Aim & Objective:** To present a rare case demonstrating the complete histopathological spectrum of fibroepithelial breast lesions in a single patient and to emphasize the importance of careful pathological evaluation for appropriate diagnosis and management. **Material & Methods:** A 46-year-old female presented with bilateral breast lumps clinically suggestive of benign breast lesions. Radiological evaluation favored fibroadenomas. Surgical excision of the breast masses was performed, followed by detailed histopathological examination of all excised specimens. **Results:** Histopathological analysis revealed three distinct fibroepithelial lesions within the same patient, including fibroadenoma, benign phyllodes tumor, and malignant phyllodes tumor. The lesions showed overlapping radiological appearances, contributing to diagnostic difficulty. Microscopic evaluation demonstrated varying stromal cellularity, atypia, mitotic activity, and tumor margins corresponding to the different pathological entities. The presence of a malignant phyllodes tumor necessitated close clinical follow-up and further oncological management. **Conclusion:** This rare case illustrates the broad histopathological spectrum of fibroepithelial breast lesions and highlights the limitations of radiological diagnosis alone. Comprehensive histopathological assessment remains essential for accurate classification, prognostication, and treatment planning. Early recognition of malignant transformation within fibroepithelial lesions is crucial to optimizing patient management and reducing the risk of recurrence.

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INTRODUCTION

Fibroepithelial tumors of the breast are a heterogeneous group of biphasic neoplasms characterized by the proliferation of both epithelial and stromal components. These lesions encompass a broad histopathological spectrum ranging from benign fibroadenomas to phyllodes tumors, which may further be classified as benign, borderline, or malignant depending on their microscopic features. Among fibroepithelial lesions, fibroadenoma is the most common benign breast tumor, particularly affecting young women, and is generally associated with an excellent prognosis. In contrast, phyllodes tumors are relatively rare fibroepithelial neoplasms, accounting for approximately 0.3–1% of all breast tumors and nearly 2.5% of fibroepithelial lesions [1,2]. Despite their rarity, phyllodes tumors are clinically significant because of their tendency for local recurrence and, in malignant cases, potential for distant metastasis.

Histologically, phyllodes tumors are graded into benign, borderline, and malignant categories according to specific pathological criteria, including stromal cellularity, nuclear pleomorphism, mitotic activity, stromal overgrowth, and tumor margin characteristics [3]. Benign phyllodes tumors usually demonstate mild stromal hypercellularity and low mitotic activity, whereas malignant variants exhibit marked stromal atypia, increased mitoses, infiltrative margins, and stromal overgrowth. Borderline tumors possess intermediate features between the two extremes. Accurate histopathological classification is essential because treatment strategies, recurrence risk, and prognosis vary considerably across these categories.

Clinically and radiologically, fibroadenomas and phyllodes tumors often present as painless, mobile, well-circumscribed breast masses, making preoperative differentiation difficult. Imaging modalities such as ultrasonography and mammography frequently reveal overlapping features, including oval or lobulated hypoechoic lesions with circumscribed margins. Consequently, definitive diagnosis often relies on histopathological examination following excision. The coexistence of different fibroepithelial lesions within the same patient is uncommon, while the simultaneous presence of fibroadenoma, benign phyllodes tumor, and malignant phyllodes tumor in a single individual is exceedingly rare. Such cases present significant diagnostic and therapeutic challenges because radiological findings may underestimate the biological behavior of the lesion [4,5]. Spectrum of fibroepithelial breast lesions from fibroadenoma to malignant phyllodes tumor **(Figure 1)**.

The present case is unique in demonstrating the entire spectrum of fibroepithelial breast tumors within one patient, emphasizing the importance of meticulous pathological evaluation and adequate sampling of all excised breast lesions. Recognition of the variable histological patterns is crucial for appropriate surgical management, prevention of recurrence, and long-term follow-up, particularly in patients harboring malignant phyllodes components.

