Original Research Article

Stromal expression of cd10 in invasive breast carcinoma and its correlation with ER, PR, HER2, NEU and KI67

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Abstract

Aim & Objective: To evaluate and correlate CD10 expression with ER, PR, HER2-Neu & Ki 67 index CD 10 expression in breast malignancies. **Methodology :** The descriptive study was undertaken in the Upgraded Department of Pathology, Osmania medical college, Hyderabad from Dec 2015 to June 2017.Total of 50 cases of invasive breast carcinomas in females were included in the study. Of these 45 cases comprised of invasive carcinoma of no special type (NST) followed by 3 cases of invasive lobular carcinoma and the remaining 2 cases were medullary carcinoma and tubular carcinoma respectively. **Results:** In the present study, the age group included were from 35-80 years with the average age being 51years and highest incidence of breast carcinoma was seen in fourth decade. Routine processing and Haematoxylin and Eosin staining of the received specimens were done followed by immunohistochemical analysis with CD10, ER, PR, HER2neu & Ki 67 antibody was done. In the present study, cytoplasmic and membranous staining of >30% of the stromal cells around the tumor cells were taken as CD 10 stromal positivity. CD 10 stromal positivity was correlated with expression of ER, PR, HER2 neu and Ki 67 index. Present study showed a slight lower negative correlation of CD10 stromal expression with ER expression which showed a higher correlation in other studies. This discordance can be attributed to the number of cases andduration of study and also to the more ER positive prevalence in the study group. Present study did not show any correlation with CD 10 expression and PR status which was much similar to the observations in other studies. Present study showed good correlation between stromal CD 10 expression and well established negative prognostic marker that is, HER2 neu overexpression and high Ki 67 index. **Conclusion:** To conclude, stroma plays a important role in progression, hormonal expression and response to chemotherapy in breast cancer

Keywords: CD10, Her2. Ki67 index, Medullay Carcinoma, stromal positivity, Immunohistochemical

Introduction

Breast carcinoma is the most common malignancy and the leading cause of cancer death in women and 12% of the breast cancer occur in women between 20-34 yrs. In India, breast cancer is next to cancer of the cervix among women. It is estimated that approximately 80,000 cases occur annually. Breast cancer survival is linked to early detection, timely appropriate treatment and genetic predisposition. The prognosis is related to a variety of clinical, pathologic and molecular features which include p histologic type, grade, tumor size and lymph node metastases[1,2]. Immunohistochemistry (IHC) has an important role in the assessment of prognostic and predictive factors in invasive breast cancer today. Prognostic factors are defined as clinical, pathological and biological features associated with the innate aggressiveness of untreated invasive breast cancers and, if adverse enough, usually result in the use of adjuvant therapies following surgery. Although a large number of potentially useful factors have been identified, only four are currently used in routine clinical practice and their assessment is mandatory. These include the estrogen receptor (ER), the progesterone receptor (PR) and the Human epidermal receptor (Her2) oncogene/ oncoprotein and ki 67 index. IHC is the most commonly used method of assessing these factors, although fluorescent in situ hybridization (FISH) also has a prominentrole in Her2 testing[3,4].

Estrogen and progesterone receptors (ER, PR) and Her-2/neu have with increasing importance influenced the management of the malignant lesions. With an established positive correlation of ER and PR with the degree of tumor differentiation, determination of ER and PR status on biopsy specimens prior to therapeutic intervention is advocated as standard practice[1].Estrogen is an important mitogen exerting its activity by binding to its receptor (ER) and is found in 50-80% of breast cancers. Endocrine treatments are assigned to antagonize the effects of estrogen. Therapeutic hormones like tamoxifen competitively blocks ER, thus antagonizing transcriptional activation of genes required for tumor growth. The presence of hormone receptors (ER and PR) in the tumor tissue correlates well with the response to hormone therapy and chemotherapy. Studies have shown that 55-60% of women with ER-positive tumors respond to additive or ablative hormone therapy, compared with about 8% of women with ER-negative tumors. Tumors that are better differentiated are more likely to be ER and PR positive and have a relatively better prognosis[1,3].PR is a surrogate marker of a functional ER and is valuable in predicting the behavior of breast carcinoma. It is expressed in 60-70% invasive breast carcinomas with higher positivity in older age and postmenopausal women. Loss of PR by tumor cells is associated with a worse prognosis. Patients with larger tumors, poorly differentiated morphology, increased number of axillary lymph node metastases and higher stage tumors have more chance of an ER and PR negative status[1,3].Her-2/neu also known as C-erb B2 (Her-2), is a proto-oncogene located on chromosome 17. It is amplified and the protein is overexpressed in 15-25% of breast carcinoma and is associated with poor prognosis. Her-2/neu encodes a transmembrane

