Cd10 as a Prognostic Stromal Marker in Breast Carcinoma

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Abstract:
Aims and objectives: *to study the stromal expression of cd10 in breast carcinoma, relationship with certain prognostic factors like 1.age and 2.nottingham's grade, to study the role of stroma in the pathogenesis of breast cancer.*
Materials and methods*: a total of 75 cases of breast cancer were included in the study. Representative sections were taken and hematoxylin and eosin staining was done. Immunohistochemistry was performed with cd10. Stromal expression of cd10 (>10% stromal positivity was considered positive) in invasive breast carcinoma was noted and was statistically analyzed with different known prognostic markers of breast carcinoma.*
Results*: stromal expression of cd10 was found to be significantly associated with increasing tumor grade (p = <0.0001). No correlation was found between cd10 overexpression and age of the patient.*
Conclusion*: the stromal expression of cd10 as well as its intensity has significant correlation with higher histological grade(grade 3), no correlation between cd10 expression and age of the patient. There is wide expression of cd10 in desmoplastic stroma of breast carcinoma and negative immunoreactivity in stromal cells of normal breast.*
Key words: *cd10 stromal expression, prognostic role*

I.   Introduction

Breast carcinoma is the commonest cancer in women. It is the leading cause of death in women, with more than one million cases occuring worldwide annually (1). Breast cancer represents an important public health issue, having a high occurence worldwide, with an obvious increasing tendency (2).

Over the last few decades there have been better advances in breast cancer. Early detection and skillfull treatment has lead to a significant decline in breast cancer deaths. It has also made improved outcome for women living with the disease. Breast cancer is no longer seen as single disease but rather a multifaceted disease consisting of diverse biological subtypes with distinct natural history. Breast cancer presents as a varied spectrum of clinical, pathological and molecular features with diverse prognostic and therapeutic implications.

Estrogen is the steroid hormone, responsible for development and maturation of primary and secondary sexual characteristics in females (3). Estrogen has an important role in pathogenesis and development of breast cancer (4).

In india, breast cancer is the **second most common** cancer in women after cervical cancer. However in indian metropolitan areas, breast cancer has become the most common cancer than cervical cancer (5). Incidence of breast cancer is 21% for the year 2015.

After remaining constant for many years, the incidence of breast cancer has begun to increase. This is due to detection of increased number of cases by means of introduction of **mammographic screening** in early 1980's (6). The main aim of screening is the detection of in situ carcinomas small predominantly er positive invasive carcinomas. Dcis is almost exclusively detected by mammography, providing an explanation for increase in the diagnosis of dcis since 1980. In the age of screening, the number of stage i cancers (small node negative carcinomas) has increased in frequency, while the number of large node positive or advanced stage breast carcinomas has fallen (6)

Cd10 is a 90-110 kda cell matrix metalloproteinase, which is a membrane bound zinc dependent endopeptidase. It is also called as "common acute lymphoblastic leukemia antigen" (7), "neutral metalloendopeptidase" in kidney and "enkephalinase" in brain (8). Matrix metalloproteinases are metallopeptidases which cleaves extracellular matrix proteins and play an important role in tissue remodeling. In normal breast, it lowers the extracellular concentration of many peptides available for receptor binding and thereby regulates their physiological action. It cleaves signaling proteins that usually promotes differentiation of early common progenitors to luminal epithelial progenitor or myoepithelial progenitor, which gives rise to luminal and myoepithelial cells and thereby maintains the early progenitor population (9).

In carcinoma, absence of cd10 expression from myoepithelial cells leads to progression from dcis to invasive carcinoma and its stromal expression correlates with poor prognosis, higher grade and negativity of estrogen receptor.

II. Methodology

The study was done during the period january 2014-july 2015. It was carried in patients with confirmed diagnosis of carcinoma breast. The study was approved by ethical committee of stanley medical college.

The study sample comprised of 75 breast cancer patients. Cases were chosen from department of general surgery, stanley medical college and hospital. Age of the patient and histological grading was obtained for all cases. 75 patients were screened for cd10 through immunohistochemical assay.

10% buffered formalin was used for fixing the specimens. The tissues were processed in various grades of alcohol and xylol using automated histokinette. Paraffin blocks were prepared and section of 5 micron thickness were cut in semiautomatic microtome using disposable blades and stained with hematoxylin and eosin. Suitable blocks were chosen for ihc.

