Original Article

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Pathology Section

Stromal CD10 Expression in Breast Carcinoma and its Association with ER, PR, and HER2/neu using Immunohistochemistry: A Cross-sectional Study

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ABSTRACT

Introduction: Breast cancer is a common and deadly malignancy affecting women worldwide. Various immune markers, such as Estrogen Receptor (ER), Progesterone Receptor (PR), and Human Epidermal growth factor Receptor 2 (HER2/neu), are commonly used to assess prognosis. Currently, ongoing research aims to evaluate molecular pathways that contribute to invasion and metastasis. One important immunomarker under investigation is CD10, a zinc-dependent Matrix Metalloproteinase (MMP) that degrades bioactive peptides. CD10 expression in the tumour stroma has been associated with the biological aggressiveness of several epithelial malignancies, including breast carcinoma.

Aim: To analyse the association between stromal CD10 expression and different prognostic factors, such as age, histological grade, and status of ER, PR, and HER2/neu markers, in patients with breast cancer.

Materials and Methods: This institutional-based, cross-sectional study was conducted at the Department of Pathology, Nil Ratan Sircar Medical College and Hospital (NRSMC) in Kolkata, West Bengal, India over a period of one and a half years (February 2021 to July 2022). It included 120 cases of breast carcinoma diagnosed through histopathological examination of formalin fixed paraffin embedded sections, which were prepared from trucut biopsies and resection specimens referred from the Department of General Surgery, NRSMC. CD10 expression was assessed by Immunohistochemistry (IHC) in all cases and scored as negative, weak, or strong. The study examined the association between CD10 expression and the following parameters: age, histopathological grade, and the status of ER, PR, and HER2/neu markers. Data were entered into Microsoft Excel (MS) for statistical analysis. The significance of the study was determined using the Chi-square test, and data were analysed using Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM, Illinois, US). A p-value of <0.05 was considered statistically significant.

Results: The study included a total of 120 cases, with 119 cases of female breast cancer (99.16%) and one case of male breast cancer (0.84%). The mean±SD age of the patients was 54±5.038 years (range 44 to 67 years). The majority of cases 102 (85.00%) were diagnosed as Invasive Ductal Carcinoma (IDC), Not Otherwise Specified (NOS), followed by IDC-special types 18 (15.00%). CD10 expression was evaluated in all cases, and stromal CD10 positivity was observed in 79 out of 120 cases (65.80%), with 39 individuals (49.40%) showing weak positivity and 40 cases (50.60%) showing strong positivity. The remaining 41 cases (34.16%) were CD10 negative. Grade 3 cancers were predominant in this study 62 (51.66%). It was noted that CD10 stromal positivity increased with higher grade. Most of the cancers in this study were negative for ER, PR, and HER2/Neu (78, 65.00%; 84, 70.00%; and 67, 55.83%, respectively). Stromal CD10 expression showed a significant association with ER (p-value=0.00001), HER2/neu (p-value=0.000089), tumour grade (p-value=0.0012), and an insignificant association with age (p-value=0.264) and PR (p-value=0.256).

Conclusion: Therefore, CD10 expression is strongly associated with well-established prognostic markers, namely higher tumour grade, HER2/neu negativity, and ER negativity. This indicates that CD10 can not only be used as an independent marker of poor prognosis but also as a target for the development of novel therapies.

Keywords: Carcinoma, Microenvironment, Stroma, Tumour

INTRODUCTION

Breast carcinoma is one of the common malignancies among women in our country. In India, it is the leading cause of death in females [1]. Depending on invasiveness and metastatic potential, there are case-to-case variations. The prognosis of breast cancer depends on the size of the tumour, histological grade, lymph node involvement, along with some familiar immunohistochemical markers like ER, PR, HER2/neu, etc. So far, a few studies have been found in the literature regarding the association between stromal expression of CD10 in breast cancers with ER, PR, and HER2/neu [1-3]. CD10 is a special type of enzyme that acts as a stem cell regulator in the breast, preventing the unchecked proliferation of mammary stem cells. Interestingly, in invasive carcinoma of the breast, there are numerous genetic alterations that trigger either the myofibroblasts or the conversion of fibroblasts to myofibroblasts or stromal cells to express and secrete CD10 extracellularly, paving the way for the cleavage of protein components of the Extracellular Matrix (ECM) [1]. In this regard, Jana SH et al., revealed that stromal expression of CD10 was significantly associated with increasing tumour grade, increasing mitotic rate, worsening prognosis, ER negativity, and HER2/neu positivity [1].