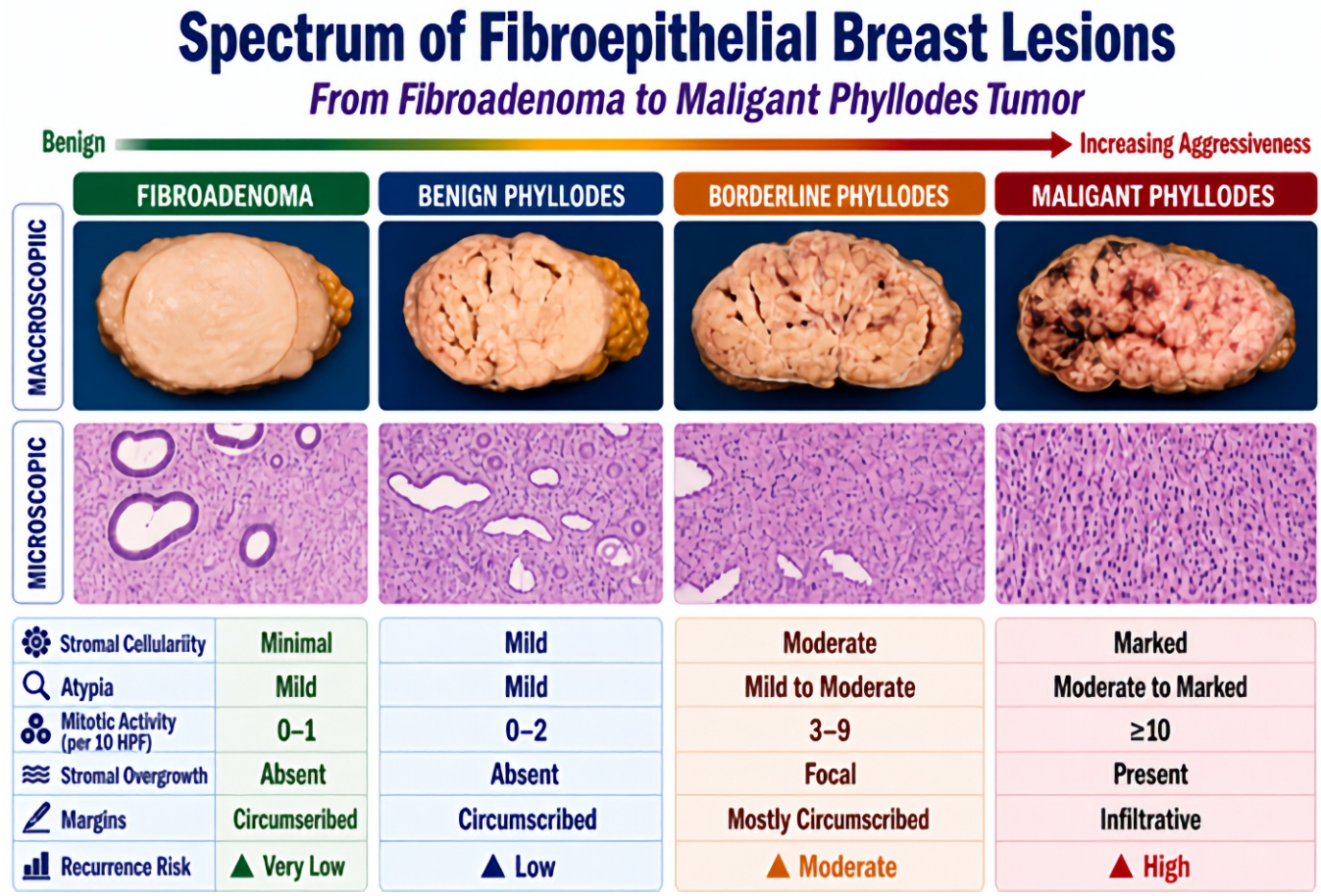

Figure 1: Spectrum of fibroepithelial breast lesions showing the macroscopic, microscopic, and histopathological progression from fibroadenoma to malignant phyllodes tumor.

CASE PRESENTATION

A 46-year-old female presented with multiple, firm, mobile, non-tender lumps in both breasts. There was no nipple discharge, skin involvement, or axillary lymphadenopathy.

Radiology: Mammography and ultrasound revealed multiple, well-circumscribed hypoechoic masses bilaterally, initially reported as fibroadenomas.

Gross Pathology: Four encapsulated masses were received:

- TP-1: 14 × 7 × 4.5 cm
- TP-2: 13 × 6 × 3 cm
- TP-3: 5 × 3 × 2 cm
- TP-4: 2 × 2 × 1 cm

Cut surfaces were firm, grey to grey-brown, with focal cleft-like areas.

