

Stromal CD10 Expression in Invasive Breast Carcinoma and Its Association with Prognostic Markers

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Abstract: ***Background:** Breast carcinoma is epithelial in origin, but its progression and metastasis are strongly influenced by the stromal microenvironment. CD10 is a membrane-bound zinc-dependent metalloproteinase expressed by stromal fibroblasts and has been associated with aggressive tumor behavior. This study evaluated stromal CD10 expression in invasive breast carcinoma and its association with established clinicopathological and immunohistochemical prognostic parameters. **Methods:** A descriptive cross-sectional study was performed on 45 paraffin-embedded tissue specimens of histopathologically confirmed invasive breast carcinoma. Representative sections were evaluated for ER, PR, HER2/neu and stromal CD10 by immunohistochemistry. ER/PR were interpreted using Allred scoring, HER2/neu according to ASCO/CAP criteria, and CD10 as negative, weak positive or strong positive according to the proportion of stromal cells stained. Associations were assessed using the chi-square test, with $P < 0.05$ considered significant. **Results:** Stromal CD10 was positive in 36/45 (80%) cases, including 16 (35.5%) weakly positive and 20 (44.5%) strongly positive cases. CD10 positivity was significantly associated with higher histological grade ($P=0.037$), necrosis ($P=0.009$), PR negativity ($P=0.030$), and HER2/neu positivity ($P=0.011$). Although CD10 positivity was more frequent in ER-negative tumors (89.2%) than ER-positive tumors (59.8%), the association was not statistically significant ($P=0.135$). CD10 positivity was also frequent in tumors showing lymphovascular invasion (85.8%), but this association was not significant ($P=0.193$). **Conclusion:** Stromal CD10 expression is frequent in invasive breast carcinoma and is associated with several adverse clinicopathological features, particularly higher grade, necrosis, PR negativity and HER2/neu positivity. These findings support the potential prognostic relevance of stromal CD10 and warrant validation in larger prospective cohorts with outcome follow-up.*

Keywords: Breast carcinoma; CD10; tumor microenvironment; immunohistochemistry; progesterone receptor; HER2/neu

1. Introduction

Breast carcinoma is the most commonly diagnosed cancer among women worldwide and represents an important public health burden. According to World Health Organization (WHO), an estimated 2.3 million women were diagnosed with breast cancer in 2020, resulting in roughly 685,000 deaths globally, with total mortalities reaching 670,000 by 2022. Beyond the malignant epithelial component, the tumor microenvironment influences tumor growth, invasion, metastasis and treatment response. The stromal compartment contains fibroblasts, myofibroblasts, endothelial cells, immune cells and extracellular-matrix components that interact with tumor cells and can modify their biological behavior. [1-3]

CD10, also known as neprilysin or common acute lymphoblastic leukemia antigen, is a cell-surface zinc-dependent metalloproteinase. In breast tissue, CD10 is normally expressed by myoepithelial cells, whereas stromal expression may be detected in invasive carcinoma. Stromal CD10 has been linked to tumor-associated fibroblast activity, extracellular-matrix remodeling and aggressive tumor behavior. [4-6]

Established breast cancer biomarkers, including estrogen

receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2), are central to prognostic assessment and therapeutic selection. Several studies have investigated whether stromal CD10 expression correlates with these markers and with histological grade, necrosis, lymphovascular invasion and nodal disease. However, published results are not completely concordant, possibly reflecting tumor heterogeneity, differences in scoring and population characteristics. [7-12]

The present study was undertaken to determine the frequency of stromal CD10 expression in invasive breast carcinoma and to evaluate its association with ER, PR, HER2/neu and other clinicopathological parameters.

2. Materials and Methods

Study design and subject

A descriptive cross-sectional study was conducted in the Department of Pathology, Maharaja Agrasen Medical College, Agroha, over a one-year period. Forty-five paraffin-embedded tissue specimens from histopathologically confirmed invasive breast carcinoma were included. Eligible specimens were obtained from patients undergoing mastectomy, excisional biopsy or trucut biopsy. Cases treated with neoadjuvant chemotherapy, radiotherapy and/or

hormonal therapy and biopsies showing crushed artefacts were excluded.