According to Puri V et al., the stroma of breast parenchyma plays a significant role during the progression of the tumour and metastasis [2]. They found that CD10 expression correlated strongly with well-established negative prognostic markers, namely, HER2/neu and Ki67 positivity, ER/PR negativity, and higher tumour grade, indicating that CD10 can be used as an independent marker indicating poor prognosis and can be used as a target for the development of novel therapies [2].

Vo TN et al., evaluated the role of the stromal microenvironment in tumour progression, growth, cell dedifferentiation, invasion, and survival, which, in turn, leads to the identification revealed that CD10 was significantly associated with higher tumour grade, lymph node metastasis, HER2/neu positivity, ER negativity, and Ki67 positivity [3].

Newer research is increasing day by day in order to understand the complex molecular pathways that enhance local invasion and metastasis. These studies can help us understand the aggressiveness of cancer and develop drugs that target these molecules [2]. Ultimately, the main aim is to reduce morbidity and mortality and improve the quality of life for patients. In this regard, one molecular study gaining importance is the expression of CD10 in the stromal tissue of the breast. CD10, also known as Common Acute Lymphoblastic Antigen (CALLA), is a 90-110 Kd membrane-bound zinc-dependent endopeptidase (a type of MMP). It regulates the physiological action of many peptides by reducing their extracellular concentration available for receptor binding. CD10 is expressed by the myoepithelial cells of the normal breast and is commonly found in pro-B lymphoblasts, lymphoid stem cells in the bone marrow, various lymphoma subtypes, endometrial stromal sarcoma, renal cell carcinoma, etc. CD10-positive stromal cells are associated with aggressiveness in different malignancies [4,5]. Significant improvements have occurred in the management of breast cancer today, from breast conservation surgeries to neo-adjuvant chemotherapies. The typing of the tumour based on the ER, PR and HER2/neu receptor over-expression, to targeted therapy against them and the incorporation of all these into standard protocols of treatment. Mortality due to breast carcinoma is primarily attributed to metastatic disease, and a better understanding of the molecular basis of metastatic disease, with a focus on CD10, would help in the diagnosis, treatment, and prognosis of breast carcinoma.

The aim of this study was to categorise breast carcinomas as either IDC-NOS or special types and to grade IDC-NOS cases as grade 1, grade 2, or grade 3 based on histopathological examination. Another objective was to study the expression of ER, PR, and HER2/neu in these patients. Additionally, the study aims to evaluate the stromal expression of CD10 in patients diagnosed with breast carcinoma through histopathological examination.

MATERIALS AND METHODS

It was an institutional-based cross-sectional observational study conducted at the Department of Pathology, in collaboration with the Department of General Surgery of the Nil Ratan Sircar Medical College and Hospital, Kolkata, West Bengal, India. A total of 120 cases of breast carcinoma were included in the study, including one case of male breast carcinoma. The study duration was one and a half years, from February 2021 to July 2022. The study was approved by the Institutional Research and Ethics Committee (Reference Number: No/NMC/441, dated 01.02.2021). All procedures were performed in accordance with the ethical principles involving research in human subjects, and informed and written consent was obtained from each subject.

Inclusion criteria: All cases of breast carcinoma diagnosed by trucut biopsy and/or excisional biopsy, regardless of age (cases referred from the Department of General Surgery). Evaluation of CD10 expression, as well as the expression of ER, PR, and HER2/neu, in all cases of breast carcinoma after establishing the diagnosis.

Exclusion criteria: Non neoplastic diseases and benign tumours of the breast were excluded from the study.