Microscopy:

- **TP-1:** Benign ducts with intact myoepithelial cells arranged in a leaf-like pattern within mildly cellular stroma, showing stromal overgrowth, hyalinization, and mild atypia - *Benign Phyllodes Tumor*.
- **TP-2:** Stromal tumor with pushing margins and focal infiltration into adjacent breast tissue. Cells were oval to spindle-shaped with moderate to marked pleomorphism, coarse chromatin, and numerous mitoses (45–50/10 HPF). Osteoclast-like giant cells, bizarre cells, stromal overgrowth, and heterologous osteoid differentiation were present - *Malignant Phyllodes Tumor*.
- **TP-3 & TP-4:** Biphasic proliferation with pericanalicular and intracanalicular patterns, bland stroma, compressed ducts - *Fibroadenoma*. Thus, the histology demonstrated the full fibroepithelial spectrum in a single patient.

RESULT

Histopathological examination of four excised breast masses from a 46-year-old female revealed the coexistence of the complete spectrum of fibroepithelial lesions within a single patient. Radiological evaluation initially suggested multiple bilateral fibroadenomas. Grossly, the tumors were well-encapsulated, firm, grey to grey-brown masses with focal cleft-like spaces. Microscopic examination of TP-1 demonstrated features of benign phyllodes tumor, including leaf like architecture, mildly cellular stroma, stromal overgrowth, hyalinization, and mild atypia. TP-2 showed features consistent with maliagnant phyllodes tumor, characterized by marked, moderate to severe pleomorphism, numerous mitotic figures (45-50/10 HPF), stromal overgrowth, infiltrative margins, osteoclast like giant cells, bizarre stromal cells, and heterologous osteoid differentiation. TP-3 and TP-4 exhibited classical features of fibroadenoma with biphasic epithelial and stromal proliferation in pericanalicular and intracanalicular patterns. The findings highlighted the rare simultaneous occurrence of fibroadenoma, benign phyllodes tumor, and malignant phyllodes tumor in the same patient, supporting the concept of a biological and histopathological continuum among fibroepithelial breast lesions.

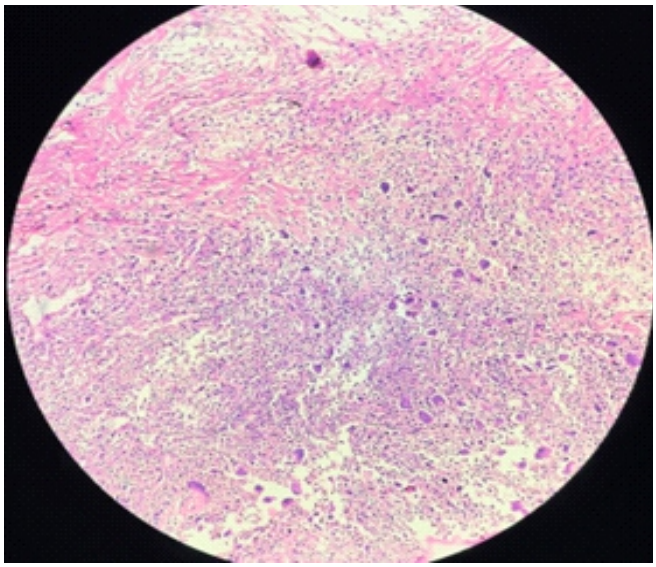

Figure 2: At 10x magnification- section shows hypercellular stromal tumour arranged haphazardly along with Multiple osteoclast like giant cells.

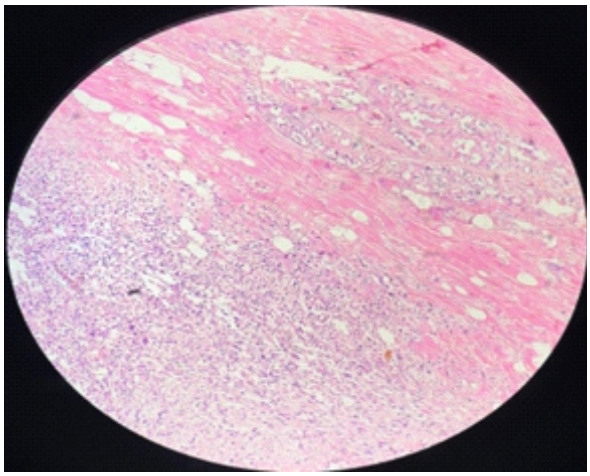

Figure 3: At 10x magnification- section shows hypercellular stromal tumour infiltrating the adjacent benign breast tissue.

