STROMAL EXPRESSION OF CD10 IN INVASIVE BREAST CARCINOMA AND ITS CORRELATION WITH KNOWN PROGNOSTIC MARKERS

Swayamprava Pradhan[1], Chandan Bajad[2], Debi Prasad Mishra[3], Anusuya Dash[4], Sulata Chowdhary[5], Samir Kumar Behera[6], Manoj Kumar Patro[7], Atanu Kumar Bal[8]

[1]Professor and HOD, Department of Pathology, SLN Medical College, Koraput, Odisha.
[2]Postgraduate Student, MKCG Medical College, Berhampur, Odisha.
[3]Professor and HOD, Department of Pathology, MKCG Medical College, Berhampur, Odisha.
[4]Associate Professor, Department of Pathology, MKCG Medical College, Berhampur, Odisha.
[5]Assistant Professor, Department of Pathology, MKCG Medical College, Berhampur, Odisha.
[6]Associate Professor, Department of Pathology, SLN Medical College, Koraput, Odisha.
[7]Assistant Professor, Department of Pathology, MKCG Medical College, Berhampur, Odisha.
[8]Assistant Professor, Department of Pathology, MKCG Medical College, Berhampur, Odisha.

ABSTRACT

BACKGROUND

Breast carcinoma is the most common non-skin malignancy in women. More recently, it has been suggested that extracellular proteinase regulates growth factors and cytokines that might contribute to tumour progression. Since CD10 is a cell surface metalloproteinase which inactivates various biologically active peptides, it might facilitate cancer cell invasion and/or metastasis.

MATERIALS AND METHODS

48 cases of Invasive Breast Carcinomas were taken up for the study along with 5 cases of benign tumour as a control group (fibro adenoma and phyllodes). Statistical Analysis: For all statistical data chi**-**square test was applied using IBM SPSS Statistics 20.

RESULTS

CD10 was found to be positive in 89% (n=43) cases of which 30.3% (n=13) cases showed weak immunoreactivity whereas strong immunoreactivity was observed in 69.7% (n=30) cases. Stromal CD10 expression correlated with well-established prognostic markers, i.e. higher tumour grade (P<0.001), lymph node metastasis (P=0.003), high mitotic rate (P=0.002), increasing NPI (P=0.003), ER negativity (P=0.032), PR negativity (P=0.041) and HER2/neu positivity (P=0.849).

CONCLUSION

Stromal CD10 expression in Invasive breast carcinomas is closely correlated with invasion and metastasis and it might play an important role in the pathogenesis.

KEYWORDS

Invasive Breast Carcinoma, Metalloproteinase, Prognostic Marker, Stromal CD10 Expression.

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BACKGROUND

Breast cancer is the most common carcinoma in women worldwide and it is more than twice as common as cancer at any other site.[1] In India, Mortality due to breast carcinoma per year is more than 70,000. According to WHO reports, United States has achieved a decrease in mortality even with an increase in the number of women diagnosed with breast cancer, which has taken several decades of untiring persistent efforts. WHO postulates, it will take another 25 to 30 years to get positive results in breast carcinoma in India, if we start today. (GLOBOCON 2012).[2] So, early detection and prompt treatment with the new therapeutic modalities should be given, to decrease the incidence.

Although breast cancer is an epithelial malignancy arising in the epithelial cells of the terminal ductal lobular unit, stromal microenvironment plays an important role in breast cancer evolution and metastasis. It has been proved beyond doubt that tissue microenvironment plays a key role in controlling cell survival, proliferation, migration, polarization, and differentiation.[3,4]

CD10 is a zinc-dependent metalloproteinase that has been called common acute lymphoblastic leukaemia antigen (CALLA). It is frequently expressed in bone marrow lymphoid stem cells, pro-B lymphoblasts, mature neutrophils, various

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Corresponding Author:
Dr. Chandan Bajad,
Plot No. 405/2, Street 15/A,
Pragati Nagar, Risali, Bhilai,
District Durg, Chattisgarh-490006
E-mail: chandan.bajad@gmail.com
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lymphoma subtypes, renal cell carcinoma and endometrial stromal sarcoma.[5] In normal breast tissue, CD10 is expressed by the myoepithelial cells only and stromal cells is mostly negative. In contrast, stromal cells in carcinoma breast are CD10 positive. Multiple studies in literature informs that the expression of CD10 in stromal cells is associated with biological aggressiveness in epithelial malignancies like gastric carcinoma, colon carcinoma and hepatocellular carcinoma.[6-8]

Several reports have provided insight on the molecular characteristics differentiating tumour associated stroma from normal stroma.[9,10] Allinen and colleagues were the first to conduct systematic profiling of different stromal cell types and noticed striking changes in the gene expression in the cells that were characterised by surface marker CD10.[11] Later Christine Desmedt et al in their study, compared gene expression profiles from tumour associated CD10 positive stromal cells with CD10 positive cells of the normal breast tissue.[12]

Stromal markers are now emerging as novel markers in assessing the prognosis and metastatic potential of invasive breast carcinoma. This justifies the current study of new stromal marker "CD10" and to find out it's correlation with other well-known prognostic markers of breast to evaluate its prognostic and predictive value.

Aims and Objectives

To estimate the frequency of expression of stromal CD10 in invasive breast carcinomas and to assess its prognostic significance and its correlation with known prognostic markers of breast carcinoma.

MATERIALS AND METHODS

The present prospective study was conducted in the department of Pathology, M.K.C.G. Medical College, Berhampur from August 2014 to July 2016, with the approval of ethical committee of this institute. Modified radical mastectomy specimen of carcinoma breast, which were sent to the department of pathology, MKCG medical college from the department of surgery, subjected to histopathological examination. Relevant history like name, age and menopausal status were recorded.

Female patients irrespective of age who underwent mastectomy with histological diagnosis of infiltrating carcinoma breast were included in our study. Five cases of lumpectomy with benign histology were taken as the control group. Specimens of needle biopsy and incisional biopsy, carcinoma of the male breast cases, carcinoma in situ cases were excluded from the study.