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glycoprotein with tyrosine kinase activity known as p185 proto-oncogene and belongs to the family of epidermal growth factor receptors. Over- expression of Her-2/neu is a good predictor of response to Trastuzumab (Herceptin), but not a positive predictor of response to chemotherapy or overall survival[5].Ki-67 is a nuclear protein being associated with cellular proliferation and was originally identified by Gerdes et al[6] in the early 1980s, using a mouse monoclonal antibody directed against a nuclear antigen from a Hodgkin's lymphoma-descended cell line. It was shown that Ki-67 nuclear antigen is expressed in certain phases of the cell cycle namely S, G1, G2, and M phases, but is non-existing in G0[7,8,9]. By means of immuno-staining with the monoclonal antibody Ki-67, it is possible to assess thegrowth fraction of neoplastic cell population

CD10 is a cell surface zinc-dependent metalloproteinase. Matrix metalloproteinases are a family of metallopeptidases that cleave the protein components of extracellular matrix and thereby play a central role in tissue remodelling.

Aims and objectives

1. To evaluate CD 10 expression in breast malignancies
2. To correlate CD10 expression with ER, PR, HER2-Neu & Ki 67 index
3. To compare the present study with literature

Materials and methods

This study was done in the Department of Pathology at OSMANIA general hospital, Hyderabad on 50 mastectomy specimens from Dec 2015 to June 2017

Inclusion criteria

- This study included mastectomy specimens and core needle biopsy specimens

Exclusion criteria

- All benign cases were excluded

Method

The specimens were fixed in 10% neutral buffered formalin. They were examined grossly according to the standard guidelines, with special emphasis on the tumor size and lymph node status of the lesion. The specimens were grossed and sections were taken from representative sites. These sections were then processed in tissue processor and embedded in paraffin wax. Four to five micron thickness sections were prepared from the corresponding paraffin blocks, one on albumin coated slide for Haematoxylin and Eosin (H&E) staining and the other on poly-L-lysine coated slide for immuno-histochemical staining.

Histologic grade /Total points

Grade 1 (well differentiated) 3-5 points Grade 2 (moderately differentiated) 6-7points Grade 3 (poorly differentiated) 8-9 points

The kits for ER, PR, Her-2/neu immunohistochemical staining was obtained from Biogenics Company. The staining was done according to the manufacturer's protocol.

Method of Immunohistochemical staining

- Immunohistochemical staining was done using peroxidase-antiperoxidase method according to the protocol described by Biogenics.
- 4 microns thin sections are taken on poly - lysine coated slides.
- Deparaffinization is done by dipping the slides in 3 changes of xylene 10 min each, followed by 3 changes of absolute alcohol for 5 min each.
- The slides are washed under running tap water for 15 minutes.
- Endogenous peroxidase activity is quenched by covering the slides with 0.5%H2O2 for 30 minutes.
- Wash under running tap water for 15 minutes.
- Antigen retrieval done by microwave with Tris buffer -1.2lg of TrisHydroxymethyl methylamine and 3.75 mg of EDTA in 100ml distilled water.
- Slides are washed with TBS buffer (9.6 g of TrisHydroxymethyl methylamineand 8.6 g of NaCl in 100 ml distilled water) pH 7.4-7.6.
- Incubated with Primary antibody (ER, PR, Her-2 neu) which is ready to use, atroom temperature in a humidifier chamber for 60 minutes.
- The sections were washed again with TBS buffer (9,6 g of TrisHydroxymethyl methylamine and 8.6 g of NaCl in 1000 ml distilled water) pH 7.4-7.6.
- Incubated with secondary antibody in a humidifier chamber for 30 minutes.
- The sections were again washed with TBS buffer.
- Chromogen DAB for 20 minutes for detection of enzymatic activity.
- Counter staining was done with Haematoxylin.
- Dehydrate in alcohol and xylene.
- Mount with DPX.
- The ER, PR and Her2, ki 67, CD 10 antibodies were ready to use vials. The following antibody clones were used.
- ER - 1D5 Mouse monoclonal antibody in PBS carrier protein and preservative.
- PR - PR88 Mouse monoclonal antibody in PBS carrier protein and preservative.
- Her2 - EP1045Y Rabbit monoclonal antibody in PBS carrier protein and preservative.
- Ki 67 rabbit polyclonal antibody immunohistochemical staining were obtained from BIOCARE (polyclonal rabbit Anti-Human Ki67 IgG) .prediluted 1:200 wasused
- CD 10 clone 56C6 DAKO –monoclonal mouse anti human antibody

