



## Stromal Expression of CD 10 in Infiltrating Duct Carcinoma Breast and Its Correlation with ER, PR, and HER 2 NEU

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### Abstract

**Background:** Breast carcinoma is an epithelial malignancy and it is hormone dependent mostly. Breast carcinoma is the most frequently diagnosed malignancy among the women of all ages worldwide. In 2012, breast carcinoma was found to be the most common malignancy amongst women in India, way ahead of cervical cancer<sup>1,2</sup>. In the year 2020 the diagnosed cases of breast carcinoma among women were 22,61,419<sup>3</sup>. Recently it has been documented that tumor progression is promoted by interaction of tumor cells with their microenvironment especially stromal cells. This understanding has brought forth new potential candidate markers like CD10. The aim of this study is to understand the Association of Stromal CD10 expression with ER, PR, HER-2/NEU, in IDC breast.

**Methods:** Fifty one cases of IDC, breast received as a specimen of modified radical mastectomy in Deptt of Pathology. IHC was done for ER, PR, Her-2/neu and CD10.

**Results:** Out of fifty one cases of IDC, stromal CD 10 positivity was seen in 84.3% of cases. ER and PR positivity was seen in 60.8% and 54.9% respectively. However HER-2/neu overexpression was observed only in 21.4% cases.

**Conclusions:** In majority of the cases of IDC, the tumor cells were positive for ER and PR. Her-2/neu was positive (score 3+) in only 21.6% of cases of IDC. Although majority (84.3%) of the cases of IDC showed stromal CD10 positivity, no statistical significant correlation was observed between stromal CD 10 expression and other IHC markers i.e ER, PR and HER-2/NEU in the cases of IDC breast in our study.

### Introduction

Breast carcinoma is a major health problem worldwide as well as in India. It is the most common cancer among women accounting for 18% of malignancies in females<sup>4</sup>. Many variables have been shown to correlate with prognosis of patients.

IHC has become an important determinant of prognosis and theranostics. Estrogen receptor (ER) is the most important prognostic and predictive marker for breast cancer. Similarly, analysis of Progesterone receptor (PR) expression is generally reported along with ER expression. Most studies have reported that expression of

estrogen and progesterone receptors indicates favorable response to hormonal therapy and good prognosis<sup>5</sup>. Another receptor is Human epidermal growth factor receptor 2 (HER-2/neu) which is an independent prognostic marker of clinical outcome in patients with metastasis deposits of IDC in lymph nodes<sup>6</sup>. Hence, new markers are being evaluated to understand their role in cancer progression.

Stromal contribution to cancer progression is important as it is related to the tumor invasion and also indicates about metastatic potential of tumors<sup>7</sup>. Stroma also contributes in carcinoma progression as it may promote tumor cell growth, de-differentiation, invasion and ectopic survival of tumor cells<sup>8</sup>. This is why the novel stromal markers are now being studied as potential prognostic markers in invasive breast cancer<sup>9</sup>. Amongst these markers one of the stromal marker is CD10, also known as Nephilysin or Common Acute Lymphoblastic/Lymphoma Antigen (CALLA). It is a 90 to 110-kDa cell surface zinc dependent metalloproteinase<sup>8,10</sup>. Commonly CD10 is expressed in myoepithelial cells of the human breast, lymphoid stem cells, pro-B lymphoblast, mature neutrophils<sup>11</sup>. It is also expressed abnormally in stroma of invasive breast carcinoma, in various subtypes of lymphomas, renal cell carcinoma and endometrial stromal sarcoma<sup>11</sup>. Expression of CD10 in the stroma of invasive breast carcinoma is associated with biological aggressiveness of tumor, higher tumor grade and decreased patient survival. Routine chemotherapeutic drugs target the epithelial cells while stromal cells are spared which could be responsible for recurrences. Therefore CD10 may prove to be a potential target for the development of novel therapies.

This study was conducted to evaluate the correlation between

Stromal CD 10 expression and other IHC marker (ER , PR , Her2/neu) in patients of Infiltrating duct carcinoma of breast.

## Material and Methods

The present study was conducted in the Department of Pathology and Department of Surgery, Indira Gandhi Medical College, Shimla. Specimens (Modified Radical Mastectomy) received were all the biopsy proven cases of Infiltrating ductal carcinoma of breast w. e. f May 01,2018 to April 30,2020.