All specimens were fixed in formalin and grossly examined and representative sections were taken and H & E staining was done. The grading of breast carcinoma was done according to the Nottingham's combined histologic grade (Elston-Ellis modification of Scarff-Bloom-Richardson grading system).[13] Nottingham's Prognostic index (NPI) was calculated in histologically confirmed case of infiltrating carcinoma.[14]

(EPG) Excellent Prognostic group-2.08 to 2.4.
(GPG) Good Prognostic group- >2.42 to = <3.4.
(MPG I) Moderate I Prognostic group- >3.42 to </ = 4.4.
(MPG II) Moderate II prognostic group- >4.42 to = <5.4.
(PPG) Poor prognostic group- >5.42 to = <6.4.
(VPG) Very poor prognostic group- >6.5 to 6.8.

Ultimately, 48 cases that fulfilled the above criterion were taken up for the study along with five cases of benign tumour as a control group (fibroadenoma and phyllodes).

Paraffin blocks which were most representative of the tumour tissue were chosen. Immunohistochemistry was done manually for evaluation of ER (Ready to use, FLEX, Monoclonal Rabbit, Anti-Human Oestrogen Receptor α, Clone EP1; English Code IS084), PR (Ready to use, FLEX, Monoclonal Mouse, Anti-Human Progesterone Receptor, Clone PgR 636, Clone 56C6; English Code IS068), HER2/neu (ready to use, polyclonal rabbit anti-human c-erbB-2 oncoprotein; Code A0485) and CD10 (Ready to use, FLEX, Monoclonal Mouse, Anti-Human CD10, Clone 56C6; Code IS648). Expression of CD10 were first studied in the tumours, following which they were compared with the respective histological grading, HER2/neu and hormonal receptors studied.

Evaluation of CD10 Index- (According to Makretsov NA et al, 2007)[7]

Grouped in three categories as follows: -

1. Group-1 ------- No staining.
2. Group-2 ------ < 30% (weak staining).
3. Group-3 -------- > 30% (strong staining).

Membrane and cytoplasmic immunostaining in tumour cells were accepted as positive; At least 500 cells were counted at 100X magnification; Tonsil was used as a positive control.

Evaluation of ER and PR immunostaining was done according to ASCO-CAP GUIDELINES 2010[15] and HER-2neu immunostaining was done according to ASCO-CAP Guidelines 2013.[16]

The significance of the results was assessed by determining the P value using the chi-square test. P-value less than 0.05 was significant and less than 0.001 was very highly significant.

RESULTS

Case distribution- Ductal NST comprised majority of the carcinoma cases i.e. 83.3 % (n=40) followed by Lobular carcinoma, 4.16% (n=02), metaplastic carcinoma 4.16% (n=02), medullary carcinoma 2.08% (n=01), colloid carcinoma 2.08% (n=01), Invasive papillary carcinoma 2.08% (n=01) and malignant phyllodes 2.08% (n=01).

Age - In our study, the oldest patient of carcinoma cases, was 80 years of age and the youngest case was 27 years of age and the mean being 47.94 years. The majority of the studied patients with infiltrating carcinomas were of (41-60) years age group 56.3% (n=27) followed by ≤40-year age group 29.2% (n=14). Amongst 27 patients of 41-60 year

age group, 10 cases were premenopausal and 17 were postmenopausal.

Size- Most of the carcinoma cases 91.7% (n=44) were of size ≥2 cm and the rest 8.3% (n=04) were of size <2 cm.

Mitotic Grade- Most of the carcinoma cases 39.6% (n=19) were of mitotic grade II followed by mitotic grade 3 37.5% (n=18) and the rest are grade I, 22.9% (n=11).

Lymph Node Status - In our study, 35.4% (n=17) cases were positive for lymph node metastasis, more than 4 axillary lymph nodes were involved in 52.1% (n=25) cases whereas 12.5% (n=06) cases were negative for axillary lymph node metastasis.

Tumour Grade- Histological grading by MBR grading system showed 29.2% (n=14), 45.8% (n=22) and 25.0% (n=12) cases belonging to Grade III, Grade II and Grade I respectively.

Nottingham's Prognostic Index- Maximum number of tumours belonged to Poor Prognostic Group (PPG), 35.4% (n=17) cases followed by Very Poor Prognostic Group (VPG), 22.9% (n=11). Excellent Prognostic Group (EPG) contributed least number of cases, i.e. 4.2% (n=02).

IHC Status

CD10 immunostaining was performed on all 53 cases along with other hormonal and HER-2/neu markers. Five benign cases comprising of fibroadenoma (n=03), giant fibroadenoma (n=01) and phyllodes (n=01), were also subjected for the CD10 immunostaining, which served as the control group.

Stromal CD10 expression was not detected in the normal breast but the myoepithelial cells show CD10 positive immunostaining. These non-neoplastic myoepithelial cells served as a built-in positive control for CD10. There was no CD10 expression in normal ductal cells, fibroblast and adipose cells in our study. However, a minor population of stromal cells has been shown to express CD10 positivity in fibroadenoma and normal breast tissue as evidenced in literature.[6]

CD10 was found to be positive in 89% (n=43) cases of which 30.3% (n=13) cases showed weak immunoreactivity whereas strong immunoreactivity was observed in 69.7% (n=30) cases.

Stromal CD10 positivity was found to have statistically significant trend with increasing grade of tumour (P <0.001), increasing mitotic grade (P = 0.002), Nodal status (P = 0.003), worsening prognosis (P = 0.003), ER (P = 0.032) and PR negativity (P = 0.041).

Percentage positivity of strong CD10 immunostaining increases from 75% to 90.9% in tumours as the tumour size increases more than 2 cm (P = 0.026).

Most patients were ER negative 64.6% (n=31) and PR negative 68.8% (n=33) and CD10 expression was statistically significant when correlated with ER (P = 0.032) and PR status (P = 0.041).