Sections for immunohistochemistry were also cut in semiautomatic microtome using disposable blades. Slides coated with chrome alum were used. Sections were subjected to antigen retrieval using pressure cooker technique using tris edta (ph 9.2) buffer solution and then treated by hrp (horse radish peroxidase) polymer technique. Cd10 staining and intensity was assessed by the following table,
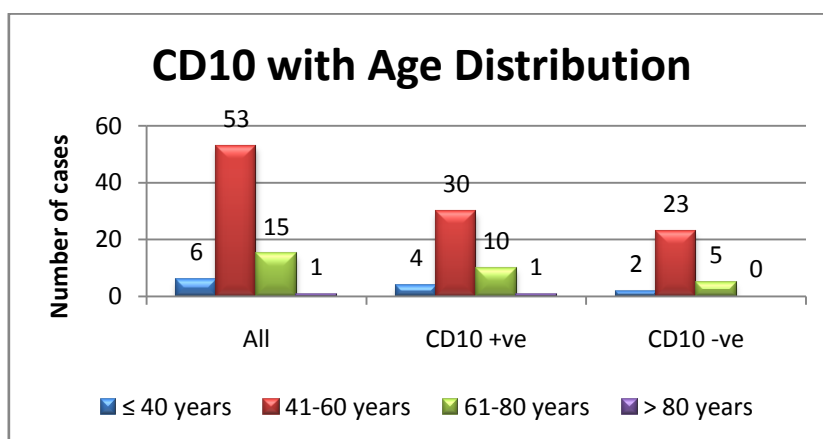
Score	Cd10 staining
Negative	<10% stromal positive cells/core
Weak	10-30% stromal positive cells/core
Strong	>30% stromal positive cells/core

Observation and results

in this study, we included 75 patients diagnosed with infiltrating ductal carcinoma fulfilling the inclusion and exclusion criteria.
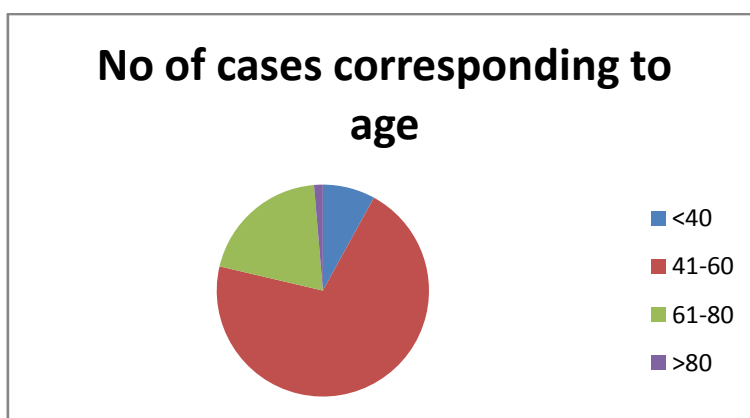

Graph 1 : Age Wise Distribution Of Number Of Cases

Graph 2: comparison of cd10 with age

Out of 6 patients (8%) among those aged less than 40 years, 4 were cd10 positive and 2 were cd10 negative. In the age group between 40-60 years (70.67%), out of 53 patients, 30 were cd10 positive and 23 were cd10 negative. In the age group of 61-80 years (20%), out of 15 patients, 10 were cd10 positive and 5 were cd10 negative. In the age group of more than 80 years (1.33%), 1 patient was included in the study and was cd10 positive. Comparison with age was not statistically significant (p value= 0.134671)