ER, PR, Ki 67 is a nuclear stain while Her-2 neu & CD 10 is cytoplasmic and membranous stain. The slides were then examined under microscope to determine the ER, PR and HER-2/neu reactivity pattern. The reactivity pattern was scored according to the guidelines of ASCO/CAP

Observation and results

This study was conducted between Dec 2015 to June 2017.A total of 50 malignantbreast cancers were studied.

In this study, the ER, PR, Her-2/neu and ki 67 was assessed and correlated with CD 10 expression. The observations –age, right/left involvement, histological type were tabulated

Age and location

The mean age was around 51 years, range being 35-80 years. The youngest subject in this study was 35years while the eldest was 80years.The common age group range being 41-50years.The right breast was more commonly involved.

Histomorphological type

Infiltrating ductal carcinoma, no special type comprised majority of our study population

CD 10 staining

No stromal expression was detected in the normal breast although the non neoplastic myoepithelial cells, whenever present,served as a built-in positive control for CD 10 .Sections of fibroadenoma were put up as control There was no expression of CD10 in normal ductal cells, fibroblasts and adipose cells .

The CD10 staining was scored as negative, weak, and strong as described in table 2

Table 1: Age distribution of breast carcinoma

AGE INCIDENCE		
AGE	NO OF CASES	PERCENTAGE
35-40years	0 2	4%
41-50years	35	70%
51-60years	10	20%
61-70 years	02	4%
71-80years	01	2%

Immunohistochemistry results and correlation

Table 2: Correlation of CD 10 with ER

CD 10	ER negative	ER positive	Total
Negative	05(10%)	10(20%)	15
Weak	1(2%)	15(30%)	16
Positive	4(8%)	15(30%)	19
Total	10	40	50

P valve is not statistically significant

Table 3: Correlation of CD 10 with PR

CD 10	PR negative	PR positive	Total
Negative	10	05	15
Positive	15	20	35
Total	25	25	50

Table 4: Correlation of CD 10 with HER2-neu

Her2-neu	CD10 Negative	CD10 Strong positive	CD 10 weakpositive	Total
Negative	10	4	5	19
Score 2+	1	3	2	6
Score 3+	4	12	9	25
Total	15	19	16	50

Table 5: Correlation of CD 10 with Ki 67

CD 10	Ki 67 low	Ki 67 high	Total
Negative	6	9	15
Weak positive	6	10	16
Strong positive	3	16	19
Total	15	35	50