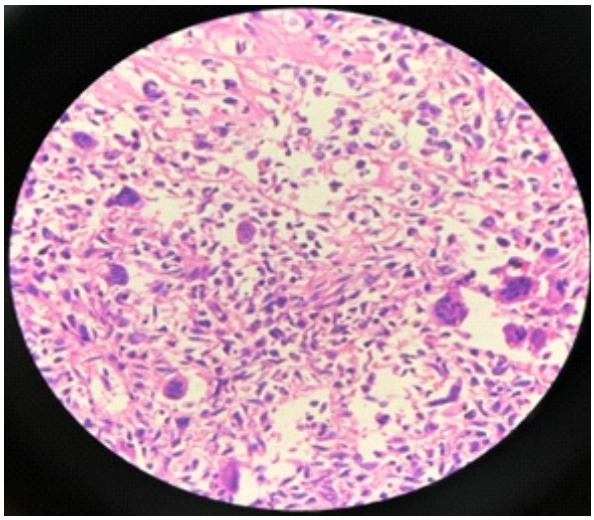

Figure 4: At 40x magnification- tumour proper composed of oval to spindle shaped cells showing moderate to marked pleomorphism, plump nuclei, coarse chromatin, inconspicuous nucleoli and moderate amount of cytoplasm. Multiple osteoclast like giant cells are also notes.

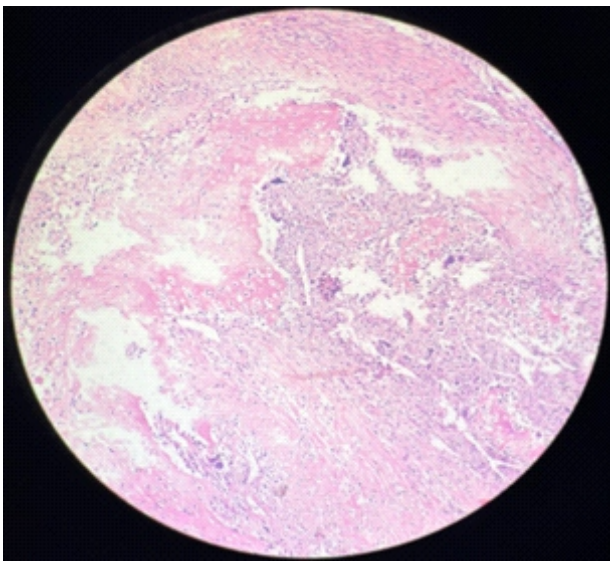

Figure 5: At 10x magnification- Section shows hypercellular stromal tumour arranged haphazardly along with heterologous component in the form of lace like pattern of osteoid formation is also noted.

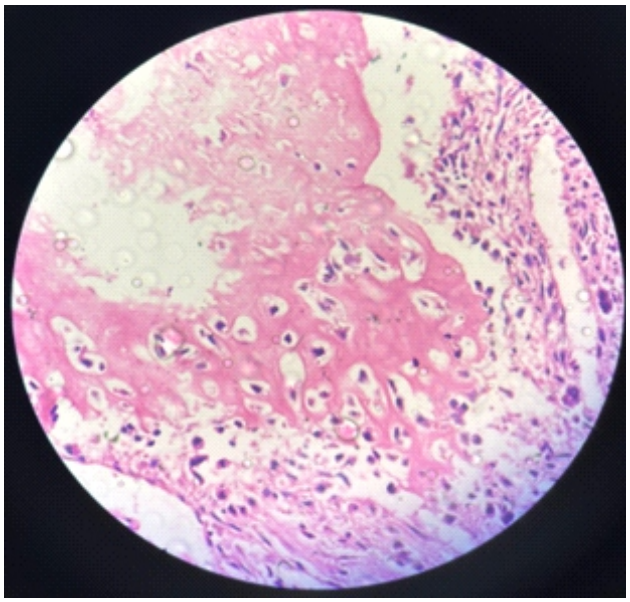

Figure 6: At 40x magnification- Section shows heterologous component in the form of lace like pattern of osteoid formation