Following observations were made:

1. ER,PR,HER-2/NEU status
2. CD10 stromal status

This study comprised of total 51 cases of IDC, breast. Benign lesions breast, carcinoma breast other than IDC and Post neo-adjuvant chemotherapy specimens were not included.

The specimens were fixed in 10% neutral buffer formalin for not less than 6 hours and not more than 72 hours<sup>12</sup>. Gross findings of the specimen were recorded.

Tissue sections were processed in the fully automated tissue processor of Leica model 6025<sup>TM</sup>.

## Immunohistochemical Staining

Staining was done as per the staining protocol in fully automated IHC BioGenex<sup>TM</sup> Xmatrix autoimmunostainer using the mouse monoclonal antibody against CD10.

IHC for ER, PR, Her2-neu were done as per the staining protocol in fully automated Biogenex<sup>TM</sup> using monoclonal rabbit antibody.

## Controls

CD10 expression in myoepithelial cells of accompanying normal breast tissue was used as the positive control<sup>13,14,15</sup>.

Known cases of IDC positive for ER, PR and HER-2/neu (score 3+) were used as external controls for the corresponding test IHC markers. Benign breast tissue in the mastectomy specimen accompanying the IDC were also used as internal controls for specificity of immunoreactions for ER and PR

Results of CD10 stromal staining were correlated with:

- ER status
- PR status
- HER-2/NEU overexpression

### Results

Allred scoring (Table no. 1) was used to evaluate Estrogen Receptor and Progesterone Receptor status. In our study, 31/51 (60.8%) cases were ER positive, and 20/51(39.2%) were ER negative. PR status showed 28/51(54.9%) cases were PR positive, and 23/51 (45.1%) were PR negative. ER -, PR + were observed in 4 /51(7.8%) cases of IDC.

Out of 51cases of IDC, 11(21.6%) cases were Her-2/neu positive with a score of 3+ and 40 (78.43%) cases were negative for Her2-neu. (assessed as per table no 2).

CD 10 stromal positivity was assessed as described in table no 3.

Benign glands with myoepithelial cells were taken as internal control (Figure 1). CD 10 stromal positivity was observed in 43/51(84.3%) However strong positivity (Figure 2) for CD10 was observed in 28 cases comprising 55% of total cases followed by weak positivity (Figure 3) in 15/51(29.4%) cases of IDC.

### Expression of Stromal CD10 in Infiltrating Duct Carcinoma breast and its Correlation with ER, PR, HER-2/Neu (Table no. 4)

Majority of ER positive cases, 26/31 (83.9%) showed positivity for CD10.

Out of all ER negative cases, a higher percentage of cases 17 (85%) showed positivity for CD10

### Table no. 2

#### For HER-2/neu:

Membranous staining was taken as positive and the following grading scheme was followed:

Staining Pattern	Score	Her-2/neu overexpression
No staining	0	Negative
Weak or incomplete membrane staining in any population of cells.	1	Negative
Complete membrane staining in <10% cells.	2	Negative
Uniform intense membrane staining in >10% cells	3+	Positive

For the present study, a score of 3+ was considered as positive immunostaining for HER-2/neu.

Majority of PR positive cases 24/28 (85.7%) showed positivity for CD10.

Out of all PR negative cases a higher percentage of cases 19 (82.6%) showed positivity for CD10

Majority of HER2-NEU positive cases 10/11 (90.9%) showed positivity for CD10.

Majority of HER2-NEU negative cases 33/40 (82.5%) showed positivity for CD10

CD10 was found to have no correlation with ER , PR and Her-2/neu in our study. P values were also not statistically significant.

### Interpretation of IHC

#### Table no. 1

The results were observed and interpreted as follows:

#### For ER and PR

Allred scoring was done

Nuclear staining was taken as positive

**Allred Score:** Total score 8

Staining Pattern	Proportion score 0-5
No cell stained	0
1/100 cell stained	1
1/10 cells stained	2
1/5 cells stained	3
2/3 cells stained	4
All cells stained	5

Staining Pattern	Intensity Score
No staining	0
Weak staining	1
Moderate staining	2
Strong staining	3

**Total score** = Proportion score + Intensity score.

Total Score of more than 3 or more than 3 was taken as positive.