Study Procedure

The specimens obtained were radical mastectomies, and relevant patient information such as age, menopausal status, and prior chemotherapy was recorded. The specimens were grossed and reported according to the College of American Pathologists (CAP) Protocol [1] for examining specimens from patients with invasive breast carcinoma. The specimens were fixed in 10% neutral buffered formalin. Representative sections were taken, and after proper tissue processing, they were embedded in paraffin. Sections 5 µm thick were cut from the formalin-fixed paraffin-embedded blocks and stained with Haematoxylin & Eosin (H&E) stain. Grading of breast carcinoma was performed according to the Nottingham combined histologic grade (Elston-Ellis modification of Scarf-Bloom-Richardson grading system) [1].

For IHC analysis of CD10, ER, PR, and HER2/neu, 3.0 µm paraffin sections were taken on poly-L-lysine coated slides and deparaffinised in xylene, followed by hydration in descending grades of ethanol. Antigen retrieval was performed. Sections were then incubated with power block (Biogenex, USA) for 10 minutes to reduce non specific antibody binding, followed by incubation with primary antibodies for one hour at 4ºC. The primary antibodies used were a rabbit monoclonal antibody against human ER (Dako Anti-human Erα, EP1-clone, Ready To Use [RTU]), a mouse monoclonal antibody against human PgR (Dako Anti-human PgR receptor, Pgr636-clone, RTU), a rabbit monoclonal antibody against human HER2 (BioGenex Anti-ErbB2/HER2, EP1045Y, RTU), and a mouse monoclonal antibody against human CD10 (Dako Anti-human CD10, 56C6-Clone, RTU). After three washes with Trisphosphate Buffer Solution (TBS), a secondary antibody was added and incubated for 30 minutes. After a further three washes with TBS, 3, 3'-diaminobenzidine substrate (DAB tetrahydrochloride) was applied to the sections for 10 minutes, and the sections were counterstained with haematoxylin, dehydrated with ethanol and xylene, and permanently mounted with DPX. Negative control sections were processed by omitting the primary antibody.

Positive controls were as follows:

1) Fibroadenoma for ER and PR.
2) Previously known positive cases of HER2/neu positive breast carcinoma for HER2/neu.
3) Endomyometrial stroma for CD10.

Negative controls were processed by omitting the primary antibody.

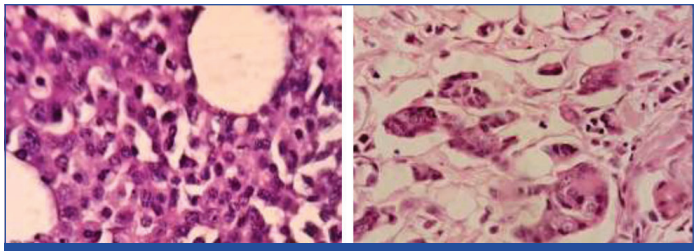
Reporting of ER, PR, and HER2/neu was done in accordance with the CAP protocol [1]. CD10 was considered negative if <10% of stromal cells were positive, weak if 10%-30% of stromal cells were positive, and strong if more than 30% of stromal cells showed cytoplasmic and membranous positivity [1].

STATISTICAL ANALYSIS

The slides were interpreted, and the collected data was entered into a Microsoft Excel (MS) sheet. For descriptive purposes, the age range and percentage were used. The significance of the study was determined using the Chi-square test with the SPSS version 23.0 (IBM, Illinois, US). Additionally, a one-way Analysis of Variance (ANOVA), including Tukey's Honestly Significant Difference (HSD), was performed to determine the association between CD10 expression and the patients' age, tumour grade, ER, PR, and HER2/neu. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 120 cases of breast carcinoma were included in the study, consisting of 119 cases of female breast cancer (99.16%) and 1 case of male breast cancer (0.84%). The mean±SD age of the patients was 54±5.038 years, ranging from 44 to 67 years, The majority of the cases (102, 85.00%) were diagnosed as IDC-NOS followed by IDC-special types 18 (15.00%), which were confirmed by H&E staining [Table/Fig-1].



