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CD 10 EXPRESSION IN FIBROEPITHELIAL LESIONS OF BREAST AND THEIR ASSOCIATION WITH CLINICOPATHOLOGICAL PARAMETERS

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ABSTRACT

Background: Fibroepithelial lesions (FELs) of the breast, encompassing fibroadenoma (FA) and phyllodes tumour (PT) [benign, borderline, malignant], are biphasic neoplasms representing one of the most diagnostically challenging groups in surgical pathology. Histomorphological overlap, particularly between cellular fibroadenoma and benign PT, necessitates ancillary immunohistochemical (IHC) markers. CD10, a zinc-dependent neutral metalloendopeptidase (neprilysin, MME gene), is expressed in myoepithelial cells and aberrantly upregulated in activated stromal fibroblasts, making it a candidate marker of progressive stromal transformation. The present study aimed to evaluate CD10 expression across the FEL spectrum and correlate it with established clinicopathological parameters.

Materials and Methods: This cross-sectional study (prospective and retrospective) included 64 excision biopsy specimens of fibroepithelial breast lesions received between January 2018 and January 2026 at the Department of Pathology, SRM Medical College and Research Institute, Potheri. All specimens were fixed in 10% neutral buffered formalin, processed to paraffin blocks, and sectioned at 4 μm for H&E staining and IHC using the Peroxidase-Anti-Peroxidase (PAP) method. CD10 IHC was performed using a monoclonal antibody (clone DBS 56C6, PATHINSITU) with microwave-based antigen retrieval. CD10 stromal expression was graded as negative/Grade 0 (<10%), weak/Grade 1 (10–30%), or strong/Grade 2 (>30%) using breast myoepithelium as an internal positive control. Statistical analysis employed the chi-square test; $p < 0.05$ was considered statistically significant.

Results: Of 64 cases, 25 (39.5%) were fibroadenomas, 24 (37.5%) benign PTs, 7 (10.7%) borderline PTs, and 8 (12.3%) malignant PTs. CD10 expression demonstrated a highly significant stepwise increase with tumour grade ($p < 0.001$). Grade 2 (strong) expression was confined exclusively to malignant PT (7/8; 87.5%), Grade 1 (mild) expression predominated in borderline PT (7/7; 100%), and Grade 0 (negative) was universal in fibroadenoma (25/25) and the majority of benign PT (19/24). The diagnostic performance of Grade 2 CD10 for malignant PT: sensitivity 87.5%, specificity 100%, PPV 100%, NPV 96.4%.

Conclusion:CD10 shows a progressive and statistically significant stepwise increase in stromal expression from fibroadenoma through benign to malignant phyllodes tumour, with Grade 2 (strong) expression confined exclusively to malignant PT. These findings support the integration of CD10 into multimarker IHC panels as a high-specificity adjunct marker for identifying malignant stromal transformation in diagnostically challenging fibroepithelial lesions of the breast.

KEYWORDS: Fibroepithelial lesions; Fibroadenoma; Phyllodes tumour; CD10; Immunohistochemistry; Stromal atypia; Stromal overgrowth; WHO classification; Breast pathology; Stromal cellularity; Mitotic activity

INTRODUCTION

Mammary fibroepithelial tumours are biphasic neoplasms characterised by the proliferation of both epithelial and stromal (mesenchymal) components. The spectrum includes fibroadenomas (simple, conventional, cellular, and complicated) and phyllodes tumours (benign, borderline, and malignant), as well as periductal stromal tumour, as defined by the WHO 5th Edition Classification of Breast Tumours.[1]

Accurate categorisation remains diagnostically challenging due to morphological feature overlap, particularly between cellular fibroadenoma and benign phyllodes tumour, as well as between borderline and malignant phyllodes tumours. Because accurate classification directly affects surgical care, margin evaluation, and recurrence risk, histomorphology alone may be insufficient in ambiguous or borderline cases, necessitating additional diagnostic tools.[2,3]

The biological behaviour of fibroepithelial lesions is principally determined by the stromal component, which has raised interest in immunohistochemical markers reflecting stromal activity and genetic alterations. CD10 has been linked to stromal activation, extracellular matrix remodelling, and tumour progression. CD10 (also known as Common Acute Lymphoblastic Leukaemia Antigen, CALLA) is a 90–110 kiloDalton zinc-dependent metalloprotease found on the cell

surface, encoded by the MME gene. It is expressed in myoepithelial cells of normal breast and aberrantly upregulated in activated stromal fibroblasts of phyllodes tumours.[4]
Despite its biological rationale as a marker of stromal activation, the diagnostic and prognostic utility of CD10 in the full spectrum of fibroepithelial lesions remains incompletely characterised. The present investigation aims to assess CD10 expression in breast fibroepithelial lesions and correlate it with recognised clinicopathological characteristics, with the goal of evaluating its potential function as a supplementary diagnostic and prognostic marker in routine surgical pathology practice.[5]

AIM AND OBJECTIVES

The specific objectives of this study were:

1. To study the expression pattern of CD10 in fibroepithelial lesions of the breast and correlate it with pathological parameters.
2. To classify fibroepithelial lesions of the breast according to the WHO 5th Edition multiparameter criteria.
3. To evaluate the diagnostic utility and prognostic significance of CD10 stromal expression across the full fibroepithelial lesion spectrum.

