

Analysis Of CD 10 Expression In Breast Carcinoma In Post Menopausal Patients.

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Abstract:

Background: Breast carcinoma is the most common cancer among women. The mortality is attributed to metastatic disease. CD10, a metalloproteinase, may play a role in degrading extra cellular matrix and collagen, providing a microenvironment favourable for invasion and metastasis.

Aim And Objectives: To study the stromal expression of CD 10 antigen in invasive ductal breast carcinoma patients (post menopausal status) and its relationship with Age, Histologic subtypes, Nottingham's grade, Nottingham's Prognostic index, Mitotic rate and Lymph node metastasis.

Materials and methods: 34 patients were included. Representative sections were taken, Hematoxylin and Eosin staining and Immunohistochemistry (CD10) (10%-30% stromal positivity was considered weak positive, >30% as strong positive) were evaluated and statistically analysed.

Results: Stromal expression of CD10 was found to be significantly associated with increasing tumor grade ($P = <0.0001$), Lymph node metastasis ($P = <0.0001$). No correlation was found between CD10 expression and age, histologic subtypes, tumour size, mitotic rate and Nottingham's Prognostic index ($P = 0.07$).

Conclusion: The stromal expression of CD10 has significant correlation with higher histological grade and lymph node metastasis. Study highlights the role of stromal CD10 expression in predicting tumor response and prognosis. Hence CD10 could be used as a prognostic marker.

Keywords: CD10, stromal expression, Breast carcinoma.

I. Introduction

Breast carcinoma is the most common cancer among women. It is the fifth leading cause of cancer death worldwide accounting for 522,000 deaths/year (2012)[1,2]. The focus of recent research is on the nature and molecular signature of stroma[3,4].

CD10 is a 90-110 kilo Dalton, cell surface metalloproteinase. Expressed by myoepithelial cells of normal breast and lymphocytes, endometrial stroma cells, etc. The interaction of tumour cells with stromal cells and extra cellular matrix leads to CD10 expression in stroma, acts to degrade extra cellular matrix and collagen, providing a microenvironment favourable for invasion and metastasis.

The search for new prognostic marker that could elucidate more effectively the metastasizing potential of breast carcinomas remains an important goal of this study.

II. Aims And Objectives

To study the stromal expression of CD 10 antigen in invasive ductal breast carcinoma patients with post menopausal status and to analyse it with the Nottingham's Prognostic index, Mitotic rate and tumor grade of the patients.

III. Materials And Methods

This cross sectional study was done from June 2014 to June 2016 in a tertiary care hospital. All invasive breast carcinoma patients (confirmed by Histopathological examination) with post menopausal status, who have undergone modified radical mastectomy were included in the study population. The institutional ethical committee approval was obtained.

Inclusion criteria: All cases reported as positive for invasive ductal carcinoma of breast, with first line of treatment as surgery.

Exclusion criteria: All cases who have undergone any other modalities of treatment are excluded in view that there can be differences or alterations in the expression of the marker of interest.

Consent: may not be required as only tissues sent for histopathological examination or blocks of tissue are to be used.

Sample size: 34 patients were chosen. The details including age, disease laterality, tumor size, histopathological grade, lymph node metastasis and treatment details were obtained and entered in DATA entry form.

Their corresponding blocks were retrieved and Haematoxylin and Eosin stained sections were prepared and evaluated. Another section was used for IHC using CD10 mouse monoclonal antibody (Pathnsitu pm150) and evaluated as in TABLE 1.

Table 1: CD 10 expression interpretation:

Interpretation	Description
Negative Fig 1	No staining <10 % cytoplasmic and membranous staining in stromal cells
Weak positive Fig 2	10-30 % focal cytoplasmic and membranous staining of stromal cells Diffuse weak staining
Strong positive Fig 3	>30 % cytoplasmic and membranous staining of stromal cells.

The data was entered into Excel sheet and statistically analysed using SPSS software version 16.0.