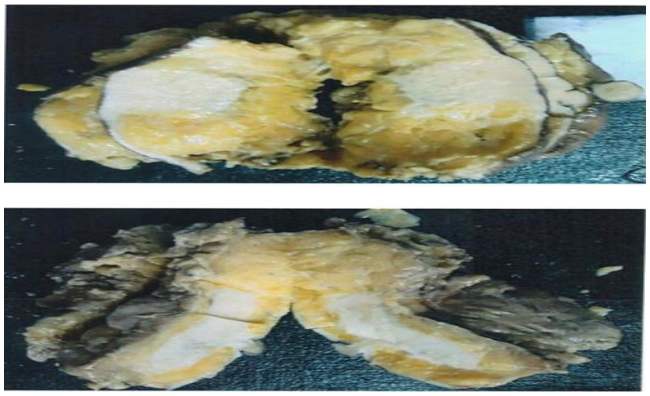

Fig 1: Gross picture of mastectomy specimens

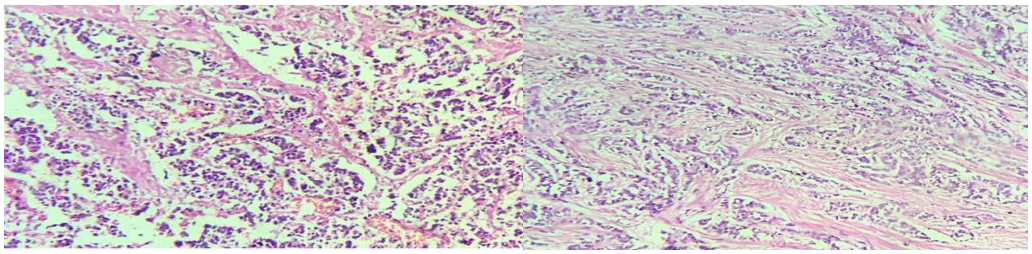

Fig 2:H&E:40X, Invasive carcinoma NST
Fig 3:H&E:40X, Invasive lobular carcinoma

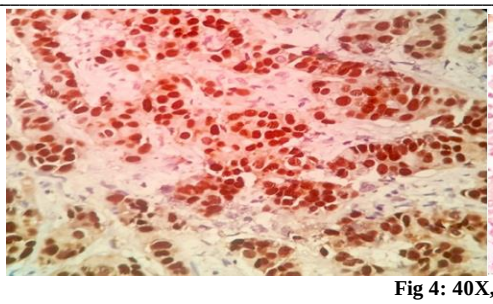
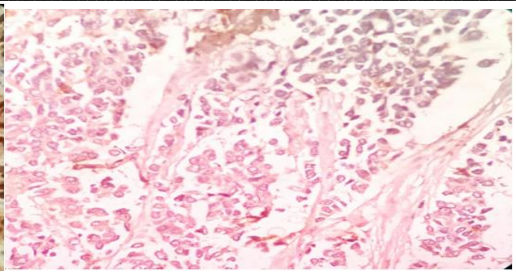

Fig 4: 40X, ER positive
Fig 5: 40X, ER negative

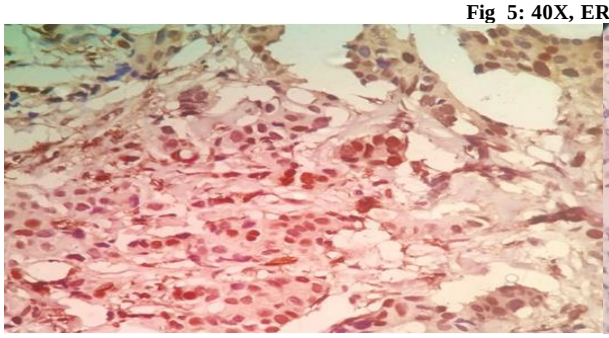
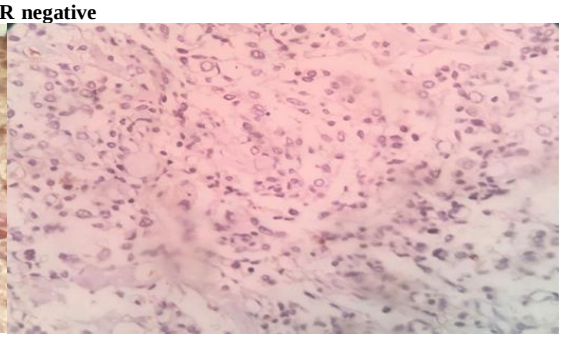

Fig 6: 40X, PR positive
Fig 7:40X PR negative

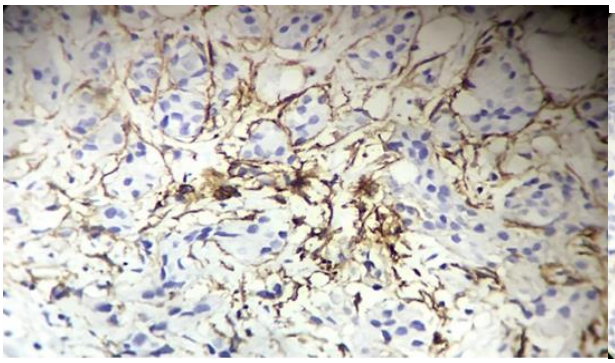
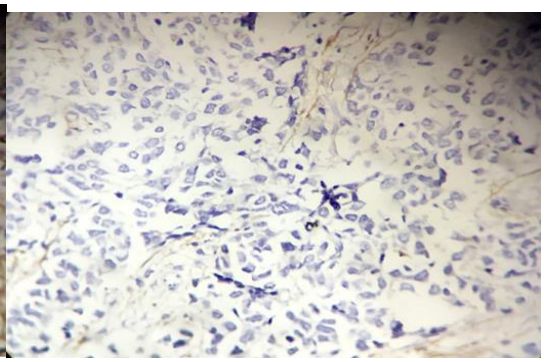