[Table/Fig-1]: H&E stained section of breast carcinoma (IDC-NOS type, 400X).

Out of the 120 specimens collected, age distribution and CD10 positive and negative values is shown in [Table/Fig-2]. Statistical analysis showed that the result was not significant (p-value=0.264).

Age (years)	n (%)	CD 10 Positive cases n (%)	CD10 Negative cases n (%)	p-value
40-49	17 (14.17)	13 (76.47)	04 (23.53)	0.264 (insignificant)
50-59	87 (72.50)	58 (66.67)	29 (33.33)	
60-70	16 (13.33)	08 (50)	08 (50)	

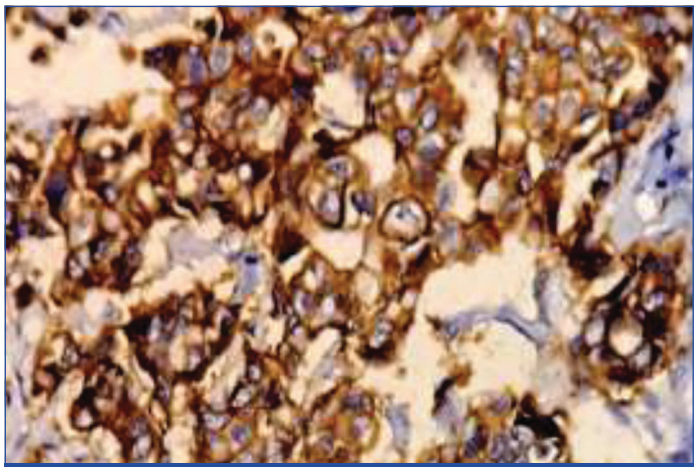
[Table/Fig-2]: Association between age and CD10 expression of breast cancer patients.
**Statistical test used: Chi-square test+ANOVA study

CD10 immunostaining was performed in all 120 cases. No stromal expression of CD10 was detected in the normal breast, and no expression of CD10 was detected in the normal ductal cells, fibroblasts, and adipose cells. The staining was scored as negative, weak, and strong [Table/Fig-3] [1].

Score	CD10 staining	n (%)
Negative	<10% stromal positive cells/core	41 (34.16)
Weak	10-30% stromal positive cells/core	39 (32.50)
Strong	>30% stromal positive cells/core	40 (33.33)

[Table/Fig-3]: CD 10 Immunostaining scoring.

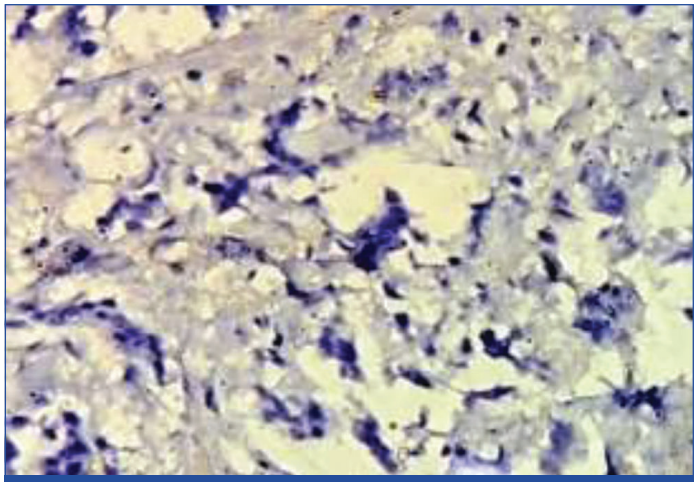
CD10 was found to be positive in 79 out of 120 cases (65.80%), with 39 individuals (49.40%) showing weak positivity and the remaining 40 cases (50.60%) showing strong positivity [Table/Fig-4], which included the single case of male breast carcinoma. The remaining 41 cases (34.16%) of breast carcinoma were CD10 negative [Table/Fig-5].



[Table/Fig-4]: Breast carcinoma showing strong CD10 positivity in the cytoplasm and cell membrane (400X).