MATERIALS AND METHODS

Study Design and Setting

This was a cross-sectional study with both prospective and retrospective inclusion, conducted over 17 months (September 2024 to February 2026) at the Department of Pathology, SRM Medical College and Research Institute, Potheri, Chengalpattu District, Tamil Nadu.

Study Population

A total of 64 excision biopsy specimens of fibroepithelial breast lesions received between January 2018 and January 2026 were included. Cases lacking archival paraffin blocks or with insufficient material for IHC were excluded.

Clinicopathological Parameters

Parameters evaluated included patient age, tumour size, quadrant involvement, and histomorphological features assessed per WHO 5th Edition criteria: stromal atypia, stromal cellularity, stromal overgrowth, mitotic activity (per 10 HPF), and tumour border characteristics.

Histopathological Processing

All specimens were fixed in 10% neutral buffered formalin, processed to paraffin blocks, and sectioned at 4 µm for H&E staining. All slides were evaluated under light microscopy and classified according to the WHO 5th Edition multiparameter criteria.

Immunohistochemistry for CD10

IHC was performed on freshly cut sections using positively charged slides. The Peroxidase-Anti-Peroxidase (PAP) method was employed for antigen detection. The primary antibody was a monoclonal anti-CD10 antibody (clone DBS 56C6, PATHINSITU) with microwave-based antigen retrieval.
CD10 stromal expression was graded using a standardised three-tier system:

- **Grade 0 (Negative):** <10% stromal cells positive
- **Grade 1 (Weak/Mild):** 10–30% stromal cells positive
- **Grade 2 (Strong):** >30% stromal cells positive

Breast myoepithelium served as an internal positive control. Stromal cell staining was specifically assessed and distinguished from myoepithelial positivity.

Statistical Analysis

Data were analysed using SPSS software employing the chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

Demographic and Lesion Distribution

Of 64 patients (age range 14–60 years), 46.4% (n=27) were in the 14–30-year age group, 38.6% (n=23) in the 31–45-year group, and 15% (n=14) in the 46–60-year group, consistent with the established epidemiology of FELs. Lesion distribution: fibroadenoma 39.5% (n=25), benign PT 37.5% (n=24), borderline PT 10.7% (n=7), malignant PT 12.3% (n=8).

Table 1: Frequency Distribution of Study Variables

Variable	N (64)	Percentage (%)
Age 14–30 years	27	46.4
Age 31–45 years	23	38.6
Age 46–60 years	14	15.0

Fibroadenoma	25	39.5
Benign Phyllodes Tumour	24	37.5
Borderline Phyllodes Tumour	7	10.7
Malignant Phyllodes Tumour	8	12.3
CD10 Grade 0	44	68.8
CD10 Grade 1	13	20.3
CD10 Grade 2	7	10.9

Histomorphological Findings

All four WHO histomorphological parameters demonstrated statistically significant associations with lesion type ($p = 0.00$ for all).

Table 2: Association of Stromal Atypia with Fibroepithelial Lesion (N=64)

Stromal Atypia	Malignant PT	Borderline PT	Benign PT	Fibroadenoma
Present	8 (12.5%)	7 (10.9%)	5 (7.8%)	1 (1.6%)
Absent	0 (0%)	0 (0%)	19 (29.7%)	24 (37.5%)
P value	**0.00***			

Table 3: Association of Stromal Cellularity with Fibroepithelial Lesion (N=64)

Stromal Cellularity	Malignant PT	Borderline PT	Benign PT	Fibroadenoma
Present	8 (12.5%)	7 (10.9%)	17 (26.6%)	2 (3.2%)
Absent	0 (0%)	0 (0%)	7 (10.9%)	23 (35.9%)
P value	**0.00***			

Table 4: Association of Stromal Overgrowth with Fibroepithelial Lesion (N=64)

Stromal Overgrowth	Malignant PT	Borderline PT	Benign PT	Fibroadenoma
Focal/Present	8 (12.5%)	6 (9.4%)	1 (1.6%)	0 (0%)
Absent	0 (0%)	1 (1.6%)	23 (35.9%)	25 (39%)
P value	**0.00***			

Table 5: Association of Mitotic Activity with Fibroepithelial Lesion (N=64)

Mitotic Activity	Malignant PT	Borderline PT	Benign PT	Fibroadenoma
>10 HPF	5 (7.8%)	2 (3.1%)	0 (0%)	0 (0%)
<10 HPF	3 (4.7%)	5 (7.8%)	24 (37.5%)	25 (39.1%)
P value	**0.00***			

CD10 Immunohistochemical Expression

CD10 stromal expression demonstrated a highly significant association with fibroepithelial lesion grade ($p < 0.001$). The stepwise escalation of CD10 expression with tumour grade is the central finding of this study.