Histopathological assessment

Routine hematoxylin and eosin sections were reviewed for histological type, modified Scarff-Bloom-Richardson/Nottingham grade, necrosis, lymphovascular invasion and lymph-node involvement where lymph nodes were available.

Immunohistochemistry

Representative tumor sections were subjected to immunohistochemistry for ER, PR, HER2/neu and CD10. ER and PR were interpreted using the Allred scoring system; a total score of 3–8 was considered positive. HER2/neu was interpreted according to ASCO/CAP categories; in the study protocol, scores 2+ and 3+ were categorized as positive. Stromal CD10 staining was assessed as 0 (negative, <10% stromal cells), 1 (weak positive, 10–30%) or 2 (strong positive, >30%). Fibroadenoma tissue served as the positive control and omission of primary antibody as the negative control.

Statistical analysis

Data were entered in Microsoft Excel and analyzed using SPSS version 20.0. Associations between categorical variables were evaluated using the chi-square test. A P value <0.05 was considered statistically significant.

3. Results

Forty-five cases were studied; all patients were female. The age range was reported as 22–82 years, with a mean age of 57.7 years. The largest proportion was in the fifth and sixth decades. The left breast was involved in 25 (55.6%) cases and the right breast in 20 (44.4%) cases. All tumors were reported as invasive carcinoma of no special type.

Lymph nodes were available in 20 cases, of which 17 (85%) contained metastatic deposits. Lymphovascular invasion was present in 35 (77.7%) cases and necrosis in 36 (80%) cases.

Histologically, 1 (2.2%) case was grade I, 24 (53.3%) were grade II and 20 (44.4%) were grade III. ER was positive in 17 (37.8%) and negative in 28 (62.2%) cases. PR was positive in 16 (35.5%) and negative in 29 (64.5%) cases. HER2/neu was positive in 22 (48.9%) and negative in 23 (51.1%) cases.

Stromal CD10 was negative in 9 (20%) cases, weakly positive in 16 (35.5%) and strongly positive in 20 (44.5%), giving an overall positivity rate of 80%. CD10 positivity increased with tumor grade: 0% in grade I, 79.2% in grade II and 85% in grade III. The association with grade was statistically significant ($P=0.037$).

Among tumors with necrosis, 32/36 (88.8%) showed stromal CD10 positivity compared with 4/9 (44.4%) of tumors without necrosis ($P=0.009$). Among tumors with lymphovascular invasion, 30/35 (85.8%) were CD10 positive; the association was not statistically significant ($P=0.193$).

CD10 positivity was observed in 15/17 (88.2%) ER-positive and 25/28 (89.2%) ER-negative tumors; however, the

categorical association was not statistically significant ($P=0.135$). For PR, 9/16 (56.3%) PR-positive tumors and 27/29 (93.1%) PR-negative tumors were CD10 positive, showing a significant association ($P=0.030$). For HER2/neu, 21/22 (95.5%) HER2-positive tumors and 15/23 (65.2%) HER2-negative tumors were CD10 positive ($P=0.011$).

Table 1: Clinicopathological profile of the study cohort

Variable	n (%)
Age, mean	57.7 years
Left breast	25 (55.6)
Right breast	20 (44.4)
Lymph-node deposits	17/20 (85.0)
Lymphovascular invasion	35 (77.7)
Necrosis	36 (80.0)
Grade I	1 (2.2)
Grade II	24 (53.3)
Grade III	20 (44.4)

Table 2: Immunohistochemical profile

Marker	Positive n (%)	Negative n (%)
ER	17 (37.8)	28 (62.2)
PR	16 (35.5)	29 (64.5)
HER2/neu	22 (48.9)	23 (51.1)
CD10	36 (80.0)	9 (20.0)