**Table no. 3**  
**CD 10 Scoring**

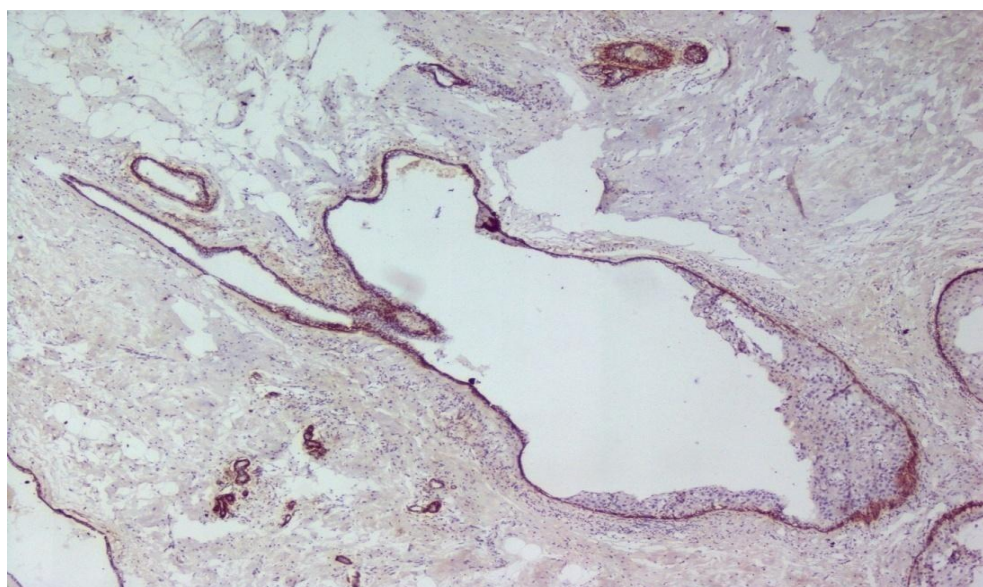
Membranous staining was taken as positive and the following grading scheme was followed:

CD 10 Staining Pattern	Score
<10% stromal positive cells	Negative
10-30% stromal positive cells	Weak positive
>30% stromal positive cells	Strong positive

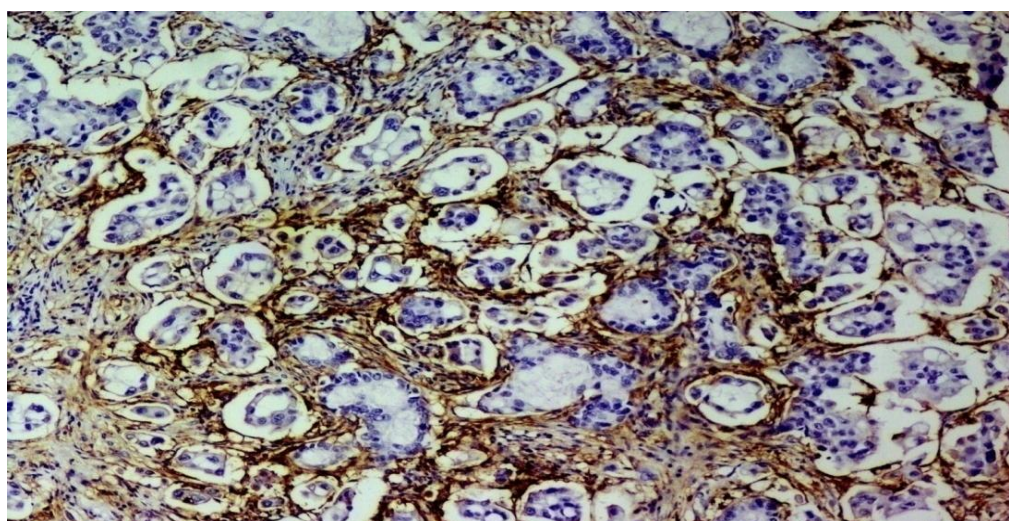
Table no 4 shows the correlation of IHC markers.