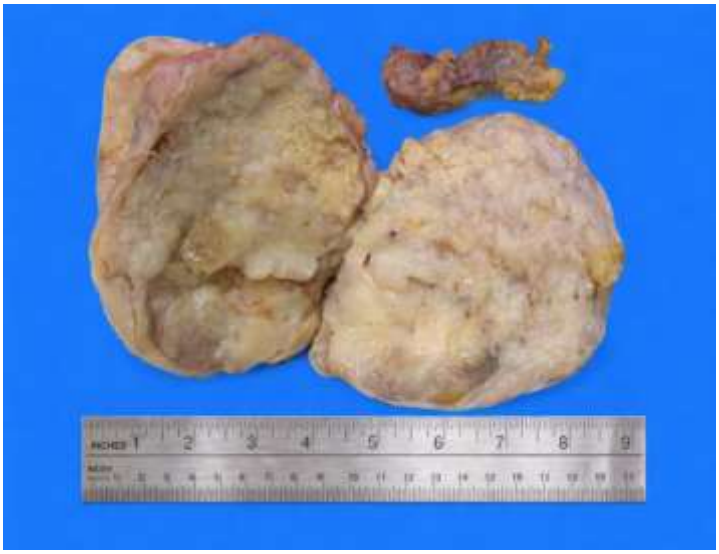

Figure 1: Malignant Phyllodes Tumour — Gross Specimen showing grey-white fleshy cut surface, irregular borders, and focal necrosis.

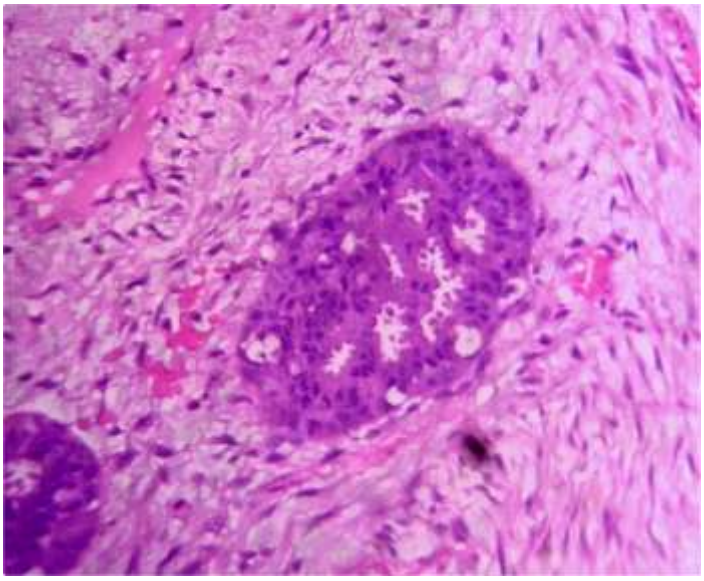

Figure 2: Fibroadenoma with Usual Ductal Hyperplasia (H&E ×400) — Epithelial proliferation within ductal lumen with streaming pattern characteristic of UDH.

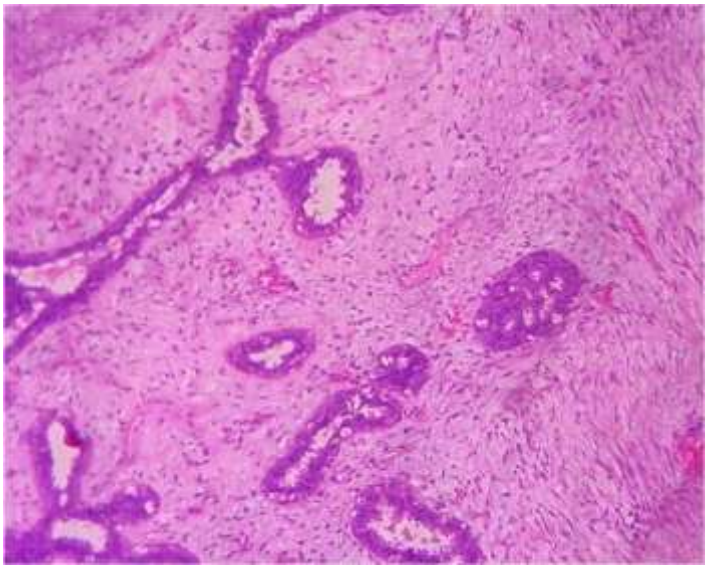

Figure 3: Fibroadenoma with UDH (H&E ×100) — Low-power view showing intracanalicular growth pattern with hypercellular ducts and fibromyxoid stroma.