Fig 8:40X, CD10 positivity
Fig 9: 40X, CD10 negative

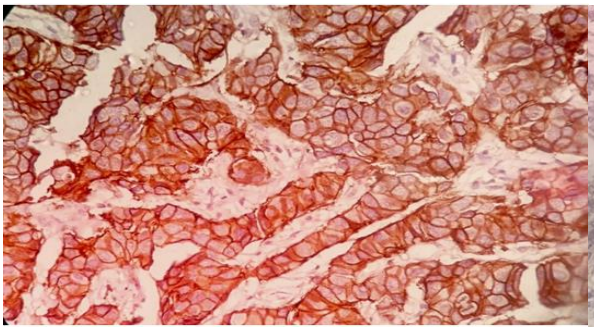
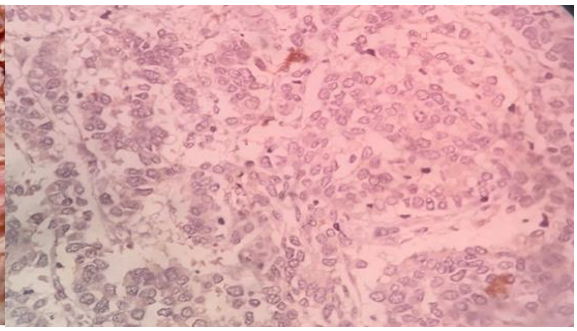

Fig 10:40X, HER2/neu expression
Fig 11: 40X, HER2/neu negative

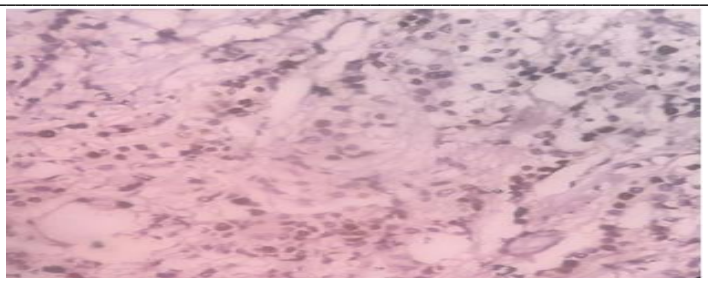

Fig 12: 10X Ki 67 proliferative index

Discussion

Immunohistochemistry (IHC) plays a pivotal role in the assessment of prognostic and predictive factors in invasive breast cancer. Estrogen, progesterone receptors (ER, PR) Her-2 neu, Ki67 have with increasing importance influenced the management of the malignant lesions.

CD 10 is a membrane bound zinc-dependent endopeptidase (a type of MMP), which degrades many bioactive peptides .CD 10 expression in tumor stroma is associated with biological aggressiveness of many epithelial malignancies Therefore, this study was done to correlate ER,PR,Her-2 neu, and Ki 67 expression with CD 10 .

There is a continuous and bilateral molecular crosstalk between normal epithelial cells and cells of the stromal compartment and it is disrupted by several factors secreted by the tumor cells themselves or by the stromal cells under the influence of cancer cells[9,10,11]. Matrix metalloproteinase (MMPs) helps in defining the role of stromal microenvironment in tumor invasion and metastasis[13]. High expression of estrogen receptors is associated with enhanced activity of MMP-2 and high expression of progesterone receptors is correlated with low TIMP-1 protein (tissue inhibitor of MMPs) levels[12].

TGF-beta (tissue growth factor –beta) a cytokine produced by carcinoma associated fibroblasts promotes tumorigenesis and stromal cell functions associated with angiogenesis, mmunosuppression and tumor progression[41]. MMPs play an important role in the formation of active TGF –beta (tissue growth factor –beta –a cytokine produced by carcinoma associated fibroblasts)

Products obtained after the cleavage of matrix components like collagen, laminin ,IGFs I & II have chemotactic activity for tumor cells, and thus help in tumor cell migration through matrix[14].

CD 10 –its role in breast cancer progression

In breast carcinoma, CD 10 expression has apparently contradictory findings, on one hand its disappearance from myoepithelial cells and basement membrane leads to the progression of DCIS to invasive carcinoma and on the other hand, CD 10expression by the stromal cells surrounding the breast tumor is correlated with poor prognosis, oestrogen receptor negativity and high grade[15].