Bloom Richardson grading was performed on all cases, and most patients belonged to grade 3 (62/120, 51.70%), followed by grade 2 (58/120, 48.30%). No grade 1 cancer was found in this study.

Out of the 58 grade 2 specimens, 32 cases (55.17%) were CD10 positive and 26 (44.88%) cases were CD10 negative. Out of the 62 grade 3 specimens, 47 cases (75.80%) were CD10 positive and 15 cases (24.19%) showed CD10 negativity. This association was



[Table/Fig-5]: Breast carcinoma showing CD10 negativity (400X).

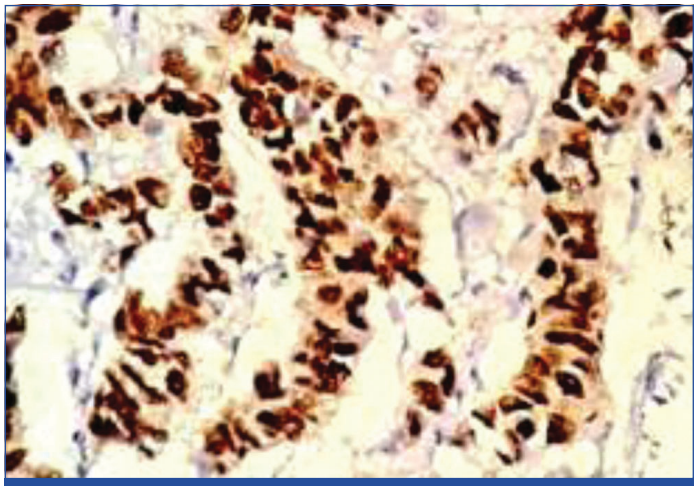
statistically significant at the p-value <0.05 level (p-value=0.0012) [Table/Fig-6].

Grade	Number of patients	CD 10+	CD10-	p-value
2	58	32	26	0.0012 Significant
3	62	47	15	

[Table/Fig-6]: Association between tumour grade and CD 10 expression of breast cancer patients.
**Statistical test used: Chi-square test+ANOVA study

The percentage positivity of CD10 increased from 55.20% in grade 2 to 75.10% in grade 3.

Out of the 120 specimens collected, 78 (65.00%) cases showed ER negativity, and 42 (35.00%) specimens showed ER positivity (37 strongly positive+05 weakly positive) [Table/Fig-7]. The single case of male breast carcinoma also showed ER negativity. Statistical analysis showed that the result was highly significant, with a p-value of 0.00001 (p-value <0.05) [Table/Fig-8].

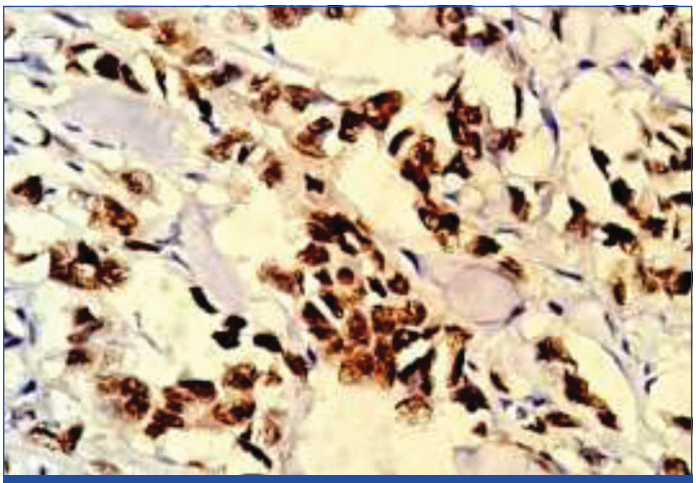


[Table/Fig-7]: Breast carcinoma showing strong ER positivity in the nucleus (400X).