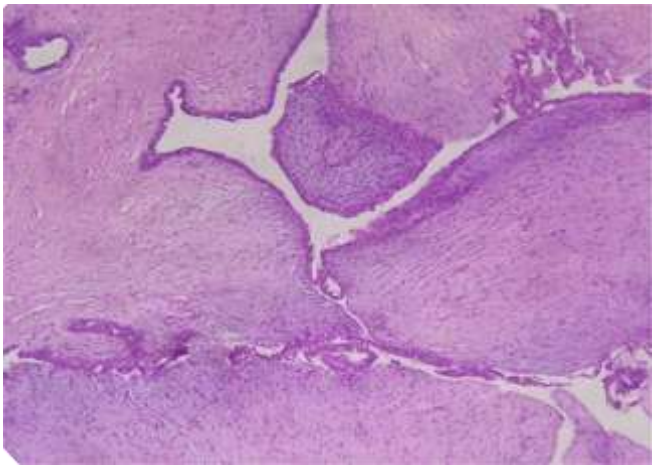

Figure 4: Benign Phyllodes Tumour (H&E ×100) — Hypercellular stroma with periglandular condensation and bland stromal spindle cells.

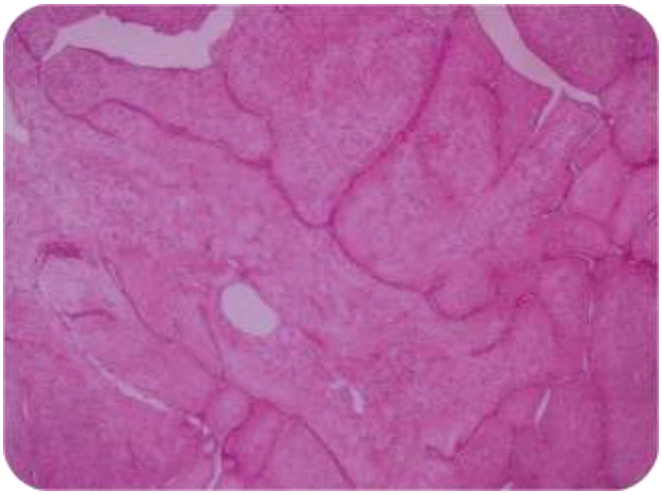

Figure 5: Malignant Phyllodes Tumour (scanner magnification) — Leaf-like stromal folds with hypercellular stroma.

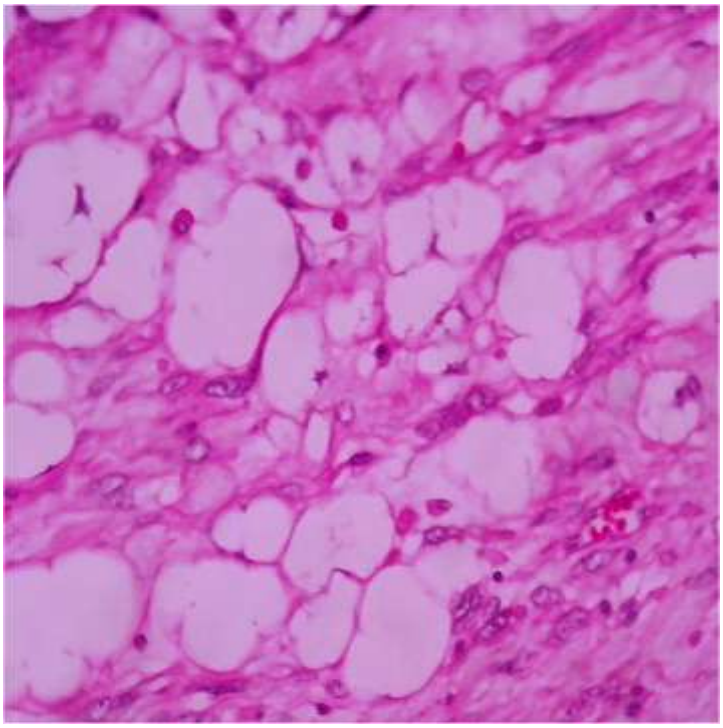

Figure 6: Malignant Phyllodes Tumour (H&E ×400) — Lipoblast-like areas in malignant stroma reflecting heterologous differentiation

Table 6: CD10 Expression by Grade in Fibroepithelial Lesions (N=64)