Maguer –satta et al (2011)[16] proposed a model which explains that an early oncogenic events in stem cells modulate the expression of CD-10 enzyme in the altered cells or even in the neighboring cellular environment. A resultant decrease in CD-10 –enzymatic function after the neoplastic transformation of early common progenitors (ECF) or progenitors (p) could induce an accumulation of unprocessed peptides in the stem cell microenvironment ,resulting in their lineage commitment and malignant proliferation .this is the proposed basis for progression of DCIS into invasive malignancy with CD10 loss

CD10 and stromal signature

A recent gene expression profiling study of breast carcinoma stroma identified two clinically significant types of stromal signatures in breast cancer, namely, solitary fibrous tumor type and desmoid type fibromatosis type which were associated with poor outcome[17]. CD 10 expression was associated preferentially with desmoid –type fibromatosis stromal signature ,and possibly ,contributed to a number of negative outcomes in invasive carcinoma of the breast with this type of stromal signatures .

Further studies have shown that, CD10 positive stroma signatures includes among others, genes involved in matrix remodeling (MMP11, MMP13 and COL10A1) and genes related to osteoblast differentiation (periostin). This stromal signature is present in DCIS but absent in invasive carcinoma –proving the fact that progression from in situ to invasive breast cancer upon the tumor microenvironment.

Age distribution of breast cancers

In the present study age ranged from 35-80years, average age was 51years at the time of diagnosis of breast carcinoma. Incidence being high in the fourth decade.

According to B.V.Anuradha Devi et al[18] most of the patients belonged to 41-50 years of age group which correlated well with our study group

Vandana puri et al[19] also had a similar study group with the mean age group being48 years and the range being 30-80years

Table 6: Age distribution in various study groups

Study and year	Age
B.V.Anuradha Devi at al (2016)[18]	41-50years
Vandana Puri et al (2011)[19]	30-80years
Present study (2017)	30-80years

Number of cases

The present study incorporated 50 cases (n=100), whereas 59 ,50 and 70 cases werethe number of cases in the studies done by B.V. Anuradha Devi (2016)[18], Vandana puri et al (2011)[19] and Sayantan H.Jana et al (2014)[20] respectively .

Table 7 : Number of cases and duration of study invarious study groups

Study group and year	No of cases	Duration of study
Vandana (2011)[19] Puri et al	50	16 months
Sayantan H Jana et al (2014)[20]	70	20 months
Present study (2017)	50	18months

Maximum number of samples were noted in the study done by Sayantan H Jana et al[20] followed in close succession by B.V.Anuradha Devi et al[18] and same number of cases were taken by Vandana puri et al[19] and the present study. This slight variation inthe study population may be due to the differences in the duration of the study period.

Histopathological-type of breast carcinoma

In the present study, among the 50 cases studied -45 (90%) cases comprised invasive carcinoma of no special type(NST) followed by three cases of invasive lobular carcinoma (6%)and the remaining two cases were medullary carcinoma (2%) and tubular carcinoma (2%)respectively. Bloom and Richardson grading was performed on all cases

Vandana puri et al[19] studied 50 cases of breast carcinoma among which majority belonged to invasive ductal carcinoma, no special type (47/50: 94%) followed by two cases (4%) of mucinous carcinoma and one case (2%) of infiltrating ductal carcinoma with extensive in situ component

Anuradha Devi et al[18] reported 59 cases of breast carcinoma, out of which 55 cases were invasive carcinoma, no special type (93%), followed by three cases of medullary carcinoma (5%) and one case of lobular carcinoma (2%).

TABLE 8 : Number of cases with predominant type ofbreast carcinoma

Study and Year	No of cases	Invasive carcinoma ofno special type(NST)	Other types
Vandana et al[19](2011)	50	47(94%)	3
B.V.Anuradha et al[18] (2016)	59	55(93%)	4

Invasive carcinoma of no special type (NST) comprised majority of our study population which correlated well with other study groups of Vandana Puri et al[19] and B.V.Anuradha Devi et al[18]

Stromal CD 10 expression

In the present study, CD 10 immunostaining was done in all the 50 cases. No stromal expression was detected in the normal breast although the non-neoplastic myoepithelial cells, whenever present, served as a built –in positive control for CD 10. CD 10 was found to be positive in 70% (35 cases) of the cases out of which 21 (60%) cases showed strong positivity for CD 10 and 14 cases (40%) showed weak immunoreactivity for stromal CD10 expression

