

CD10 expression by stromal cells in carcinoma of breast and its correlation with ER, PR, HER2neu and Ki67-A tissue microarray study in a tertiary care hospital

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Abstract

Introduction: CD10 is a metalloproteinase (Zinc dependent) which is expressed in stroma of various epithelial malignancies. It is associated with biological aggressiveness of the tumor. Till now very few studies has been undertaken correlating CD10 with other prognostic markers like lymphnode status, tumor grade, stage, ER, PR, HER2-neu and ki67 in breast carcinoma.

Aim: To see the CD10 expression in breast carcinoma and correlate it with ER, PR, HER2 neu and ki67.

Materials and Methods: 55 cases of carcinoma breast were diagnosed on histology. Tissue microarray blocks were prepared and Immunohistochemistry was performed for ER, PR, HER2neu, Ki67 and CD10.

Result: 32(58%) cases are CD10 positive and 23 (42%) cases are CD10 negative. Out of this 32 positive cases, 12 (22%) cases are weak positive and 20 (36%) cases are strong positive. CD10 is positively correlated with tumor grade. CD10 is negatively correlated with ER and PR status which is not statistically significant and no correlation is found between CD10 and HER2-neu. A positive correlation is seen between CD10 and ki67, but it is not statistically significant.

Conclusion: CD10 expression is positively correlated with Ki67 and increasing tumor grade and whereas inversely correlated with ER and PR status. No correlation is seen between CD10 with lymph node status and HER2-neu.

Introduction

Carcinoma breast is a growing menace world wide. It is taking its toll relentlessly. It is estimated that about 1,15,000 new patients are added and approximately 53,000 deaths occur in every year¹ due to carcinoma of breast. Human breast carcinomas are a heterogeneous group of tumors that are diverse in behavior, outcome and response to therapy.² prognostic factors like lymphnode status, grade, stage, ER, PR, HER2 neu are routinely performed in breast carcinoma.³

Though Breast carcinoma is an malignancy of epithelial origin, but stroma plays an important role in pathogenesis of progression of tumor and metastasis. Proliferation rate is also found to be a good predictor of aggressiveness of the tumor. Hence new markers such as Ki 67 gene over expression and CD10 have been added to the armament for the prognostication of these tumors. More recently, a combination of CD10 with the established four markers (ER, PR, HER2-neu, Ki67) has been shown to have a strong prognostic impact that is similar to that of gene expression assays that has been described in many studies.³ CD10 is a metalloproteinase (Zinc dependent). It is expressed in mature neutrophils, Pro B lymphoblast and bone marrow lymphoid stem cells. Various studies also revealed that stromal CD10

expression is associated with biological aggressiveness in many epithelial malignancies.¹⁶

Till now very few studies have been done correlating expression of CD10 with ER, PR, HER2neu and only one study has been done correlating CD10 with Ki67. So our aim was to study the stromal CD10 expression in breast carcinoma and correlating CD10 with ER, PR, HER2neu and Ki67.

Materials and Methods

Study was done in the Department of Pathology, KIMS, Bhubaneswar, Odisha from September 2015 to August 2017. It is a prospective study. 55 cases of carcinoma breast were selected on which modified radical mastectomy was performed and diagnosed on histology as invasive breast carcinoma, NST. The clinical data like age, gender, laterality of the tumor were noted. Grading and pathological TNM staging was done. Microarray blocks were prepared from the donor tissue blocks as described by Nazar⁴ et al. The desired area of tumor tissue was selected manually. Tissue microarray blocks are constructed. cylindrical tissue core biopsies was extracted from different donor paraffin blocks and re-embedded these in to single recipient block. Immunohistochemistry was performed for ER, PR, HER2-

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neu, Ki67 and CD10. Scoring was done for each of these according to the standardised scoring system. CD10 immunostaining was considered as negative when <10 % tumor cells showed staining, weak when there is diffuse weak staining or weak or strong staining in 10-30% tumor cells and strong when there was > 30% tumor cells with strong staining, according to the standard scoring criteria followed by Makretsov⁹ et al. Fibroadenoma was used as a standard positive control. Negative controls were prepared by omitting the primary antibody. Statistical analysis was done by Chi square test and Fisher's exact test. It was considered to be statistically significant when P value is <0.05.

Results

In our study mean age of the patient is 50.07 years (range-30-80years). Most of the patients in our study belong to tumor grade II (28/55 i.e, 51%) followed by grade III (25/55 i.e, 45%) and grade I (2/55 i.e, 4%). Majority of our cases belong to N0, 22/55(40%) of all. N1 and N3 has equal number of cases 12/55 (22%) each of cases. N2 has 9/55 (16%) cases. Majority of the tumors belong to size range of 2-3.9cm (44%), followed by 4-4.9 cm (16%) and 5-5.9cm (13%). Range of tumor size is from 1.5 - 10 cm. In the present study, 26/55(47%) of the cases are ER positive and 29/55(53%) are ER negative. 25/55(45%) cases are PR positive and 30/55(55%) cases are PR negative.31/55 (56%) of cases are HER2-neu positive and 24/55 (44%) are HER2neu negative. Of these HER2-neu positive cases, 2+ positivity is shown by 5(9%) cases and 3+ positivity is shown by 26 (47%) cases.20/55 (36 %) cases show <14% Ki67 or low score where as 35/55 (64%) cases show >14% Ki67 score or high score.