CD10 Grade	Malignant PT (n=8)	Borderline PT (n=7)	Benign PT (n=24)	Fibroadenoma (n=25)
Grade 0 (Negative)	0	0	19	25
Grade 1 (Mild)	1	7	5	0
Grade 2 (Strong)	7	0	0	0
P value	**<0.001***			

Key observations: (1) Grade 2 (strong) CD10 expression was confined exclusively to malignant PT (7/8; 87.5%) and was entirely absent from borderline PT, benign PT, and fibroadenoma. (2) Grade 1 expression predominated in borderline PT (7/7; 100%), reflecting intermediate stromal activation. (3) Grade 0 (negative) expression was universal in fibroadenoma (25/25; 100%) and the majority of benign PT (19/24; 79.2%). (4) Diagnostic performance of Grade 2 CD10 for malignant PT: sensitivity 87.5%, specificity 100%, positive predictive value 100%, negative predictive value 96.4%.

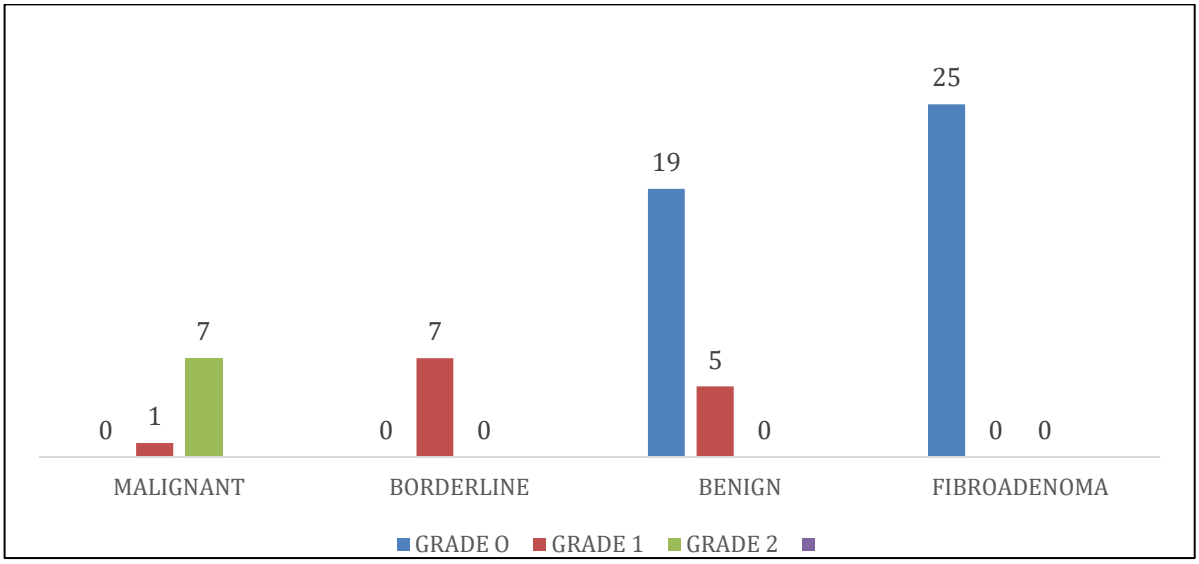

Figure 7: Expression of CD 10 in fibroepithelial lesions of the breast

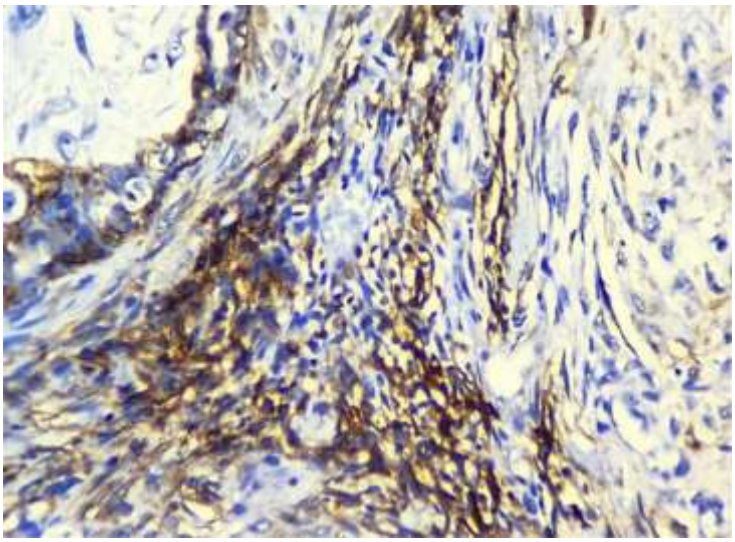

Figure 8:Malignant Phyllodes Tumour — CD10 Expression (Grade 2) IHC, ×400: Strong diffuse cytoplasmic/membranous CD10 stromal positivity (>30% stromal cells), consistent with Grade 2

