

RESEARCH ARTICLE

STROMAL CD 10 EXPRESSION IN INVASIVE CARCINOMA BREAST AND ITS CORRELATION WITH CLINICOPATHOLOGICAL FEATURES

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..... Abstract Manuscript Info

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Introduction: Tumor stroma plays a key role in modulating tumour invasion and metastasis in carcinoma breast. Matrix metalloproteinase CD10 may cause more invasiveness by facilitating matrix degradation and remodelling. Many studies showed higher expression of this marker in higher grade tumours and in tumours with lymph node metastasis.

Objectives: a) To study the expression of stromal CD10 in invasive b)To assess prognostic significance of Stromal breast carcinomas CD10 expression and its correlation with clinicopathological features

Materials and Method: Stromal expression of CD10 studied in 96 mastectomy specimens and the association with clinicopathological features evaluated using the chi-square test. P value <0.05 was considered statistically significant.

Observations: CD10 scoring was increased in high grade tumours which is statistically significant with(p value 0.017). No significant association could be established statistically for age, menopausal status, tumour size and lymph node status.

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Introduction:-

Breastcarcinoma is an epithelial malignancy in whichstroma plays an important role in tumour invasion and metastasis [1].In invasive breast cancer stromal markers are now emerging as novel marker for assessing the prognosis which have not been studied extensively till date. This emphasises the role of the current study of stromal prognostication in invasive breast carcinoma.CD10 is a zinc-dependent marker CD10 for metalloproteinase, expression of which is associated with biological aggressiveness in many epithelial malignancies [2, 3, 4, 5]. Since CD10 is a matrix metalloproteinase, it may support more invasiveness of the carcinoma cells by facilitating matrix degradation and remodelling. Few studies in literature discovered stromal expression of CD 10 and correlated this expression of CD 10 in stromal cells of breast carcinoma with other prognostic factors [2, 4]Attempts to establish a prognosis based upon generally accepted factors such as tumour size, grade and axillary lymph node status are successful to some extent, but still fail to accurately predict the clinical course for all patients because the intrinsic metastatic potential of cancer cells vary in each individual patient. Many studies have shown that varied survival rates among similar group of patients, explaining the heterogeneity of breast cancers and the need for further molecular research and a better stratification of patients. Hence the search for new prognostic markers that could elucidate more effectively the metastasizing potential and thereby get integrated as additional prognostic factor in the treatment algorithm of breast carcinomas remains an important goals for patient care. The

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aim of the study is to estimate the frequency of expression of stromal CD10 in invasive breast carcinomas and the prognostic significance of Stromal CD10 expression and its correlation with clinicopathological features like age, menopausal status, tumour size, grade and lymph node status.

Objectives:-

- 1. To study the frequency of expression of stromal CD10 in invasive breast carcinomas
- 2. To assess prognostic significance of Stromal CD10 expression and its correlation with other clinicopathological factors like age, menopausal status, and tumour size, grade and lymph node status.

Materials and Method:-

This study is aHospital based cross sectional study conducted at Department of Pathology, Government Medical College Thrissur.96mastectomy specimens done for invasive breast carcinoma were included in the study and samples insufficient for doing immunohistochemistry was excluded.Patient's age,menopausal status, tumour size, number of lymph nodes werenoted. Haematoxylin and eosin staining was done on 4 μ sections and grading doneby Modified Bloom Richardson's grading system.4 μ sections were taken on poly-L-Lysine coated slides and immunohistochemistry for CD10 done. Stromal expression of CD10 (positivity in>10% stromal cells considered positive) in invasive breast carcinoma was studied. CD10 scoring was done and scored as negative, weak positive and strong positive. Negative staining was given score 1(less than 10% stromal cells positive) weak positive staining was given score 2 (10–30% stromal positive cells/core) and strong positive staining was given score 3(>30% stromal positive cells/core).Data obtained was entered in Microsoft office excel 2010 sheet and analysed using software SPSS version16.0. The association between stromal CD10 expression and clinicopathological features evaluated using the chi-square test. P value <0.05 was considered statistically significant.