Majority of our subjects, 52.1% (25) cases were HER-2/neu positive while 47.9% (n=23) cases were HER-2/neu negative. Chi-square test showed no significant statistical correlation between stromal CD10 expression and HER-2/neu status (p = 0.849).

CD10 immunostaining had a significant correlation with molecular subtypes (P=0.015) of breast cancer. CD10 positivity having strong association with triple negative subtype and CD10 negativity with luminal A subtype.

Statistical Analysis

For all statistical data Chi-square test was applied using IBM SPSS Statistics 20.

Sl. No.	Histological Subtype	Frequency	%
1.	Ductal NST	40	83.3
2.	ILC (Invasive Lobular Carcinoma)	2	4.16
3.	Invasive Papillary Carcinoma	1	2.08
4.	Medullary Carcinoma	1	2.08
5.	Malignant Phyllodes Tumor	1	2.08
6.	Metaplastic Carcinoma	2	4.16
7.	Colloid Carcinoma	1	2.08
	Total	**48**	**100**

Table 1. Distribution of Different Histological Subtypes

Sl. No.		Histological Subtype	Frequency	Percentage
1.	Control	Fibroadenoma	4	80
2.	Group	Benign phyllodes	1	20
		Total	5	100

Table 2. Distribution of Different Histological Subtypes of Control Group

		CD10 Expression			P value
Total Number N (%)		**Negative N (%)**	**Weak N (%)**	**Strong N (%)**	
Menstrual Status					
Premenopausal	22 (45.2)	1 (4.5)	6 (27.3)	15 (68.2)	0.460
Postmenopausal	26 (54.8)	4 (15.4)	7 (26.9)	15 (57.7)	
Age (in years)					
≤40	14 (29.2)	1 (7.1)	4 (28.6)	9 (64.3)	
41-60	27 (56.2)	3 (11.1)	7 (25.9)	17 (63.0)	0.988
>60	7 (14.6)	1 (14.3)	2 (28.6)	4 (57.1)	
Tumour Size					
<2 cm	4 (8.3)	1 (25)	3 (75)	0 (0)	0.026
≥2 cm	44 (91.7)	4 (9.1)	10 (22.7)	28 (68.2)	

Mitotic Grade as in Nottingham's Grading 1 2 3	11 (22.9) 19 (39.6) 18 (37.5)	3 (27.3) 1 (5.3) 1 (5.6)	7 (63.6) 3 (15.8) 3 (16.6)	1 (9.1) 15 (78.9) 14 (77.8)	0.002
Nodal Status Negative 1-4 >4	6 (12.5) 17 (35.4) 25 (52.1)	3 (50) 1 (5.9) 1 (4.0)	2 (33.3) 7 (41.2) 4 (16.0)	1 (16.7) 9 (52.9) 20 (80.0)	0.003
Tumour Grade Grade 1 Grade 2 Grade 3	12 (25.0) 22 (45.8) 14 (29.2)	5 (41.7) 0 (0) 0 (0)	7 (58.3) 5 (22.7) 1 (7.1)	0 (0) 17 (77.3) 13 (92.9)	<0.001
NPI (Prognosis) EPG GPG MPG1 MPG2 PPG VPG	2 (4.2) 6 (12.5) 4 (8.3) 8 (16.7) 17 (35.4) 11 (22.9)	1 (50) 2 (33.3) 1 (25.0) 1 (12.5) 0 (0) 0 (0)	1 (50) 4 (66.7) 2 (50) 2 (25) 4 (23.5) 0 (0)	0 (0) 0 (0) 1 (25) 5 (62.5) 13 (76.5) 11 (100)	0.003
ER Status Negative Positive	31 (64.6) 17 (35.4)	1 (3.2) 4 (23.5)	7 (22.6) 6 (35.3)	23 (74.2) 7 (41.2)	0.032
PR Status Negative Positive	33 (68.8) 15 (31.2)	1 (03) 4 (26.7)	9 (27.3) 4 (26.7)	23 (69.7) 7 (46.6)	0.041
HER2/neu Status Negative Positive	23 (47.9) 25 (52.1)	3 (13.0) 2 (08)	6 (26.1) 7 (28)	14 (60.9) 16 (64)	0.849
Histologic Subtype Ductal NST Invasive Lobular Carcinoma Medullary Carcinoma Metaplastic Carcinoma Malignant Phyllodes Tumour Colloid Carcinoma Invasive Papillary Carcinoma	40 (83.2) 2 (4.2) 1 (2.1) 2 (4.2) 1 (2.1) 1 (2.1) 1 (2.1)	3 (7.5) 0 (0) 0 (0) 1 (50) 0 (0) 1 (100) 0 (0)	10 (25) 1 (50) 1 (100) 1 (50) 0 (0) 0 (0) 0 (0)	27 (67.5) 1 (50) 0 (0) 0 (0) 1 (100) 0 (0) 1 (100)	0.065
Molecular Subtypes Luminal A Luminal B Triple negative HER2-enriche	10 (20.8) 9 (18.8) 13 (27.1) 16 (33.3)	3 (30) 1 (11.1) 0 (0) 1 (6.3)	5 (50) 1 (11.1) 1 (7.7) 6 (37.5)	2 (20) 7 (77.8) 12 (92.3) 9 (56.2)	0.015

Table 3. The Correlation between CD10 Expression and Clinicopathological Parameters

		Tumour Grade			P value
Total Number N (%)		**Grade - I N (%)**	**Grade - II N (%)**	**Grade - III N (%)**	
ER Status Negative Positive	31 (64.6) 17 (35.4)	03 (9.7) 9 (52.9)	15 (48.4) 7 (41.2)	13 (41.9) 1 (5.9)	0.001
PR Status Negative Positive	33 (68.8) 15 (31.2)	5 (15.2) 7 (46.7)	15 (45.5) 7 (46.7)	13 (39.3) 1 (6.6)	0.019
HER2/neu Status Negative Positive	23 (47.9) 25 (52.1)	8 (34.8) 4 (16)	4 (17.4) 18 (72)	11 (47.8) 3 (12)	0.001