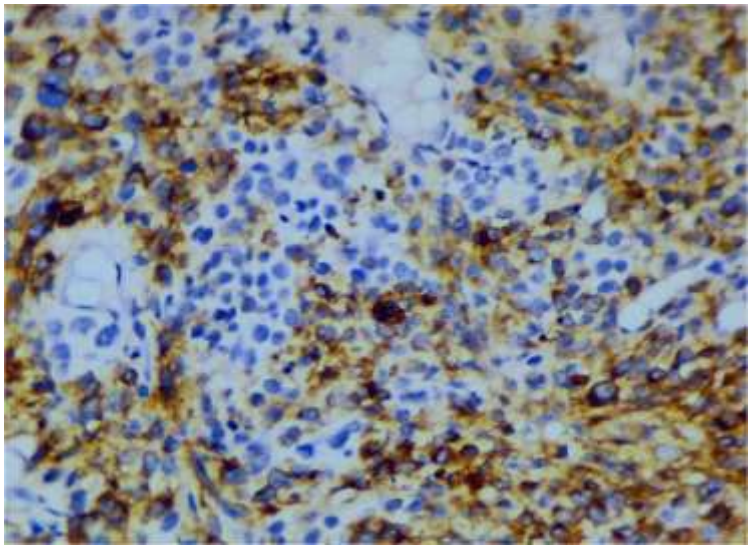

Figure 9: Malignant Phyllodes Tumour — CD10 Expression (Grade 2)IHC, ×400: Diffuse strong stromal CD 10 staining throughout tumour confirming Grade 2 expression

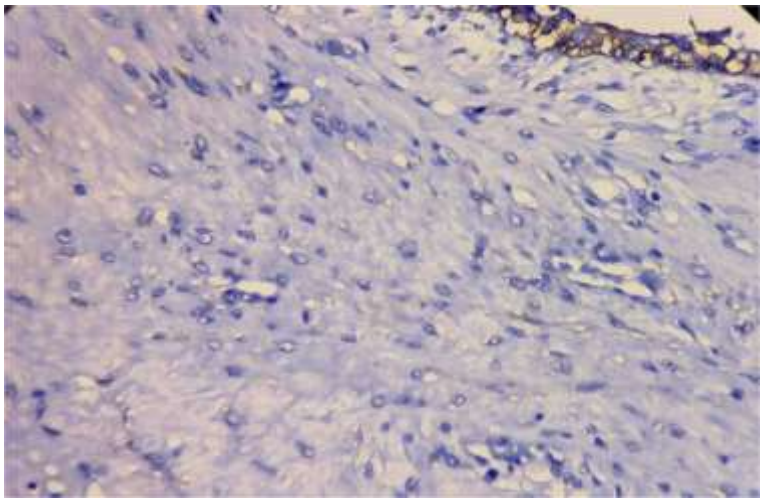

Figure 10: Borderline Phyllodes Tumour IHC X 400 — CD10 Expression (Grade 0)
IHC, ×400 — Focal CD10 positivity confined to myoepithelial layer (internal control positive); stromal staining <10%, Grade 0

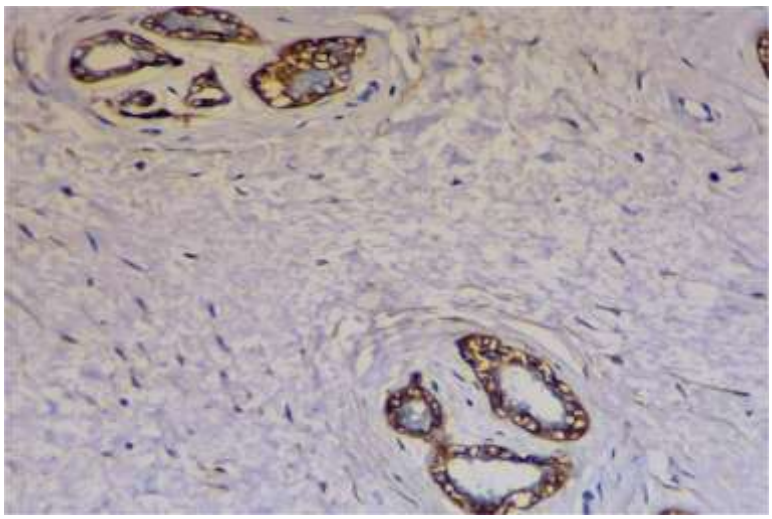

Figure 11:Fibroadenoma — CD10 Expression (Grade 0, Negative) IHC, ×400 — CD10 positivity confined to myoepithelial cells (internal control); stromal cells negative (<10%), Grade 0