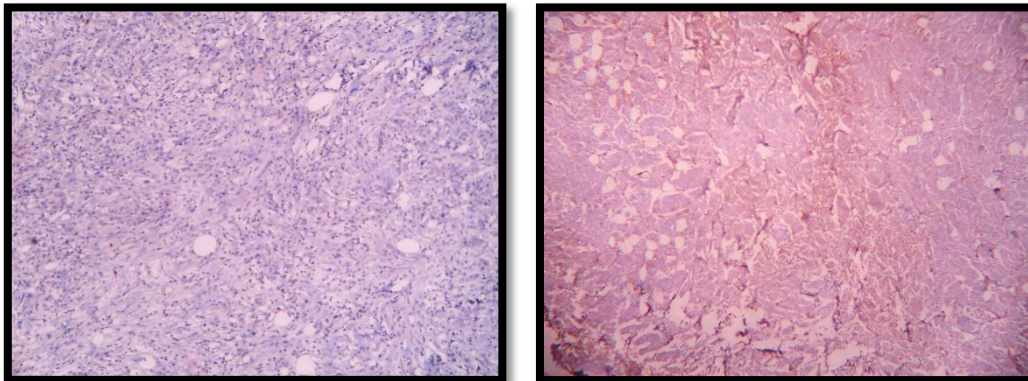


Fig.1: IHC CD10, Negative staining, 200 x **Fig.2:** IHC CD 10, Weak positive, 200 x

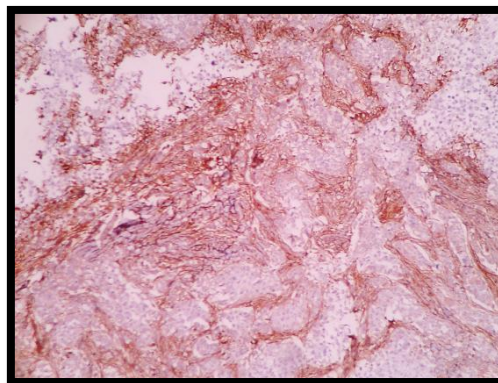


Fig.3: IHC CD 10, Strong positive, 200 x

IV. Observations And Results

Out of 34 patients 20 were the age group 51-70 years, 19 patients showing positive CD10 expression. Though not statistically significant (P value 0.51). With 25 out of 31 with IDC NST histological subtype showed positive CD10 immunoreactivity, the association could not be proved statistically (p value 0.52). 25 patients had tumour size 2-5cm, though increase in intensity of staining was observed the significance still could not be proved (P value 0.22). Study had maximum number of patients with mitotic grade 2, though showing strong positive immunoreactivity with CD10 expression, it could not reach statistical significance (P value 0.44).

Analysis of lymph nodes both based on number of nodes involved (P value 0.017) and also by lymph node staging (p value 0.032) in correlation with CD 10 expression showed statistical significant association. Histologically, grade 2 had the maximum number of patients with strong positive reaction and it had a statistical significance with P value 0.04.

Finally out of the 34 patients we had most of them with NPI of Moderate prognostic group. Also increase in intensity was noted with Poor prognostic group and Very poor prognostic group. This could not be proved statistically.

Table 2: P value for comparison of CD 10 expression with prognostic groups based on NPI

Nottingham's index	Prognostic	Number of patients	CD 10 Negativity	CD 10 Weak Positivity	CD 10 Strong Positivity
EPG(2.08 to 2.4)		0	0	0	0
GPG(>2.42 to <3.4)		1	0	1	0
MPG I (>3.42 to <4.4)		12	5	5	2
MPG II (>4.42 to <5.4)		8	2	4	2
PPG (>5.42 to <6.4)		11	0	3	8
VPG (>6.5 to <6.8)		2	0	0	2
Total		34	7	13	14

P value 0.07

Nottingham's Prognostic index(NPI): = [size (cm) ×0.2] + lymph node stage (1-3) + Grade (1-3)

EPG: Excellent prognostic group; GPG: Good prognostic group; MPG: Moderate prognostic group; PPG: Poor prognostic group; VPG: Very poor prognostic group.