ER	n (%)	CD 10+ n (%)	CD 10- n (%)	p-value
Negative (-)	78 (65)	64 (82.05)	14 (17.95)	0.00001 (Significant)
Positive (+)	42 (35)	15 (35.71)	27 (64.29)	
PR				0.256 (insignificant)
Negative (-)	84 (70)	58 (69.05)	26 (30.95)	
Positive (+)	36 (30)	21 (58.33)	15 (41.67)	
Her 2 Neu				0.000089 (significant)
Negative (-)	67 (55.83)	34 (50.75)	33 (49.25)	
Positive (+)	53 (44.17)	45 (84.91)	08 (15.09)	

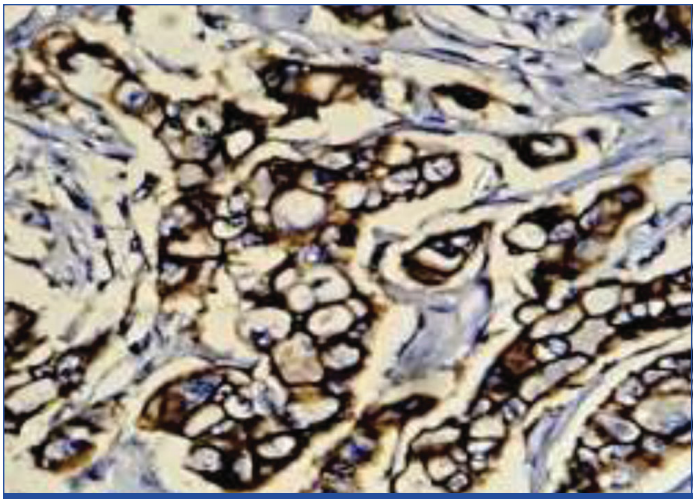
[Table/Fig-8]: Association of ER, PR, and HER2/neu expressions with CD 10 expressions in breast cancer patients.
**Statistical test used: Chi-square test +ANOVA study

Out of 120 specimens, 84 (70.00%) specimens were PR negative, and 36 (30.00%) were PR positive (30 strongly positive+06 weakly positive) [Table/Fig-9]. The single case of male breast carcinoma showed PR negativity. Statistical analysis showed that the result was not significant at the p<0.05 level (p-value=0.256) [Table/Fig-8].



[Table/Fig-9]: Breast carcinoma showing strong PR positivity in the nucleus (400X).

Among the 120 specimens collected, 67 (55.83%) showed HER2/neu negativity, and 53 (44.16%) specimens showed HER2/neu positivity (45 strongly positive+08 weakly positive) [Table/Fig-10]. The single case of male breast carcinoma showed HER2/neu negativity. Statistical analysis showed that this result was highly significant at the p-value <0.05 level (p-value=0.000089) [Table/Fig-8].



[Table/Fig-10]: Breast carcinoma showing strong HER2Neu positivity in the cell membrane and cytoplasm (400X).

DISCUSSION

Breast cancer is a major health issue worldwide, causing a significant number of deaths each year [1]. It is an epithelial malignancy that originates from the epithelial cells of the terminal duct lobular unit. The tissue microenvironment plays a crucial role in the invasion and metastasis of breast carcinoma. Interactions between normal epithelial cells and stromal cells are disrupted by various factors, including the influence of cancer cells and secreted products by tumour cells, such as MMP [6-9]. MMPs regulate the stromal microenvironment and are involved in tumour invasion and metastasis [10]. Elevated MMP activity and upregulated ECM gene expression are associated with poor prognosis [11]. MMP-2 activity is associated with high expression of ER, while low levels of tissue inhibitor of MMPs (TIMP-1) are associated with high expression of PR [10]. MMPs also play a role in the production of cytokines, such as Transforming Growth Factor-β (TGF-β), which promote angiogenesis, tumour progression, and immunosuppression [10]. MMPs can cleave matrix components, generating chemotactic and migratory factors for tumour cells, as well as important growth factors [12]. The prognostic role of CD10, a novel stromal marker and a type of MMP, is less studied in the literature. CD10 is a zinc-dependent endopeptidase with a molecular weight of 90-110 Kd, attached to the cytoplasmic membrane. It regulates the physiological actions of bioactive peptides by reducing their extracellular concentration available for receptor binding [13].