DISCUSSION

Demographic Profile

The cohort of 64 FEL patients with ages ranging 14–60 years showed the largest proportion (46.4%) in the 14–30-year age group. This distribution is consistent with the established epidemiological pattern of FELs, wherein fibroadenomas

predominate in younger women and phyllodes tumours tend to present approximately one decade later. Tan et al.[6] documented fibroadenomas characteristically presenting between 15–35 years and phyllodes tumours between 40–50 years. Phyllodes tumours collectively accounted for 60.5% of all FELs in this series — a proportion higher than typically reported in Western series but consistent with data from Asian populations, as documented by Liberman et al.[7] and Sotheran et al.[8]

Histomorphological Parameters

All four WHO histomorphological grading parameters demonstrated highly statistically significant associations with lesion type ($p = 0.00$ for all four). Stromal cellularity showed the strongest association, being universally present in all malignant and borderline PT cases and in only 8% of fibroadenomas — concordant with Karim et al.[9] and Mishra et al.[10] Stromal overgrowth was confined exclusively to the phyllodes tumour category and was universal in all malignant PT cases (100%), consistent with Spitaleri et al.[11] Elevated mitotic activity (>10/10 HPF) was restricted to malignant PT (62.5%) and borderline PT (28.6%), validating the WHO's mitotic count threshold as a grade-defining criterion.

CD10 Expression - Central Findings

The most clinically significant finding of this study is that Grade 2 (strong/diffuse) CD10 stromal expression was confined exclusively to malignant PT cases (7/8; 87.5%) and was entirely absent from all other diagnostic categories. This Grade 2 CD10 specificity for malignant PT, combined with a diagnostic sensitivity of 87.5% and specificity of 100%, establishes CD10 Grade 2 as a high-value adjunct IHC marker in the differential diagnosis of fibroepithelial lesions.

The stepwise increase in CD10 expression from Grade 0 (fibroadenoma) through Grade 1 (borderline PT) to Grade 2 (malignant PT) reflects the progressive activation of stromal metallopeptidase pathways with increasing tumour grade. This biological gradient is consistent with published data from Sukumar et al.[12] ($p<0.001$ for stepwise CD10 increase), Amir and Sheikh[13] (82% positivity in malignant PT), Shehata et al.[14] (78% in malignant PT), and Bhargava et al.[15] (14.3% in fibroadenomas — virtually identical to the 14.1% Grade 1 positivity in fibroadenomas in the present study).

The Grade 1 CD10 positivity observed in 9 of 25 fibroadenoma cases (36%) reflects physiological CD10 expression in preserved myoepithelial cells, which are constitutively positive for CD10 in the normal breast. This background myoepithelial positivity does not indicate stromal activation and was correctly distinguished from the stromal CD10 positivity seen in phyllodes tumour cases. This distinction underlines the critical importance of evaluating stromal versus myoepithelial CD10 staining patterns.

The complete absence of Grade 2 CD10 expression in all borderline PT cases (0/7) in the present study, while diverging from some published series reporting 25–40% positivity in borderline PT (Nagi et al.[16]; Bhargava et al.[15]), is most plausibly explained by the small borderline PT sample size (n=7), with 95% confidence intervals for 0/7 extending to 41%.

Clinical Implications

The exclusive confinement of Grade 2 CD10 to malignant PT cases has direct translational implications. If CD10 IHC is evaluated on preoperative core needle biopsy specimens from biphasic breast lesions, a strong stromal CD10 signal may provide preoperative evidence for malignant PT, prompting primary wide excision rather than conservative local surgery. Current consensus guidelines recommend wide local excision (WLE) with minimum 1 cm clear margins for benign PT, and wider margins or mastectomy for borderline and malignant PT.[17,18] The integration of CD10 into the preoperative assessment framework, alongside established markers such as CD34 and Ki-67, represents the most evidence-based current strategy for improving surgical planning in diagnostically challenging FEL cases.

CONCLUSION

This study systematically evaluated CD10 immunohistochemical expression across a cohort of 64 fibroepithelial breast lesions spanning the full diagnostic spectrum. The key conclusions are:

1. All four WHO histomorphological grading parameters (stromal atypia, stromal cellularity, stromal overgrowth, and mitotic activity) demonstrated statistically significant associations with lesion grade ($p < 0.05$ to $p = 0.00$), validating the WHO 5th Edition multiparameter classification framework in this South Asian institutional setting.

2. CD10 showed a progressive and statistically significant stepwise increase in stromal expression from fibroadenoma through benign to malignant phyllodes tumour ($p < 0.001$), with Grade 2 (strong/diffuse) expression confined exclusively to malignant PT (87.5% of cases).

3. The diagnostic performance of Grade 2 CD10 for malignant PT (sensitivity 87.5%, specificity 100%, PPV 100%, NPV 96.4%) supports its integration as a high-specificity adjunct marker in the IHC workup of diagnostically challenging fibroepithelial lesions.