The study conducted by B.V.Anuradha Devi et al[18] (2016) over samples from 59 cases for CD10 immuno expression in breast carcinoma 81%(48 cases) showed positive ,out of which 54% (32 cases) showed weak immunoreactivity and 27%(16 cases) showed strong immunoreactivity

CD 10 immuno expression studied by Vandana et al[19] in breast carcinoma was found to be positive in 80% of cases (40/50) out of which 40% (16 cases) showed weak immunoreactivity whereas strong positivity was observed in 60% (24 cases) which included one case of IDC with extensive in situ component. Myoepithelial cells werestrong CD10 positive in extensive in situ component and the same case showed fociof stromal CD10 positivity indicating invasion.

TABLE 9: Various studies showing cd 10 stromal expression

Study group and year	No.of cases inthe study	CD10 Strong positive	CD 10 weakpositivity	CD 10 Negativity
B.V.Anuradha et al[18] (2016)	59	16 (27%)	32 (54%)	11(19%)
Vandana et al[19] (2011)	50	24(48%)	16(32%)	10(20%)

The CD 10 expression of the present study (2017) is 42% and is almost similar to the values observed by Vandana et al (2011)[19] but little higher when compared to the study done by B.V.Anuradha et al (2016)[18]

Makrestov et al[21] found stromal CD10 expression in 79% of invasive breast carcinomas that is close to the frequency observed in the present study which is around 70%

CD 10 Expression and its correlation with ER

Makretsov et al (2007)[21] showed significant correlation between strong CD 10 staining and ER negativity in a study done over 21 years which accumulated a total of 438 cases

Vandana et al (2011)[19] also showed good negative correlation with ER which was around 87% of 50 cases. The study had 35 ER negative cases with 60% of these cases showing negative correlation with strong CD 10 positivity

The present study showed 8% cases with negative correlation between ER negative and CD 10 positive tumors. The low percentage in the study is attributed to the overall ER negative cases seen in the study i.e 10/50 .Therefore 40% of the ER negative tumors in this study showed negative correlation with CD 10 strong positivity

Sayantan H.Jana et al[20] showed good negative correlation with strong CD 10 expression and ER negativity .The study was done on a total of 70 cases out of which 37 cases showed ER negativity .Out of these 37 cases ,26 cases(70%) showedCD 10 positivity .

This slight discordance of CD 10 positivity and ER negativity of our study with other studies may be attributed to the sample size and to the overall low ER negative cases in the study.

TABLE 10: Various studies showing correlation of CD 10 expression and ER status

Study Groupand Year	Number fcases studied	Total numberof ER negative cases	Cases with ER Negative With CD10 Positive
Vandanapuri et al[19] (2011)	50	35	21(60%)
Sayantan. H Jana et al[20] (2014)	70	37	26(70%)
Present Study (2017)	50	10	8(40%)

CD 10 expression and its correlation with PR

Makretsov et al[21]. found no statistical significance between stromal CD10expression and PR status Similar findings were seen by the study done by Vandana puri et al[19].Sayantan .H. Jana et al[20] showed 50 PR negative cases out of which 27 cases (54%) showed CD 10 positivity but it was not statistically significant.In the present study, 25 cases showed PR negativity out of which 15 cases (60%) were CD 10 Positive. PR expression did not show any significance in the above studies and even thepresent study.

Vanadana et al[19] found a negative correlation between stromal CD10 expression on one hand and ER and PR status on the other.

Makrestov et al[21] and Kim et al showed a statistically significant negative correlation between stromal CD10 expression and ER status .However, Makrestov et al[21] found no statistically significant correlation between stromal CD10 expression and PR status .

CD 10 Expression and its correlation with HER2-NEU

Vandana puri et al[19] showed strong positive correlation between CD 10 stromal expression and Her2-neu expression. Out of the 40 cases which showed CD 10 positivity 28 cases (70%) were HER 2-Neu positive.In the present study, there were 35 positive CD10 cases out of which 26 cases (74%)showed Her2-neu overexpression.