Table 4. The Correlation between Tumour Grade and (ER, PR, HER2/neu Status)

Name of Study	Sample Size	Positive Correlation CD10	No Correlation	Uncertain
Present study (2016)	48	Tumour size Higher grade Nodal status Increasing Mitosis Bad prognosis ER PR	Age Menstrual status HER-2neu status Histological subtype	

		Molecular Subtype		
Jana, et al (2013)	70	Higher Grade Increasing Mitosis Bad Prognosis ER - Her2 + Molecular subtype	Age Tumour Size Stage/TNM Lymph node positivity PR	Histological type Chemotherapy
Thomas S et al (2013)	29	ER - Her 2 + Chemotherapy and clinical response		
Makretsov NA et al (2007)	453	Higher grade Decreased Survival ER	Tumour size Lymph node Status PR, Her 2 Histologic Subtype	
Iwaya K et al (2002)	123	Lymph node Mets Decreased DFS/OS	Age Tumour size Histologic grade Clinical stage	

Table 5. Correlation of Present Study with Other Studies

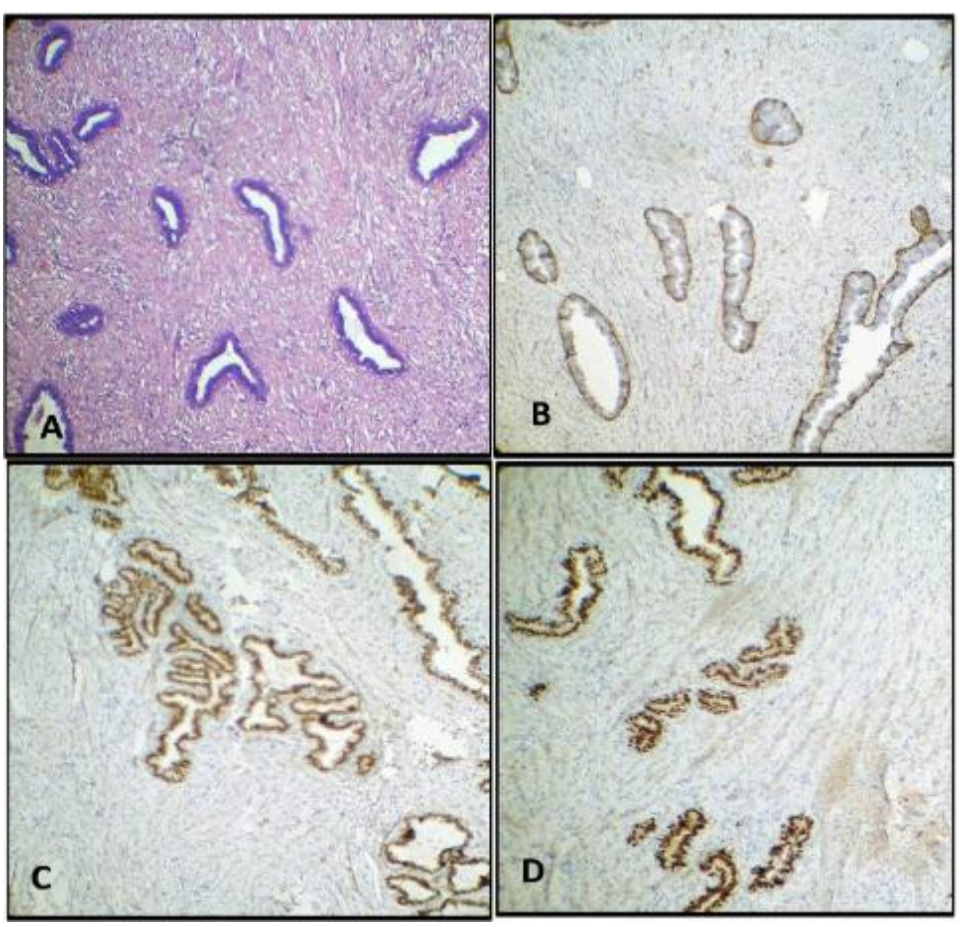

Figure 1. Fibroadenoma of Breast

A - HE 100X.
B - Myoepithelial cell is positive whereas stroma is Negative for CD10 (100X).
C - ER positive in epithelial and myoepithelial cells (100X).
D - PR positive in epithelial and myoepithelial cells (100X).