**Table 4:** Correlation of IHC Markers

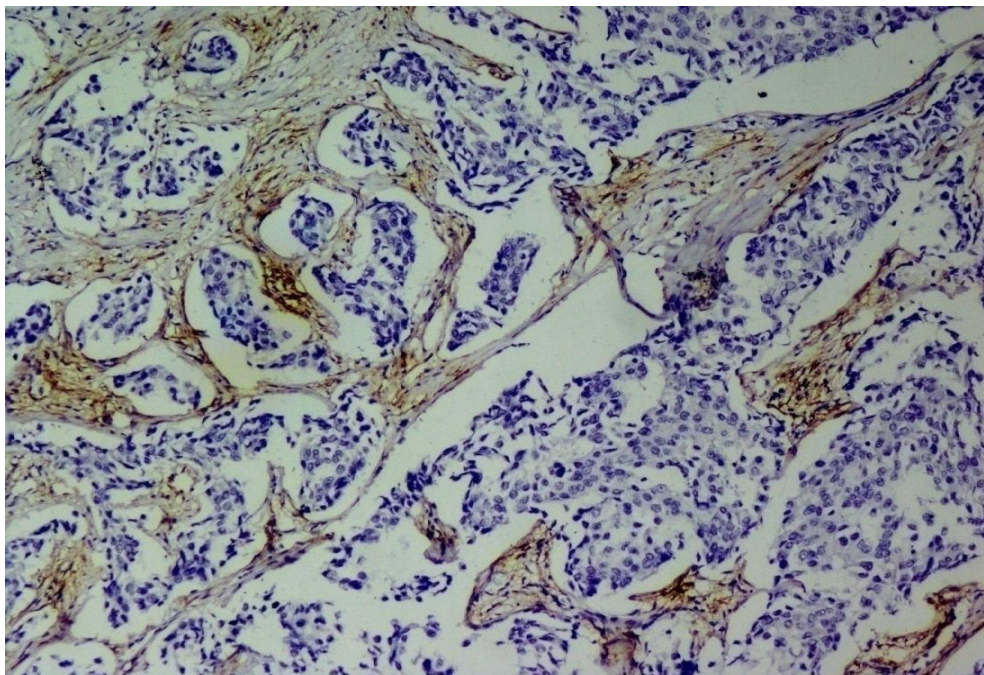
RECEPTORS	CD10 NEGATIVE	CD10 WEAK POSITIVE	CD10 STRONG POSITIVE	TOTAL
ER positive	5	9	17	31
ER negative	3	6	11	20
PR positive	4	7	17	28
PR negative	4	8	11	23
Her2-neu postivity	1	2	8	11
Her2-neu negative	7	12	21	40



**Figure 1:** CD 10 expression in myoepithelial cells in benign breast glands (x200)



**Figure 2:** Strong stromal CD 10 positivity in Infiltrating Duct Carcinoma, breast (x200)



**Figure 3:** Weak stromal CD 10 positivity in Infiltrating Duct Carcinoma , breast (x200)

### Discussion

CD 10 also known as Common Acute Lymphoblastic Leukemia Antigen (CALLA), is a 90-110 kilo dalton cell surface, membrane bound, zinc dependent matrix metalloproteinase. It is lost in case of IDC with disappearance of myoepithelial cells.<sup>16,17</sup>

Among various studies in the past it was concluded that CD10 expression by the stromal cells surrounding the breast tumor was correlated with poor prognosis<sup>4,16,17</sup>.

In the present study majority of the cases i. e 84.3% showed positivity for CD10 which is value intermediate between those observed by Puri V et al and Dhande AN et al. However a study done in 2017 by Azza et al observed strong positivity only in 16.7% of cases.

In ER positive cases in IDC, CD10 positivity varies widely. However only in studies by Taghizadeh K et al<sup>16</sup> and Azza M et al<sup>4</sup> there was positive correlation between CD 10 expression and ER positivity<sup>16,17</sup>. In our study we also found 83.8 % of ER positive cases of IDC to be CD 10 positive. But this correlation has not been statistically significant. Puri V<sup>18</sup> et al and Mohammadzadeh F<sup>19</sup> et al had also observed no statically significant correlation between ER

positivity and CD 10 expression.

Similarly we found CD10 positivity in 85.2% of PR positive cases of IDC but no statistically significant correlation was found between PR positivity and CD 10 expression with a p value of 0.7. This is in accordance with the study by Mohammadzadeh F et al.

A strong correlation between CD10 stromal positivity and Her-2/neu status was observed in the study by Puri V et al. A statistical significant correlation had been found only with a p value of 0.000. In comparison to that our study, had showed CD10 positivity in 91% of Her-2/neu positive cases. But statistically the correlation was not found to be significant similar to other studies in the literature<sup>19</sup>.

We failed to establish any statistical significant correlation between stromal CD10 status and other markers (ER, PR and Her-2/neu). These discrepancies in the results can be due to following limitations.

### Limitations

- Sample size was less probably due to the COVID -19 pandemic.
- Equivocal Her-2/neu scores i.e 2+ were not further evaluated by FISH.

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