Sayantan .H Jana et al[20] studied 70 cases. Out of which 34 cases were CD 10 positive among which 16 cases (47%) were Her2 neu positive

Sayantan .H Jana et al[20] proposed that CD 10 positive stromal signature also carried prognostic value in the HER2 positive breast

cancer, and is associated with a poor response to therapy.
In this study, stromal CD10 expression and Her2 neu status was not significantly correlated. While the same observation was reported by Makretsov et al[21]However, the exact tumor-epithelium interactions explaining the specific clinical relevance of the stroma in HER2 positive breast cancer needs further research

Table 11: Various studies showing correlation between CD10 expression and Her 2 neu over expression

Study group and year	No of cases	CD 10 Positive cases	CD 10 Positive with HER2 NEU Positivity
Vandana Puri et al[19] (2011)	50	40	28(70%)
Sayantan H Jana et al [20] (2014)	70	34	16(47%)
Present study(2017)	50	35	26 (74%)

CD 10 expression and its correlation with Ki-67 index

The study by Vandana puri et al[19] (2011) is the only one that has investigated the relationship between stromal CD10 expression and Ki 67 index in breast carcinoma.According to the results of this study, there is a statistically significant positive correlation between stromal CD10 expression and Ki67 index.According to the study done by Vandana puri et al[19] out of the 50 cases studied 47 cases showed ki67 positivity (94%).
In the present study out of the 50 cases studied 35 cases were showing high ki 67index

Table 12: Various studies showing Ki 67 positivity

Study group and year	Number of cases	Ki 67 Cases Positive
Vandana et al[19] (2011)	50	47(94%)
Present study (2017)	50	35(70%)

According to Vandana et al[19] out of the 47 cases which showed Ki 67 positive 39 cases were CD 10 stromal positive. In the present study, among the 35 cases which showed high Ki 67 index 26 casesshowed stromal CD 10 positivity.

Table 13: Comparison of CD 10 and Ki 67 IN THE STUDYGROUPS

Study group and year	KI 67 Positive cases	CD 10 Positive cases
Vandana et al[19] (2011)	47(94%)	39(82%)
Present study (2017)	35(70%)	26(74%)

The observation of Vandana et al[19] concerning the positive correlation between stromal CD10 expression and Ki 67 index in breast carcinoma supports the potential role of CD10 positive stromal cells in inducing carcinoma cells to proceed through the cell cycle.
Explaining the association between CD 10 positivity and hormonal status of breast cancer is difficult. Most studies have shown that CD 10 positivity to be associated with ER negativity and Her2 neu positivity.
In the present study, CD10 positivity was associated with the Her2 neu subtype while negativity with luminal subtypes. Molecular studies have shown that in breast cancer, basal like (ER-/PR-/Her2-) and Her2E (ER+/HER2+) subtype are more associated with PTEN loss, than luminal type (ER+). CD 10 positivity in basal and HER2E subtype can be explained by assuming that in spite of high CD10 expression, defective signaling by CD10 in cancer cells leads to defective PTEN function, causingcancer progression and angiogenesis
Also, the initial oncogenic events in progenitor cells that cause PTEN loss may upregulate CD10 function in mesenchymal stem cells, leading to accumulation of CD10 cleaved peptides that prevent epithelial differentiation. That both CD10 positivity and PTEN loss are found more in the basal and HER2 subtype and absent in the luminal subtype raises the suspicion that there is some relation between CD10 and PTEN in causing breast cancer. However further research is required to see the exact role played by CD10 and PTEN in breast carcinoma and their influence on the hormonal signature of tumor cells.

Limitations of the study

The following were the limitations of the present study which could be worked uponin the future:

- The nodal status and recurrences of the tumor at the same site or at distant sites could be studied and compared
- The tumor size and grade could be compared with the CD 10 stromal positivity
- The duration of study and number of cases could be increased which would have increased the number of ER negative cases and increased the significance of correlation between CD 10 stromal expression and ER status

Conclusions

- Breast masses specially in the young age group are source of anxiety for the patients and surgeons because of the increasing prevalence of carcinoma and their increasing incidence of metastasis at the time of diagnosis
- To conclude, stroma plays a important role in progression, hormonal expression and response to chemotherapy in breast cancer
- CD 10, a novel stromal marker plays an important role in normal breast involution and its development and progression to breast carcinoma
- Stromal expression of CD10 correlates with HER2 neu over expression and high ki 67 which are bad prognostic markers
- CD 10 can be used as a independent marker indicating poor prognosis and can be used as target for development of novel therapies
- Thus, core needle biopsy should be done as a preoperative workup and along with the traditional panel of markers, CD 10 can be used up routinely as a prognostic marker in all breast cancer patients.
- Treatments targeted to decrease the role of CD10 positive stromal component in aggressive behavior of breast carcinoma may be promising in this regard

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