Observations:-

The age of the patient included in this study ranged from 33 to 78 years. The maximum number of patients was in the age group of 51-60 years. 68% ofpatients had attained menopause and 69% of patients had tumour size between 2and 5cm. 62 patients (65%) had MBR grade II and 21 patents had grade 3 (22%) and 13 patients grade1 (13%). Majority of the patients (49%) had lymph node with reactive change only (51%) 26% showed 1-3 lymph nodes, 15% had 4-9 lymph nodes and 8% had more than 8 lymph nodes. Majority of patient had strong CD10 positivity-Score3 (68%) 19% had score2 and13% had score1.

		FREQUENCY	PERCENTAGE	
	31-40	4	8	
	41-50	23	24	
AGE	51-60	34	36	
	>60	31	32	
	1	13	13	
	2	62	65	
MBR GRADE	3	21	22	
	1	13	13	
	2	18	19	
CD 10 SCORE	3	65	68	

Table 1:- Showing distribution of age, MBR grade and CD10 scoring.

The relation between MBR grade and CD 10 expression was statistically significant p-value 0.017

MBR Grade	CD10 score 1	CD10 score 2	CD10 score 3
Grade 1	4	4	5
Grade 2	4	13	45
Grade 3	5	1	15

Table 3:- Correlation of Tumor size, Age, Lymph node status and Menopausal status with CD10 Scoring.

		CD10 SCORE1	CD10 SCORE2	CD10 SCORE3
TUMOR SIZE	<2cm	2	1	4

	2-5cm	6	12	48
	>5cm	5	5	9
AGE	30-40	1	2	5
	41-50	5	3	15
	51-60	4	7	23
	>60	3	6	22
LYMPH NODE	no	6	10	33
	1-3	3	4	18
	4-9	3	4	7
	>10	1	0	7
MENOPAUSE	not attained	6	5	20
	attained	7	13	45

The relation between tumour size, Age, Lymph node metastasis, Menopausal status and CD 10expression was not statistically significant withp-value of 0.198,90, 0.632, 0.502respectively

Discussion:-

Breast cancer is one of the most common cancers among Indian women and is the leading cause of death in women. The increased mortality of breast carcinoma is attributed to metastatic disease.

A better understanding of the molecular basis of metastatic disease would have practical implications in the clinical areas of diagnosis, treatment and prognosis. Tumor stroma has an important role in the pathogenesis of carcinoma of breast. Stromal markers can be used for assessing the prognosis of breast cancer. CD10 expressing metalloproteinase in stroma degrade extra cellular matrixand collagen, providing a microenvironment favourable for invasion and metastasis. Expression of CD10 in stroma of carcinoma breast and its scoring can be used to asses the invasiveness of the malignancy and can be integrated as additional prognostic factor in the treatment algorithm of breast carcinomas.

In the present study 96 cases of invasive carcinoma breast were included. Age and menstrual status of the patient, size of the tumour, lymphnode metastasis and MBR grade were determined for each cases based on routine H&E section and all the cases were stained with the immunohistochemical marker CD10. CD10 expression of the stroma were scored based on percentage of stromal staining. Negative score if only 10% stromal cells are positive, weak positive if 10-30% stromal cells are positive and strong positive if >30% stromal cells are positive.

The most frequent age group in the present study is between 51 and 60 years and the patients ranged from 33 to 78 years. Out of 96 cases studied 8 cases belong to age group 31-40 years, 24 cases belong to age group 41-50 years, 36 cases belong to age group 51-60 years and 32 cases belong to age group >60 years. The mean age of the patient is 56 years. A study conducted by Vandana puri et al (6) in the year 2011 included patients from 30 to 80 years with a mean age of 48.5 years.Comparison of the CD10 expression with age, age group 51-60 years showed maximum association with positivity for CD10 expression. But it could not achieve statistical significance (P value 0.890). Fereshteh Mohammadizadeh et al (2012) in his study concluded that age parameter was not significantly associated with CD10 expression (p value 0.49).