Table 3: Stromal CD10 expression according to clinicopathological variables

Variable	CD10 negative	CD10 weak	CD10 strong	P value
Grade I (n=1)	1	0	0	0.037
Grade II (n=24)	5	12	7	
Grade III (n=20)	3	4	13	
Necrosis present (n=36)	4	15	17	0.009
Necrosis absent (n=9)	5	1	3	
LVI present (n=35)	5	13	17	0.193
LVI absent (n=10)	4	3	3	

Table 4: Stromal CD10 expression according to ER, PR and HER2/neu

Marker status	CD10 negative	CD10 weak	CD10 strong	P value
ER positive (n=17)	6	5	6	0.135
ER negative (n=28)	3	11	14	
PR positive (n=16)	7	6	3	0.03
PR negative (n=29)	2	10	17	
HER2/neu positive (n=22)	1	10	11	0.011
HER2/neu negative (n=23)	8	6	9	

4. Discussion

The present study demonstrated stromal CD10 expression in 80% of invasive breast carcinomas, with strong staining in 44.5% and weak staining in 35.5%. This frequency is comparable with several published series, although reported positivity varies considerably. Gaffoor and Krishnamurthy reported stromal CD10 expression in 82.3% of cases, while Sumithasree et al. reported 86.5% positivity and Patil and Barate reported 80%. [7,8,10] Such variation may reflect differences in case mix, tissue sampling and interpretation of stromal staining.

A significant association was observed between increasing histological grade and stromal CD10 expression. Strong positivity was particularly frequent in grade III tumors. This

finding is concordant with studies reporting increased stromal CD10 in higher-grade breast carcinomas and supports the concept that CD10-positive stromal cells may be a marker of an activated, tumor-promoting microenvironment. [5,8-11]

Necrosis was another significant correlate. CD10 was positive in 88.8% of tumors with necrosis. Necrosis is commonly associated with biologically aggressive breast carcinoma, and the present finding suggests that stromal CD10 expression may accompany other morphological indicators of aggressive disease. Similarly, although CD10 positivity was frequent in tumors with lymphovascular invasion, the association did not reach statistical significance. This may be related to the modest sample size and intratumoral heterogeneity.

The association with hormone receptors was not uniform. ER-negative tumors showed a higher proportion of CD10 positivity than ER-positive tumors, but the difference was not statistically significant. Previous studies have produced mixed results, with some reporting a significant inverse association between ER and stromal CD10 and others finding no significant relationship. [5,7,9,11]

In contrast, PR negativity was significantly associated with stromal CD10 expression. More than 90% of PR-negative tumors were CD10 positive. This finding agrees with studies reporting higher stromal CD10 expression in PR-negative breast carcinoma, although other series have not demonstrated a significant relationship. [7,8,11,12]

HER2/neu positivity was also significantly associated with stromal CD10 expression. Almost all HER2-positive tumors in the present cohort showed stromal CD10 positivity. Gaffoor and Krishnamurthy and Sumithasree et al. similarly reported high CD10 positivity among HER2-positive tumors. [7,8] The biological relevance may relate to the association of HER2-positive tumors with proliferative and aggressive phenotypes; however, the present study does not establish a causal relationship.

The study has limitations. The sample size was small, the design was cross-sectional, and survival or treatment-response data were not available. Only representative tumor blocks were assessed, which may not capture the full heterogeneity of stromal CD10 expression. In addition, the findings should not be interpreted as proof that CD10 is an independent prognostic or predictive biomarker. Larger multicenter studies incorporating standardized scoring, molecular classification and longitudinal outcome data are needed.

5. Conclusion

Stromal CD10 expression was frequent in invasive breast carcinoma and was significantly associated with higher histological grade, tumor necrosis, PR negativity and HER2/neu positivity. Although CD10 positivity was common in ER-negative tumors and tumors with lymphovascular invasion, these associations were not statistically significant in this cohort. Stromal CD10 may therefore represent a useful adjunctive marker of an aggressive tumor microenvironment, but its independent prognostic and therapeutic value requires validation in larger prospective studies with clinical outcome

data.

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Ethics Statement

Ethical approval for the study was obtained from the Institutional Ethics Committee of Maharaja Agrasen Medical College, Agroha.

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Conflict of Interest

The authors declare no conflicts of interest.

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