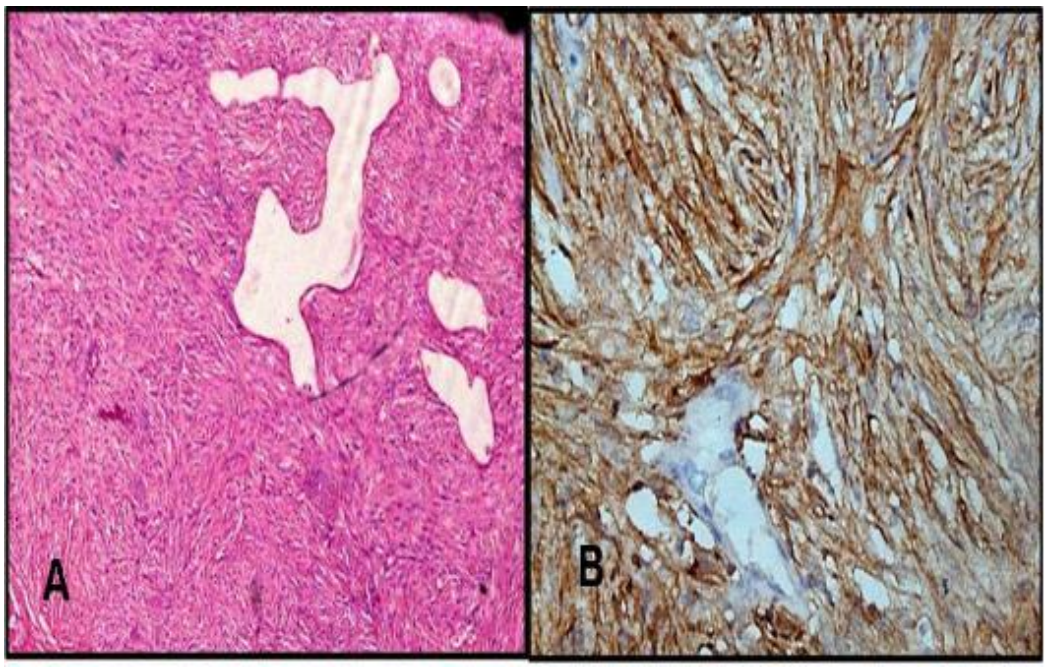

Figure 2. Malignant Phyllodes Tumour of Breast

A - HE 400X, B - Stroma is strongly positive for CD10 (400X).

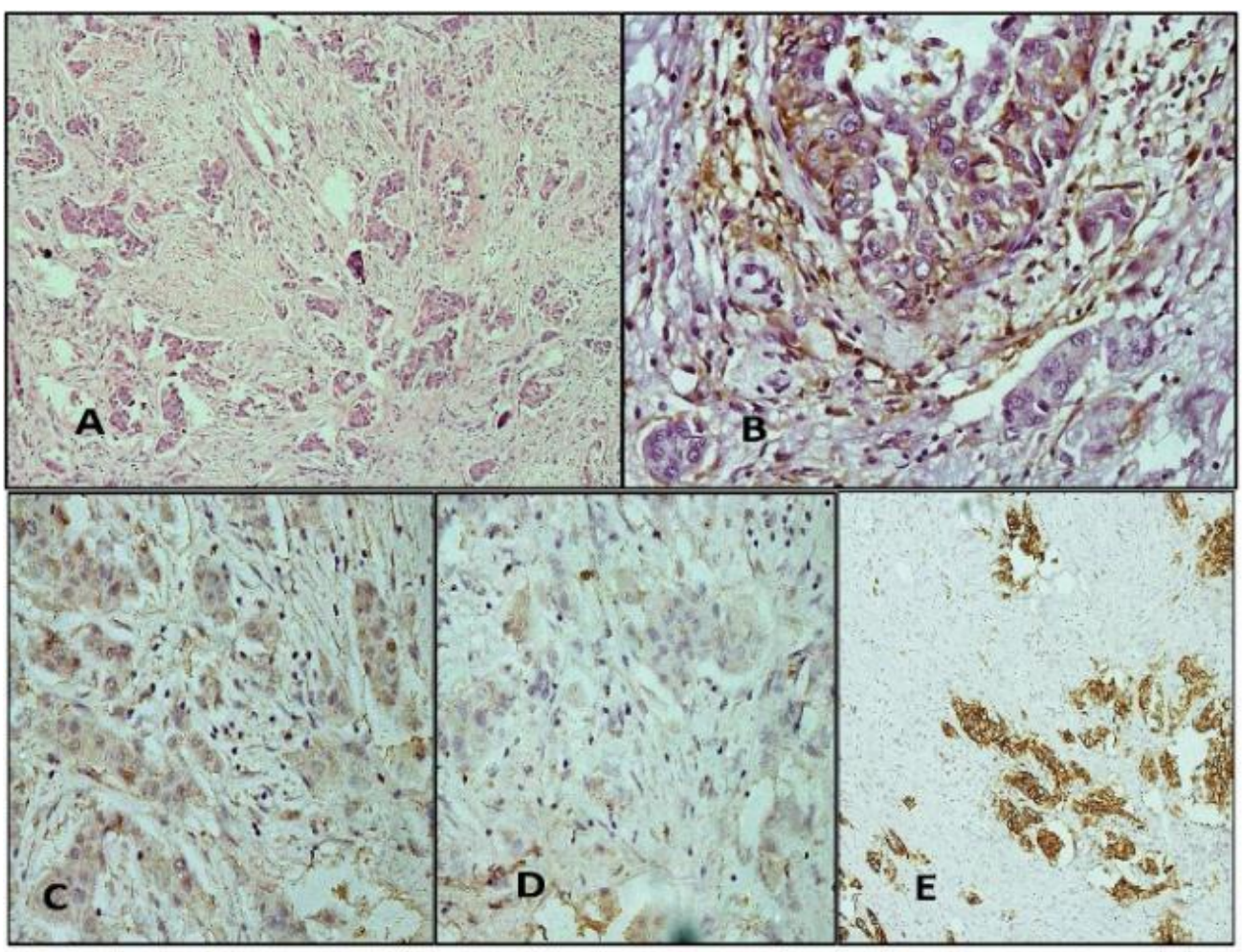

Figure 3. Invasive Carcinoma of No Special Type Grade II

A - HE 100X, B - Stroma is CD10 weakly positive (400X), C - ER negative 400X, D - PR negative 400X, E - HER2/neu 2+ 100X.