2. Tumor grade
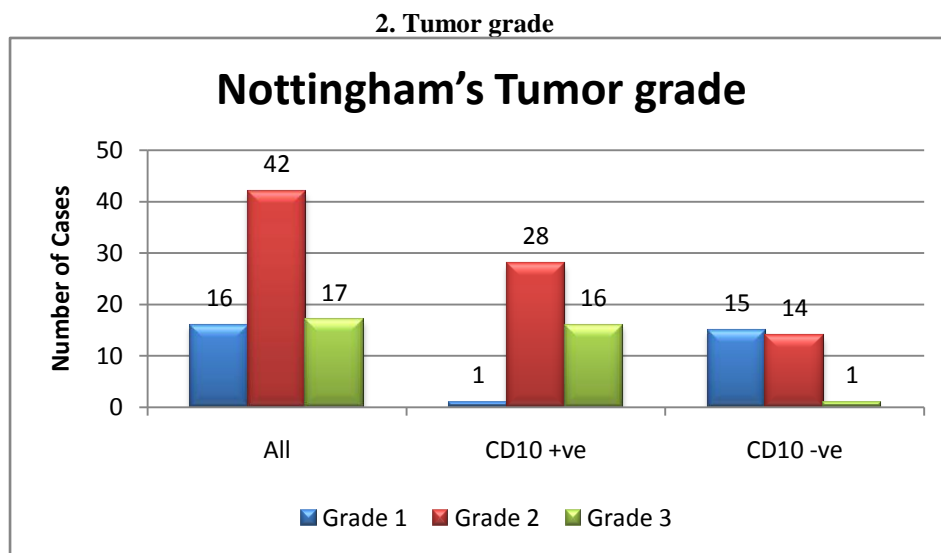
Graph 3: comparison of cd10 with histological grading

Out of 16 patients with histological grade, 1 was cd10 positive, 15 were cd10 negative. Out of 42 patients with histological grade 2, 28 were cd10 positive and 14 were cd10 negative. Out of 17 patients with grade 3, 16 were cd10 positive and 1 was cd10 negative. The correlation was statistically significant (p value <0.0001)
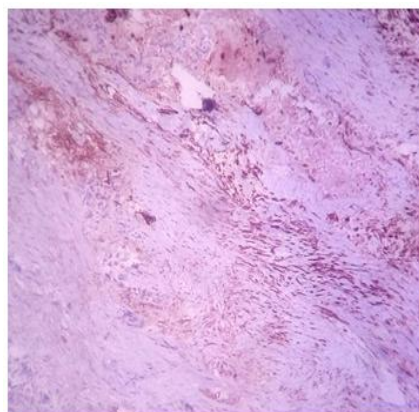

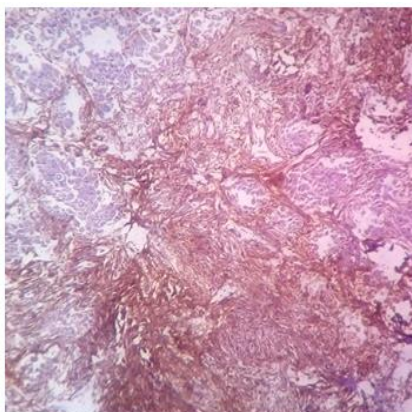**Figure 1:** CD10 weak positivity   **Figure 7**: CD10 strong positivity

III.   Discussion

1.   Age distribution

The age group of patients included in our study varied from less than 40 to more than 80 years with most of the patients belonging to 41-60 years (**graph 1**). Mean age was 54 years

sayantan et al (8) in the year 2014 conducted a study which included patients with age less than 40 to more than 60 years (56). A study conducted by vandana puri et al (7) in the year 2011 included patients from 30 to 80 years with a mean age of 48.5 years (58) in the year 2013, a study conducted thomas s babu rj et al (10) included patients from 34 to 55 years with a mean age of 45 years (60)

2.   Comparison of cd10 with age

In this present study, 53 out of 75 patients (70.67%) belonged to age group 41-60 years. Out of 53 patients, 30 were cd10 positive and 23 were cd10 negative. Number of positive cases increased as the age advances but as overall when comparing patients of all age groups, comparison with cd10 positivity was not statistically significant (p value – 0.134671)

Name of study	Age group	Cd10 positivity	P value
Present study	41-60 years	30 out of 53	0.134671
Sayantan h jana et al (9)	40-60 years	19 out of 45	0.3572
Ali taghizadeh- kermani et al (11)	41-60 years	44 out of 67	0.21

3. Comparison of cd10 with histological grading

In the present study, out of 75 cases, 16 (21.33%) cases belonged to grade 1, 42 (56%) cases belonged to grade 2 and 17 (22.67%) cases belonged to grade 3 (**graph 3**). Out of 17 grade 3 cases, 16 (35.56%) were cd10 positive. The comparison between grade and cd10 was statistically significant (<0.0001)

Name of study	Grade 3 cases	Cd10 positivity	P value
Present study	17	3	<0.0001
Sayantan h jana et al (9)	22	13	0.0413
Ali taghizadeh- kermani et al (11)	28	26	<0.001
Nikita a makretsov (12)	68	62	0.02
Keiichi iwaya et al (8)	22	3	0.488

IV.   Conclusion

➢ The stromal expression of cd10 has significant correlation with **higher histological grade** (**grade 3**)
➢ There is no correlation between cd10 expression and age of the patient
➢ The intensity of cd10 positivity also increased with increasing histological grade
➢ There is wide expression of cd10 in desmoplastic stroma of breast carcinoma and negative immunoreactivity in stromal cells of normal breast

This study highlights the role of stromal cd10 expression in predicting tumor response and prognosis and therefore cd10 could be included as a routine marker before giving chemotherapy

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