V. Discussion

5.1 Comparison of CD 10 expression with age

Comparison of the CD10 expression with age, showed no statistical significance (P value 0.51) correlating with other studies namely Keiichi Iwaya et al study[5] (P value 0.95), Fereshteh Mohammadzadeh et al[6] (2012) study (p value 0.49), Sayantan H Jana et al [7] (2014) (P value- 0.3572), Ali Taghizadeh-Kermani et al[8] (2014), study (P value- 0.21), B.V. Anuradha Devi et al [9] (2016).

5.2 Histologic subtype

Maximum number of patients were of IDC NST subtype. The other subtypes were IDC with mucinous differentiation. Though maximum positive immunoreactivity was seen with IDC NST, no statistical significance was achieved (p value 0.52), probably due to sparse distribution of other subtypes.

5.3 Tumor size

Our study had maximum number of patient with tumor size 2-5cm but their CD10 expression could not be proved statistically (P value 0.31), while Fereshteh Mohammadzadeh et al (P value 0.01), Ali Taghizadeh-Kermani et al study (P value 0.04), B.V. Anuradha Devi et al study (P value 0.003) all had statistically significant association of CD 10 expression with tumour size.

The dissimilarities of study results could be due to regional differences and other confounding factors.

5.4 Mitotic grade

Our study had maximum number of patients with mitotic grade 2, but this parameter showed no statistical significance (P value 0.44).

Sayantan H. Jana et al had statistically significant association (P value 0.03). This maybe due to difference patient distribution in each grade.

5.5 Lymph node status and grading

In our study we had tried to analyse lymph node metastasis by evaluating total number of lymph nodes involved and also by lymph node staging of TNM. All patients of stage 3 showed positive immunoreactivity with CD10 expression. It was also seen that with increase in the number of lymph node metastasis, stronger the intensity of CD10 expression. This association was proved statistically (P value 0.01), correlated with studies done by Keiichi Iwaya et al and Fereshteh Mohammadzadeh et al (0.02), Ali Taghizadeh-Kermani et al (P value <0.01) and B.V. Anuradha Devi et al (P value 0.0005).

All the studies showed significant association of CD10 expression with lymph node metastasis except Sayantan H Jana et al which may be due to difference in assessing lymph node involvement. They had used lymph node ratio instead of direct metastasis.

5.6 Histopathological grading

In our study with increasing grade, the CD 10 expression increased potentially conveying it as a marker of aggressiveness of carcinoma. This relationship was statistical significance. (P value 0.04).

Our results were in concordance with studies done by Nikita A Makretsov et al (P value 0.02), Fereshteh Mohammadzadeh et al (P value 0.004), Sayantan H. Jana et al (P value 0.04), Ali Taghizadeh-Kermani et al (P value <0.001), Hala N. Hosni et al[10] (P value <0.05), B.V. Anuradha Devi et al (P value 0.001) and Maha E Salama et al [11] (P value <0.001).

5.7 Nottingham's Prognostic index

Though 100% strong immunoreactivity was seen in VPG, proving that CD 10 expression correlated well with prognostic index it could not attain statistical significance (p value 0.05). Comparing with other studies of Sayantan H Jana et al (p value of 0.01) and B.V. Anuradha Devi et al (P value 0.0023), this could be due to regional variations, number of patients in each group.

VI. Conclusion

The stromal expression of CD 10 showed statistically significant correlation with lymph node metastasis, histopathological grade.

No significant association could be established statistically for age, tumor size, histopathological subtype, mitotic grade and Nottingham's prognostic index, though increase in intensity of expression was noted. Further studies are needed to establish the CD10 stromal expression in invasive ductal breast carcinoma for predicting overall survival rates and disease free survival rates, post chemotherapy alterations, response to doxorubicin, its prodrugs and chemoresistance elaborately to add clarity to molecular understanding.

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