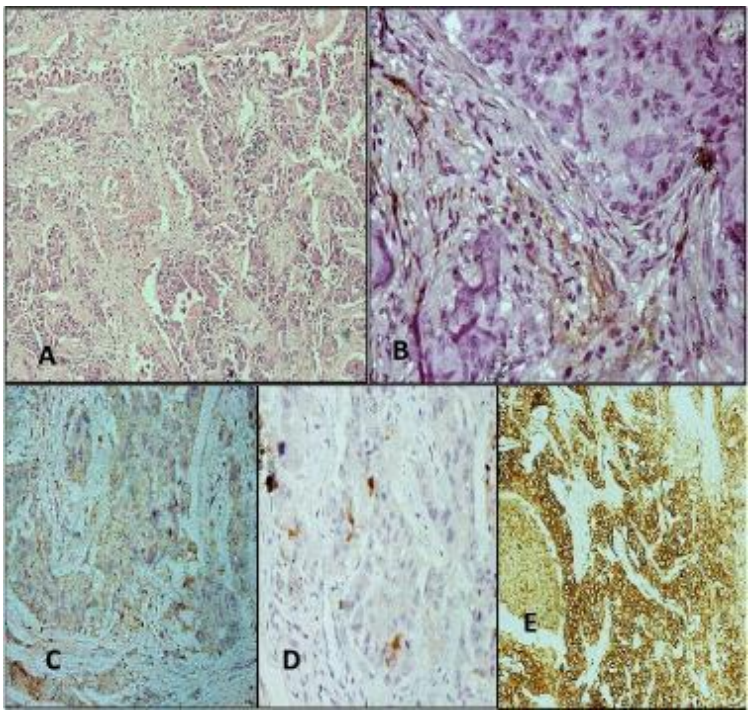

Figure 4. Invasive Carcinoma of No Special Type Grade I

A - HE 100X, B - Stroma is CD10 weakly positive, C - ER negative 400X, D - PR negative 400X, E - HER2/neu 3+ 100X.

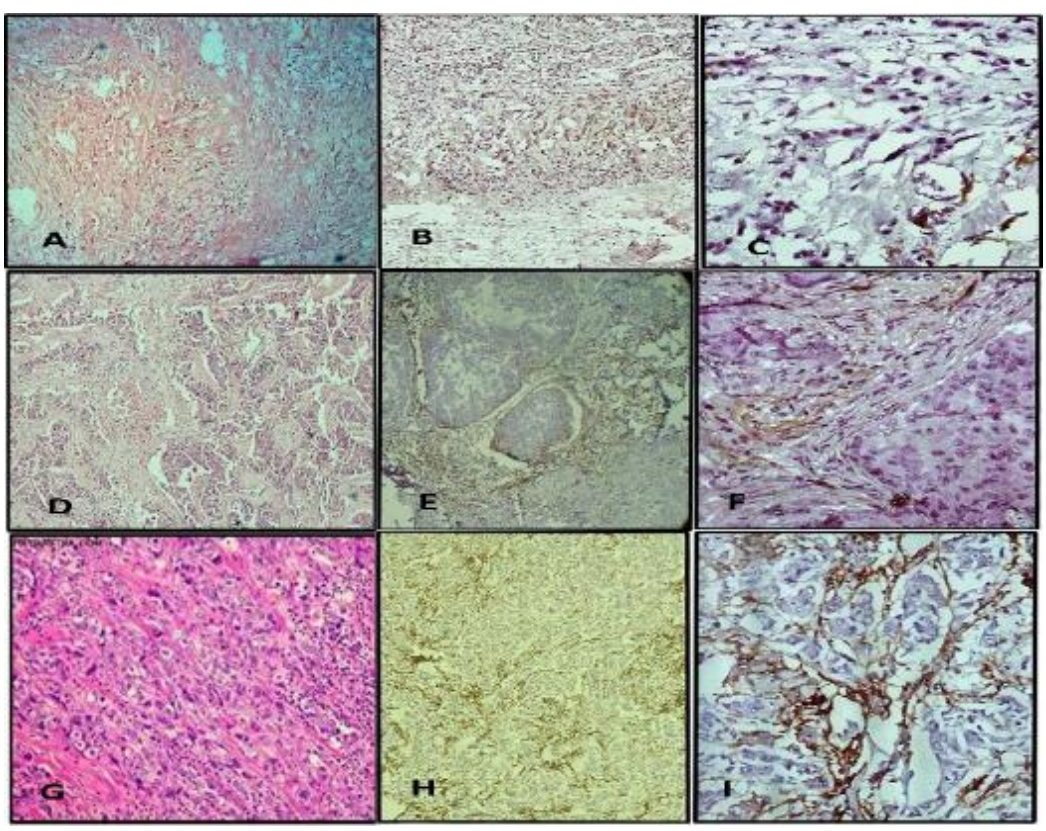

Figure 5. Photomicrograph Showing Comparative Results of CD10 Immunostaining in increasing Grades of Invasive Carcinoma of No Special Type

A, B, C - showing HE (100X), CD10 (100X) and CD10 (400X) invasive carcinoma NST grade I respectively with CD10 being weakly positive.
D, E, F - showing HE (100X), CD10 (100X) and CD10 (400X) invasive carcinoma NST grade II respectively with CD10 being strongly positive.
G, H, I - showing HE (100X), CD10 (100X) and CD10 (400X) invasive carcinoma NST grade III respectively with CD10 being strongly positive.