In the present study 65 out of 96 patients were in the post-menopausal group. 58 of them showed positivity with CD 10 expression (13 were weakly positive and 45 were strongly positive) and no statistical correlation was achieved (P value 0.502). The study conducted by Ali Taghizadeh-Kermani et al(7) had equal distribution of patients with 50 in each group and showed higher CD 10 positivity in post-menopausal age group, but was statistically insignificant (P value 0.28). B.V. Anuradha Devi et al (9) had 33 out of 59 patients in pre-menopausal age, with 19 out of 33 showing positive CD 10 expression. But no statistical association could be proved (P value 0.21).66 out of 96 patients were having a tumour size 2 to 5 cm. 60 showed positive immunoreactivity with CD 10 (12 were weakly positive and 48 were strongly positive) but could not be prove a statistical relationship of CD 10 with tumour size. (P value 0.198). The study conducted by Keiichi Iwaya et al(10)had 86 out 110 patients having a tumour size less than 5cm. 16 out the 86 showed positive CD10 expression. The comparison of CD10 expression with tumour size had not been statistically associated (P value 0.82). The study conducted by Fereshteh Mohammadizadeh et al also compared tumour size with CD10 expression and found the association to be statistical significant (P value 0.01). Lymph node metastasis was analysed by evaluating total number of lymph nodes involved. 49 out of 96 patient had

reactive change lymph node and 33 out of them showed strong positivity for CD10. 25 patients had 1-3 lymph node metastasis and 18 out of them showed strong positivity for CD10. 14 patients had 4-9 lymph node metastasis and 7 out of them showed strong positivity for CD10 score.8 patients had >10 lymph node metastasis and 7 showed strong positivity for CD10.But there is no statistically significant correlation (P value 0.632).The study conducted by Fereshteh Mohammadizadeh et al, 23 out of 49 patients with no lymph node metastasis and 16 out of the 23 patients had positive CD10 expression. On comparison of CD10 expression with lymph node metastasis, statistical significance was proved (p value 0.02). In study conducted by Sayantan H. Jana et al,(9)30 out of 70 patients had lymph node metastasis showed no statistical significance (P value 0.18).The study conducted by B.V. Anuradha Devi et al,(8) 18 out of 59 patients had no lymph node metastasis. 10 out 18 had positive CD10 immunoreactivity. On statistical analysis the association was found to be significant (P value 0.0005).

In the study, 62 out of the 96 patients (65%) were grade2, 13 out of 96 patients (13%) were grade1 and 21 out of 96(22%) patients were grade3. 45 out of 62 grade2 tumour showed strong positive CD 10 expression. 22 patients belonged to grade 3 and 15 of them showed strong positive immunoreactivity with CD 10 expression. This shows that with increasing grade, the CD 10 expression increases potentially conveying it as a marker of aggressiveness of carcinoma. The relationship of MBR grade and the CD 10 expression revealed statistical significance. (P value 0.017).Nikita A Makretsov et al, similar to the present study, had 139 put of 258 patients in histopathological grade II. 100 of whom showed positive CD10 expression. The comparison of CD10 with grade showed statistical association (P value 0.02).Fereshteh Mohammadizadeh et al had 49 patients out of which 25 was in grade 2 and 20cases showed CD10 expression. The comparison was statistically proved to be significant (P value 0.004), similar to the present study showed 28 out of 70 patients in histopathological grade 2 and 16 cases showed CD10 positivity. Comparison of CD10 expression with tumour grade was associated significantly (P value 0.04), similar to the present study.

Conclusion:-

CD 10 expression increases with increase in tumourgrade conveying it as a marker of aggressiveness of carcinoma which is statistically significant (P value 0.017).No significant association could be established statistically for age, menopausal status, tumour size and lymph node status.

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