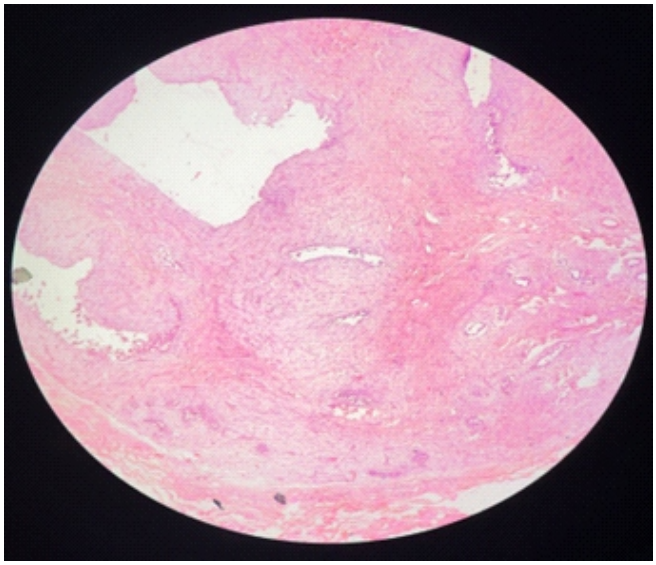

Figure 7: At 4x magnification- tumour proper shows benign ducts with intact myoepithelial cells arranged in a leaf-like pattern within mildly cellular stroma, showing stromal overgrowth, hyalinization, and mild atypia

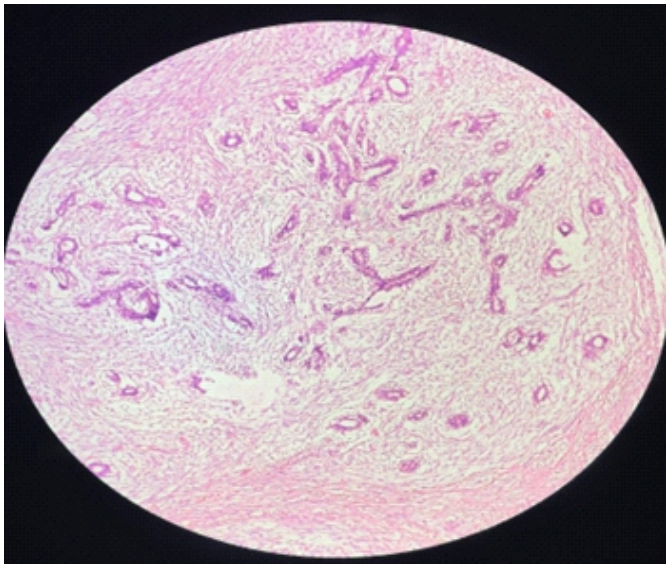

Figure 8: At 10x magnification- Biphasic proliferation with pericanalicular and intracanalicular patterns, bland stroma, compressed ducts - *Fibroadenoma*

DISCUSSION

Fibroadenoma is the most common benign fibroepithelial tumor of the breast and predominantly occurs in women younger than 35 years of age. These lesions are typically well-circumscribed, hormonally responsive tumors composed of proliferating stromal and epithelial elements arranged in pericanalicular or intracanalicular growth patterns. Most fibroadenomas demonstrate an indolent clinical course and are managed conservatively or by simple excision because recurrence and malignant transformation are rare. Molecular studies have shown recurrent MED12 mutations in fibroadenomas, supporting a shared molecular background with other fibroepithelial lesions [4]. In contrast, phyllodes tumors are uncommon fibroepithelial neoplasms that usually present in women during the fourth and fifth decades of life as rapidly enlarging palpable breast masses. Grossly, they are lobulated tumors with characteristic slit-like cystic spaces, while microscopically they exhibit exaggerated intracanalicular architecture with leaf-like stromal projections lined by benign epithelium accompanied by variable stromal hypercellularity.