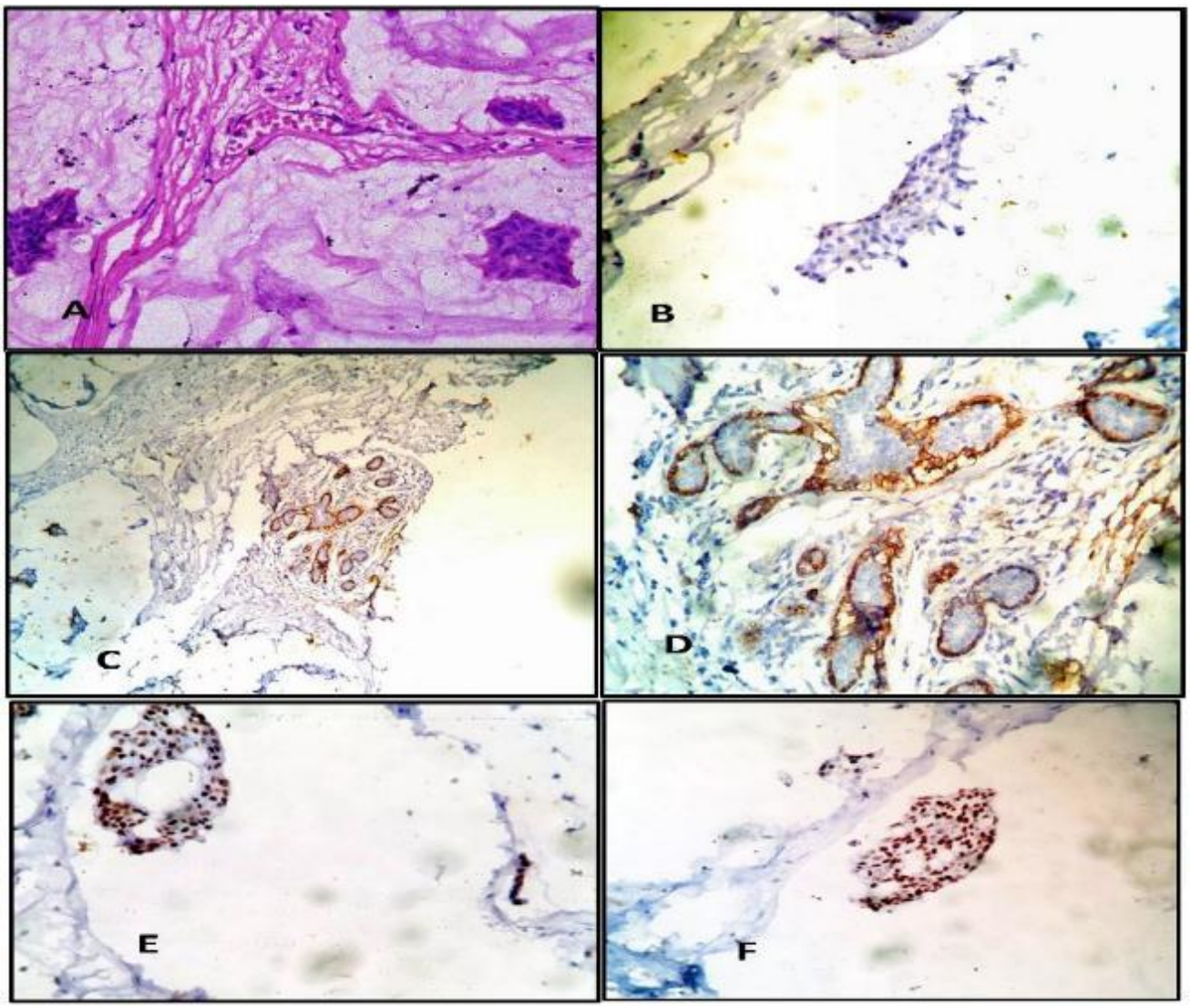

Figure 6. Colloid Carcinoma (Mucinous Carcinoma)

A - HE 400X, B - 400X tumour cells are HER2/neu negative, C - 100X CD10 is negative in tumour cells as well as stroma
D - 400X TDLU showing CD10 positive at the basement membrane, E - 400X, tumour cells are ER positive,
F - 400X, tumour cells are PR positive.

DISCUSSION

Breast cancer is a major public health problem for woman throughout the world and it is one of the leading cause of death amongst women. In India, it accounts for 27% of all cancers in women.[1] There are multiple recognised prognostic factors (which include molecular markers) of breast carcinoma. The detection of these molecular markers play a major role in planning treatment strategy.

Several studies suggested that CD10 expression in the tumour stroma of invasive Breast carcinoma is associated with aggressiveness of tumour. So CD10 constitute a clinically important prognostic marker and a potential target for the development of novel therapies.

In the present study, Ductal NST comprised 83.3% of the carcinoma cases, (n=40) followed by Lobular carcinoma, 4.16% (n=02), metaplastic carcinoma 4.16% (n=02), medullary carcinoma 2.08% (n=01), colloid carcinoma 2.08% (n=01), Invasive papillary carcinoma 2.08% (n=01) and malignant phyllodes 2.08% (n=01). Similarly, Ductal NST comprised the majority in studies done by Makretsov et al[7] and Ahmed AbdElAziz et al.[17]

Age in the present work ranged from 27 to 80 years with mean age being 47.94 years. In the present study, majority i.e. 56.3% (n=27) patients belonged to the age group [41-60 years]. Somewhat similar results were obtained from Putti et al.[18]and Yamaguchi et al.[19] Dissimilar to our results, a higher mean patient's age of 60.2, 61, and 62 was recorded in the work done by Van der Vegt et al,[20] Makretsov et al. 2007.[7] and Lu et al[21] respectively.

In our study, 91.7% (n=44) cases in our study showed tumour size >2 cm. Correspondingly, Christine Desmedt et al[12] and Ali Taghizadeh-Kermani et al.[8] observed in their study, 57% and 81% cases of tumours were greater 2 cm in size. On the other hand much smaller size tumours were observed in the study done by Makretsov et al.[7] They found in 46.1% cases, the tumour size was less than equal to 2 cm.

In the current study, lymph node metastasis was

negative in 12.5% (n=06) cases. The rest of which showed lymph node metastasis being positive in one to four lymph nodes in 35.4% (n=17) cases and more than four lymph nodes were involved in 52.1% (n=25) cases. These results showed significant correlation between lymph node positivity and CD10 status (P=0.003).

In the current study, majority of the invasive carcinoma patients belonged to the grade II – 45.8% (n=22) followed by grade III- 29.2% (n=14) whereas grade I tumours were noted in 25% (n=12) cases. Correspondingly in the studies conducted by Yamaguchi et al,[19] Makretsov et al,[7] Ahmed AbdElAziz et al[17] and B. V. Anuradha Devi et al[22]; they observed that the most prevalent grade was Invasive duct carcinoma grade II representing 40%, 53.8%, 52.8% and 54% respectively in their studies.

In contrary to our results, Puri et al[5] found grade III as the most prevalent grade - 53.06% followed by grade II - 34.29% and grade I - 12.24% cases. Predominant grade III tumours in the study group was also noted by Christine Desmedt et al[12] and S.K. Nema et al.[23]

CD10 in Carcinoma Breast

We immunohistochemically demonstrated that CD10 is expressed by the stromal cells within the area of invasive carcinoma, but not in the stromal cells of normal breast, fibroadenoma and benign phyllodes tumour, which were taken as the control group in our study.