CD10 plays a role in differentiating Early Common Progenitors (ECP) into Luminal Epithelial Progenitor (LEPPs) or Myoepithelial Progenitor (MEP). These progenitors give rise to luminal and myoepithelial cells, respectively. Therefore, CD10 acts as a stem cell regulator in the breast through its enzymatic functions, aided by β1-integrin, to prevent uncontrolled proliferation of mammary stem cells [14].

In this study, no significant association was observed between CD10 stromal expression and age (p-value=0.264) [Table/Fig-2], which was consistent with the findings of Dhande AN et al., (n=60, p-value=0.89) [15]. CD10 was positive in 79 out of 120 cases (65.80%), with 39 individuals (49.40%) showing weak positivity and the remaining 40 cases (50.60%) showing strong CD10 positivity [Table/Fig-3], including the single case of male breast carcinoma. The remaining 41 cases (34.16%) of breast carcinoma were CD10 negative. These findings were in line with the study by Dhande AN et al., where stromal CD10 positivity was seen in 78.30% of cases (n=60), with 32 (53.30%) cases strongly positive, 15 (25.00%) cases weakly positive, and 13 (21.70%) cases negative [15]. The positivity rates for ER, PR, and HER2 were 31.70%, 33.30%, and 65.00%, respectively. Puri V et al., also reported 40 CD10 positive cases (80.00%) out of a total of 50 cases [2]. According to the study by Maguer-Satta V et al., the progression of Ductal Carcinoma In Situ (DCIS) to invasive breast carcinoma occurs due to the disappearance of CD10 from myoepithelial cells and the basement membrane [13]. This mechanism suggests that during the early stages of carcinogenesis, there are oncogenic modulations of stem cells that lead to high CD10 enzyme activities in mesenchymal stem cells and/or proliferated and transformed epithelial cancer stem cells [13]. As a result there are accumulations of local CD10-cleaved peptides that inhibit epithelial cell differentiation and maintain cancer stem cells [13]. That's why the CD10 positive stromal cells surrounding tumour cells is associated with a high histological grade of the tumour. CD10 also plays a role in tumour cell migration via the PI3K-FAK pathway and can block the normal function of the tumour suppressor gene PTEN, stimulating angiogenesis, cell survival, and inhibiting apoptosis [1]. This explains the increased expression of CD10 in carcinomas with a high histological grade and subsequently higher NPI (undifferentiated carcinomas) [13]. In this study, there were more grade 3 cancers (n=62) than grade 2 cancers (n=58), and high-grade cancer showed higher CD10 positivity and a significant statistical association (p-value=0.0012) [Table/Fig-6], consistent with the studies by Puri V et al., (n=50, p-value=0.000), Makretsov NA et al., (n=438, p-value=0.01), and Dhande AN et al., (n=60, p-value=0.01) [2,5,15]. However, Iwaya K et al., (n=110, p-value=0.25) did not find any statistically significant relationship between tumour grade and CD10 expression [16]. CD10 also cleaves Fibroblast Growth Factor-2 (FGF-2), inducing endothelial cell growth and angiogenesis through the Akt pathway [13].

In this study, ER-negative cancer was predominant (N=78) (65.00%) and showed a higher CD10 positivity compared to ER-positive

cancers [Table/Fig-8] (N=42) (35.00%). With increasing CD10 positivity, the proportion of ER-negative cases increased from 35.00% to 65.00%, and this association was highly statistically significant (p-value <0.05) (p-value=0.00001) [Table/Fig-8], similar to the findings of Makretsov NA et al., (n=438, p-value=0.002) [5]. However, Puri V et al., (n=50, p-value=0.32) and Dhande AN et al., (n=60, p-value=0.35) did not find a statistically significant association between ER status and stromal CD10 expression [2,15].

The explanation for the association between ER negativity and CD10 positivity is similar to the explanation provided by Maguer-Satta V et al., regarding the high-grade nature of the cancers in their study [13]. Targeted therapy for ER-positive cancer typically involves the use of anti-oestrogenic drugs like tamoxifen, which has a good prognosis [1]. ER negativity indicates a higher proliferative index and poorly differentiated types, as observed in present study (78 ER-negative cases and 62 poorly differentiated cases) [2].