CD10 immunostaining is done on all 55 cases. Of these 32 (48%) cases are CD10 positive and 23 (42%) cases are CD10 negative. Out of this 32 positive cases 12 (22%) cases are weak positive and 20 (36%) cases are strong positive (Table 1).

Table 1: Expression of CD10

CD 10 Expression	No. of Cases (n=55)	Percentage (%)
Negative	23	42
Weak	12	22
Strong	20	36

There is a positive correlation is seen between CD10 expression and tumor grade which is statistically significant (p=0.045) and no correlation is seen between CD10 expression with lymphnode status. It is observed that ER negative case percentage rises with stronger CD10 expression (38 to 41%); whereas ER positive status decrease with stronger CD10 expression (42 to 31%). Hence, a negative correlation is observed between ER status and CD10 expression which is not statistically significant (p=0.742). There is negative correlation seen between CD10 and PR in our study but it is not statitically significant. There is increase in HER2-neu positive status with increase

in CD10 expression. However the opposite is not noticed in HER2-neu negative cases i.e, increase in CD10 expression is also seen with HER2-neu negativity. Hence, there is no correlation noted and also not statistically significant (p value =0.509). The possible reason for this could be that the cases scored as equivocal are not eventually followed up by FISH. CD10 expression increases when Ki67 values increases from 34% to 42% and expression of CD10 decreases when Ki67 value decreases from 50% to 25%. Therefore, it is concluded that there is a positive correlation exist between CD10 expression and Ki67.But the findings are not statistically significant (p=0.374) in our study possibly due to limited number of cases. (Table 2).

Table 2: Correlation of CD10 with Ki67

CD10 Expression	Ki67		Total
	Low	High	
Negative	10 (50%)	12 (34%)	22 (40%)
Weak	5 (25%)	8 (23%)	13 (24%)
Strong	5 (25%)	15 (42%)	20 (36%)
Total	20 (36%)	35 (64%)	55

Discussion

In this study, 32 (48%) cases are CD10 positive were as 23 (42%) cases were CD10 negative. Out of this 32 positive cases, 12 (22%) cases are showing weak positivity and 20 (36%) cases are showing strong CD10 positivity. CD10 is positively correlated with tumor grade and the value was statistically significant (p=0.045). Present study is in accordance with the studies done by Makretsov et al.³ (p=0.01), Hosni¹⁰ et al. (p<0.0002), Ahmed¹¹ et al. (p<0.0002), Jana¹² et al. (p=0.04), Emad¹³ et al. (p<0.001), Mohammadzadeh et al.¹⁴ (p=0.004), Tagizadeh¹⁵ et al (p<0.001). Positive correlation between CD10 and tumor grade was seen in the study done by Puri¹⁶ et al. and no correlation was found in the study done by Ogawa¹⁷ et al. (2002). Our study showed a negative correlation with ER status which is in accordance with studies done by Makretsov et al. (p=0.002), Jana et al. (p=0.0001), Mohammadzadeh et al., Tagizadeh et al. (p=0.003) and Emad et al. (p<0.001). The studies by Hosni et al. and Ahmed et al. do not show any correlation between the two. There was negative correlation seen between CD10 and PR in our study but was not statitically significant and such was described by Puri et al., Mohammadzadeh et al. Studies by Makretsov et al., Hosni et al., Ahmed et al., Jana et al., Tagizadeh et al. did not show any correlation between CD10 expression and PR status. But Emad et al. in his study showed significant correlation between CD10 and PR(p<0.0001). In our study, there is no correlation found between CD10 and HER2-neu studies done by Makretsov et al., Hosni et al., Ahmed et al. and Tagizadeh et al also showed the similar findings. However it was statistically significant in studies done by Puri et al. (p=0.0001), Jana et al. (p=0.0057), Mohammadzadeh et al. and Emad et al. (p<0.001). Positive correlation is seen between CD10 and Ki67 but it is not statistically significant .One study has

been performed by Puri et al correlating CD10 expression with Ki67 and it is statistically significant($p=0.027$).

No correlation is found in our study between CD10 and lymph node. Similar findings were also noted in the studies done by Makretsov et al., Hosni et al. and Jana et al. Statistically significant correlation was found in the study performed by Ogawa et al ($p=0.038$), Mohammadzadeh et al.($p=0.02$), Tagizadeh et al. ($p<0.001$) and Emad et al.($p<0.001$).

Conclusion

In our study CD10 positivity is seen in 48% of breast carcinoma cases. Its expression is positively correlated with increasing tumor grade and Ki67 status but it is inversely correlated with ER and PR status. This suggests that CD10 can be used as an independent marker for predicting poor prognosis and it can be used as a target for development of novel therapies. No significant correlation is achieved between CD10 and tumor size, lymph node status, HER2-neu status.

Though positive and negative correlations are noted in our study but statistical significance is not achieved probably because of limited number of cases. To see the correlation between stroma and hormonal expression in breast carcinoma further studies with large number of cases are recommended for better treatment options particularly in triple negative breast carcinomas.

Conflict of Interest: None.

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