In the present study, positive stromal cells were observed in 89% cases (n=43) of invasive carcinomas. CD10 positive stromal cells were distributed around the cancer cells where the staining intensity was also high.

CD10 with Age and Menopausal status

Our study did not achieve any significant correlation between stromal CD10 immunostaining intensity with respect to patient's age (P=0.988) and menopausal status (P=0.460). Similarly, Emad Sadaka et al[24] and none of the studies available, found any significant correlation of CD10 immunostaining with age and menopausal status.

CD10 and Tumour Size

We found statistically significant correlation between CD10 immunostaining and the tumour size (P=0.026). This finding was similar to those of Mohammadizadeh et al,[25] Ali Taghizadeh-Kermani et al,[8] Kim et al[26] and B. V. Anuradha Devi et al,[22] which also showed significant correlation of CD10 immunostaining with tumour size.

CD10 and Nodal Status

CD10 stromal cells were also detected in metastatic lymph nodes. CD10 positivity was significantly correlated with nodal metastasis (0.003). The rate of metastasis between CD10 positive and CD10 negative tumours came out to be statistically significant.

Significant correlation was also concluded by several studies like Iwaya et al,[6] Masaki et al,[27] Kim et al,[26] Mohammadizadeh et al,[25] Ali Taghizadeh-Kermani et al,[8] Emad Sadaka et al,[24] B. V. Anuradha Devi et al[22] and S.K. Nema et al,[23] between CD10 immunostaining expression. The intensity as well as positivity of stromal CD10 immunostaining were significantly higher in cases associated with axillary lymph node metastasis.

In contrast, Makretsov et al[7] and B. V. Anuradha Devi et al[22] found that CD10 immunostaining intensity was not affected by lymph node status.

CD10 and Tumour Grade

In this study, Positive stromal CD10 immunostaining was observed in all grade III cases-100% (n=14), in all grade II cases-100% (n=22) and in seven out of twelve grade I tumours i.e 58.3%. We found the relationship between Tumour grade and CD10 immunostaining to be strongly statistically significant (P<0.001).

Similar to our results, several authors like Makretsov et al[7], Kim et al,[26] Emad Sadaka et al,[24] Mohammadizadeh et al,[25] B. V. Anuradha Devi et al,[22] Ahmed AbdElAziz et al[17] and H Jana et al[28] found significant correlation between CD10 immunostaining positivity and the tumour grade.

Contradictory results were concluded by Iwaya et al[6] and Puri et al[5] who found insignificant correlation between CD10 positivity and tumour grade.

Considering the intensity of CD10 immunostaining, strong CD10 positivity was found to be the highest in grade III tumours followed by grade II and grade I tumours. The significant correlation between CD10 immunostaining and tumour aggressiveness may be attributed to the fact that CD10 being one of the matrix metalloproteinase cleaves the protein component of extracellular matrix, thereby play a central role in tissue remodelling. Therefore, in infiltrating carcinomas, CD10 degrades the extracellular matrix and helps in tumour cell invasion.[29]

CD10 with Mitotic Rate and NPI

CD10 immunostaining positivity was found to have increased with increasing mitotic rate (P=0.002) and worsening prognosis, indicated by NPI (P=0.003). The findings were similar to the study done by H Jana et al[28] who found statistically significant correlation of CD10 with respect to mitotic rate and NPI.

CD10 with Hormonal Receptor Status

Positive stromal CD10 immunostaining was observed in most of the patients showing negative staining for oestrogen and progesterone receptors. So, in our study, negative correlation was found between CD10 immunostaining and ER status (P=0.032) as well as PR status (P=0.041).

Concurrently, Emad Sadaka et al[24] also showed significant correlation of CD10 positivity with ER and PR negativity. Whereas Puri et al[5] and Ahmed AbdElAziz et al[18] found insignificant correlation of CD10 immunostaining with respect to ER and PR status.

With regards to ER in particular, similar results were found by H Jana et al,[28] Kim et al,[26] Ali Taghizadeh-Kermani et al[8] and Thomas S et al[30] who found it's significant negative correlation with CD10 immunostaining. On the other hand,

no correlation was found by Mohammadizadeh et al[25] and S.K. Nema et al.[23]

CD10 with HER2/neu Status

HER2/neu positivity was found in 52.1% cases (n=25) and it was statistically insignificant when correlated with CD10 immunostaining (P=0.849). Similar insignificant correlation was found in the study done by Ahmed Abdel Aziz et al[17] and Mohammadizadeh et al.[25]

Similar conclusion was drawn by Makretsov et al[7] with respect to oestrogen receptor confirming a significant correlation between CD10 immunostaining positivity and oestrogen receptor negativity. In the same study, he got insignificant correlation of CD10 immunostaining with progesterone receptor and HER2/neu receptor status.

In contrast, significant correlation of CD10 immunostaining with HER2/neu is concluded in the study done by Thomas S et al[30] and Emad Sadaka et al.[24] In our study, the insignificant correlation may be attributed to small sample size.

CD10 with Molecular Subtype

CD10 immunostaining had a significant correlation with the molecular subtypes of breast cancer (P=0.015). CD10 positivity having strong correlation with HER-2 subtype and triple negative subtype and CD10 negativity with luminal subtype, which has the best prognosis among molecular subtypes. These findings were similar to that of the study done by H Jana et al.[28]

CONCLUSION

Stroma plays an important role in development and metastasis of tumour and CD10 is a novel marker. CD10 expression correlated strongly with well-established prognostic markers, i.e. higher tumour grade, lymph node metastasis, high mitotic rate, increasing NPI, ER/PR negativity and HER-2neu positivity. So, we recommend CD10, to be used as a marker of poor prognosis and must be included along with the routine prognostic markers of carcinoma breast. Targeted therapy should be developed against CD10 to check overall and/or metastasis free survival of the patient.

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