In present study, most cases were PR-negative (n=84) (70.00%) compared to PR-positive (n=36) (30.00%) [Table/Fig-8]. Among the negative cases, most of them showed CD10 positivity (N=58) (69.05%). However, no significant association was found between PR status and CD10 (p-value=0.256) [Table/Fig-8], similar to the findings of Puri V et al., (n=50, p-value=0.21), Makretsov NA et al., (n=438, p-value=0.23), and Dhande AN et al., (n=60, p-value=0.43) [2,5,15]. PR acts as an adjuvant marker, predicting response along with ER. If both ER and PR are positive, a response rate of 60-70% is observed, compared to 40% with only ER positivity and less than 10% if both are negative [2].

There is upregulation of CD10 function in mesenchymal stem cells following PTEN loss in progenitor cells, which can lead to the production and accumulation of CD10-cleaved peptides in the stroma. These peptides are responsible for epithelial undifferentiation. CD10-positive breast cancer is commonly HER2 positive, according to Desmedt C et al., [17]. CD10 positivity has poor prognostic value and is associated with a poor response to therapy [16]. Desmedt C et al., and Cabioglu N et al., offer a possible explanation that increased expression of CXCL12, a specific protein, is seen following stromal expression of CD10, leading to transactivation of HER2/neu and ultimately increased expression of HER2/neu [17,18]. Predictive response and survival are dependent on this marker to some extent. HER2/neu positivity is associated with a favourable response to anthracyclines but a poor response to alkylating agents [13]. Targeted therapy against HER2/neu with trastuzumab shows a 20% response rate [14]. In the present study, there were more HER2/neu -negative cancers (n=67) (55.83%) than HER2/neu -positive cancers (n=53) (44.17%), and among the negative cases, most were CD10 positive (N=34) (50.74%). This finding showed a significant association between CD10 positivity and HER2/neu (p-value=0.000089) [Table/Fig-8], similar to the studies by Puri V et al., (n=50, p-value=0.000) and Dhande AN et al., (n=60, p-value=0.001) [2,15]. However, Makretsov NA et al., (n=438, p-value=0.23) did not find a statistically significant association in this regard [5].

Currently, there is ongoing research on the development of drugs that can modify the tumour microenvironment/stroma to have a better drug delivery system with minimal toxicity and maximum efficacy, not directed against the cancer epithelial cells as currently being used. This new concept has led to the development of peptide prodrugs cleavable by peptidases present in the tumour environment. Since CD10 is a type of metalloprotease, it can cleave peptide prodrugs (CPI-0004Na), such as N-succinyl-alanyl-L-isoleucyl-L-alanyl-leucyl-Dox. After proteolytic cleavage, leucyl-Dox is generated, which can easily enter cancer cells and generate intracellular Dox with higher potency than Dox alone. The cytotoxicity of CPI-0004Na is inhibited by phosphoramidon, a known inhibitor of CD10 enzymatic activity [3]. Therefore, routine immunostaining of CD10 could help in deciding the line of treatment for breast cancer cases.

Limitation(s)

1) In this study, HER2/neu was assessed only by the IHC method. Evaluation by Fluorescent In Situ Hybridisation (FISH) technique should have been done, especially for the equivocal cases with HER2/neu expression 2+, but could not be proceeded due to limited resources.
2) The association of CD10 with tumour size, tumour staging, and axillary lymph node status was not studied.
3) Since this study was single-centred in Kolkata, the results cannot be generalised to all regions.

CONCLUSION(S)

All these findings indicate that the stromal microenvironment plays an important role in the carcinogenesis of breast cancer as well as for prognostic purposes. High-grade breast cancers, ER-negative, and Her2/neu negative cancers are commonly associated with increased CD10 positivity and carry a poor prognosis. Therefore, as an independent prognostic marker, CD10 should be included in routine histopathology reports. Lastly, CD10 could potentially serve as a target for newer drug development.

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