4. Large-scale prospective multicentre studies incorporating molecular validation, formal interobserver agreement analysis, and long-term clinical outcome data are warranted to refine CD10-assisted diagnostic algorithms.

REFERENCES

1. Tan PH, Ellis I, Allison K, et al. WHO Classification of Tumours of the Breast. 5th ed. Lyon: IARC; 2019.
2. Thike AA, Tan PH. Update on the histopathology of fibroepithelial tumours of the breast. Pathology. 2016;48(1):22–35.
3. Mishra RK, Agarwal G, Kapoor R, et al. Stromal CD10 expression and its correlation with histological grade in phyllodes tumour of the breast. Indian J Pathol Microbiol. 2018;61(4):506–510.

4. Wei J, Tan YT, Cai YC, et al. Expression of p53, Ki-67 and CD10 in breast phyllodes tumors and their correlation with clinicopathologic parameters. Ann Diagn Pathol. 2017;31:33–40.
5. Karim RZ, Scolyer RA, Tse GM. Pathogenic mechanisms in the progression of phyllodes tumours of the breast. Pathology. 2019;51(6):605–612.
6. Tan PH, Tse G, Lee A, Simpson JF, Hanby AM. Fibroepithelial tumours. WHO Classification of Tumours of the Breast. 4th ed. IARC Press; 2012:142–147.
7. Liberman L, Bonaccio E, Hamele-Bena D, et al. Benign and malignant phyllodes tumors: mammographic and sonographic findings. Radiology. 1996;198:121–124.
8. Sotheran W, Domjan J, Jeffrey M, Wise MH, Perry PM. Phyllodes tumours of the breast — a retrospective study. Ann R Coll Surg Engl. 2005;87:339–344.
9. Karim RZ, Gerega SK, Yang YH, et al. Phyllodes tumours of the breast: a clinicopathological analysis of 65 cases. Breast. 2009;18:165–170.
10. Mishra SP, Tiwary SK, Mishra M, Khanna AK. Phyllodes tumor of breast: a review article. ISRN Surg. 2013;2013:361469.
11. Spitaleri G, Toesca A, Botteri E, et al. Breast phyllodes tumor: a review of literature. Crit Rev Oncol Hematol. 2013;88:427–436.
12. Sukumar C, Yadav SK, Singh G, Singh S, Sarin N. Comparison of P-53, Ki-67 and CD-10 expression between fibroadenoma, benign phyllodes tumor and malignant phyllodes tumor. Ann Pathol Lab Med. 2021;8(1):A1–8.
13. Amir RA, Sheikh SS. CD10 expression in phyllodes tumors of the breast: an immunohistochemical analysis of 80 cases. Int J Clin Exp Pathol. 2016;9:4320–4328.
14. Shehata IA, Alobaid AS, Abdelzaher E. Immunohistochemical expression of CD10 and CD34 in fibroepithelial lesions. Diagn Pathol. 2017;12:24.
15. Bhargava R, Beriwal S, Dabbs DJ. Utility of immunohistochemistry in the classification of phyllodes tumors. Appl Immunohistochem Mol Morphol. 2001;9:226–231.
16. Nagi C, Guttuso TP, Polydorides A, et al. CD10 expression in spindle cell lesions of the breast. Arch Pathol Lab Med. 2005;129:593–597.
17. Chaney AW, Pollack A, McNeese MD, et al. Primary treatment of cystosarcoma phyllodes of the breast. Cancer. 2000;89:1502–1511.
18. Belkacemi Y, Bousquet G, Marsiglia H, et al. Phyllodes tumor of the breast. Int J Radiat Oncol Biol Phys. 2008;70:492–500.
19. Rosai J. Rosai and Ackerman's Surgical Pathology, 10e. Elsevier; 2011.
20. Puri V, Jain M, Mahajan G, Pujani M. Critical appraisal of stromal CD10 staining in fibroepithelial lesions of breast. J Cancer Res Ther. 2016;12(2):667–670.
21. Mohapatra S, et al. Expression of CD-10 in phyllodes tumor and its correlation with histological grade. Int J Pharm Clin Res. 2024;16(11):466–468.
22. Wang S, Xiao Y, An X, et al. A comprehensive review of the literature on CD10: its function, clinical application, and prospects. Front Pharmacol. 2024;15:1336310.
23. Turner AJ, Isaac RE, Coates D. The neprilysin (NEP) family of zinc metallopeptidases. Biochim Biophys Acta. 2001;1512:1–15.
24. Ibrahim RE, Sciotto CG, Weidner N. Stromal CD10 expression in phyllodes tumors of the breast. Ann Diagn Pathol. 2011;15(3):157–161.
25. Abe M, Miyata S, Nishimura S, et al. Malignant transformation of breast fibroadenoma to malignant phyllodes tumor. Breast Cancer. 2011;18:268–272.