According to the WHO classification, phyllodes tumors are categorized as benign, borderline, or malignant based on several histological parameters including stromal cellularity, nuclear pleomorphism, mitotic activity, stromal overgrowth, and tumor margins [3]. Benign tumors show mild stromal cellularity and low mitotic activity, whereas malignant phyllodes tumors display marked stromal atypia, increased mitotic figures, infiltrative margins, and stromal overgrowth. In some malignant cases, heterologous sarcomatous differentiation such as liposarcoma, chondrosarcoma, or osteosarcoma may also be identified, reflecting their aggressive biological behavior. Recent molecular studies further suggest that fibroepithelial lesions represent a biological continuum, with MED12 exon 2 mutations being common across fibroadenomas and phyllodes tumors, while additional genetic alterations including TERT promoter mutations, TP53 mutations, EGFR amplification, and chromosomal instability are more frequently associated with borderline and malignant phyllodes tumors [5,6]. These findings support the hypothesis that progression from fibroadenoma to phyllodes tumor may occur through the accumulation of stromal genetic alterations. One of the greatest diagnostic challenges in breast pathology is distinguishing cellular fibroadenoma from benign phyllodes tumor, particularly on core needle biopsy specimens where sampling may be limited. Both lesions can demonstrate increased stromal cellularity and overlapping architectural patterns, often leading to indeterminate diagnoses. However, features favoring phyllodes tumor include stromal heterogeneity, exaggerated intracanalicular growth, leaf-like architecture, stromal condensation around ducts, infiltrative margins, nuclear atypia, and increased mitotic activity [7]. In difficult cases, the descriptive diagnosis of "fibroepithelial lesion with cellular stroma" followed by complete excision is considered appropriate to allow adequate histological evaluation and definitive grading.

Management strategies differ considerably between fibroadenomas and phyllodes tumors because of their differing recurrence potential and biological behavior. Fibroadenomas generally require conservative follow-up or simple excision, whereas phyllodes tumors, particularly borderline and malignant variants, necessitate wide local excision with histologically negative margins to minimize recurrence risk [8]. Recurrence rates increase with higher tumor grade, stromal overgrowth, and positive surgical margins. For malignant phyllodes tumors, surgical margins of at least 1 cm are generally recommended [9]. Although the role of adjuvant radiotherapy remains controversial, it may reduce local recurrence in borderline or malignant tumors with close or positive margins or in recurrent lesions. Chemotherapy has shown limited benefits and is usually reserved for metastatic or unresectable malignant phyllodes tumors [10].

The present case is particularly remarkable because it demonstrated the complete histopathological spectrum of fibroepithelial lesions within a single patient, including fibroadenoma, benign phyllodes tumor, and malignant phyllodes tumor. Such coexistence is exceedingly rare and provides important insight into the morphologic and biological heterogeneity of fibroepithelial neoplasms. The case further emphasizes the concept of a pathological continuum between fibroadenoma and phyllodes tumor and highlights the critical importance of meticulous histopathological examination, extensive tissue sampling, and careful stromal assessment for accurate diagnosis and grading. Recognition of malignant transformation within fibroepithelial lesions is essential because it directly influences surgical management, prognosis, risk of recurrence, and long-term follow-up strategies.

CONCLUSION

We report a rare and diagnostically challenging case in which a single patient demonstrated the complete histopathological spectrum of fibroepithelial breast lesions, including fibroadenoma, benign phyllodes tumor, and malignant phyllodes tumor. Although these lesions share overlapping clinical and radiological features, their biological behavior and prognosis differ significantly. In the present case, imaging findings favored fibroadenoma; however, detailed histopathological examination revealed progressive stromal changes ranging from benign fibroadenoma to malignant phyllodes tumor with stromal atypia, increased mitotic activity, and infiltrative margins. This case highlights the marked morphologic heterogeneity of fibroepithelial tumors and emphasizes the critical role of meticulous histopathological evaluation, adequate tissue sampling, and long-term follow-up for accurate diagnosis, appropriate surgical management, and prevention of recurrence.

CLINICAL SIGNIFICANCE

The clinical significance of this study lies in its potential to bridge the gap between research findings and practical healthcare applications. It emphasizes the importance of translating scientific observations into meaningful improvements in patient care, diagnosis, and treatment outcomes. By highlighting real-world relevance, the study contributes to evidence based medical practice and supports informed clinical decision making. Ultimately, the findings aim to enhance patient quality of life, optimize therapeutic strategies, and promote better disease management in clinical settings.

ABBREVIATIONS

WHO: World Health Organization
MED12: Mediator Complex Subunit 12
TERT: Telomerase Reverse Transcriptase
TP53: Tumor Protein p53
EGFR: Epidermal Growth Factor Receptor

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AUTHOR CONTRIBUTIONS

All authors significantly contributed to the study conception and design, data acquisition, or data analysis and interpretation. They participated in drafting the manuscript or critically revising it for important intellectual content, consented to its submission to the current journal, provided final approval for the version to be published, and accepted responsibility for all aspects of the work. Additionally, all authors meet the authorship criteria outlined by the International Committee of Medical Journal Editors (ICMJE) guidelines.

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CONFLICT OF INTEREST

Authors declared that there is no conflict of interest.

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