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Original Article

Immunohistochemical expression of CD10 in invasive breast carcinoma: A clinic-pathologic study

Pathology

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ABSTRACT:

Background: Prior research has established a correlation between CD10 and the biological aggressiveness exhibited by many human malignancies.

Objective: This research aimed to assess CD10 expression in invasive breast carcinoma and its correlation with clinic-pathological characteristics.

Methodology: This descriptive cross-sectional study included 60 cases diagnosed as invasive breast carcinoma, aged between 30 and 70 years. They were submitted to the histopathology lab at Al-Zahraa University Hospital. An immunohistochemical method was used to show expression of CD10 in the cases of invasive breast carcinoma.

Results: In 78.4% of the cases, the expression of CD10 was detected in the cytoplasm of stromal fusiform cells (46.7% as weak expression and 31.7% as strong expression). The incidence of stromal CD10 positivity was considerably higher in tumors that had metastases to lymph nodes ($p = 0.038$), a notable quality with increased tumor differentiation ($p \leq 0.05$), and tumor size ($p = 0.017$). Additionally, CD10 correlated with estrogen receptor (ER) expression ($p \leq 0.05$), progesterone receptor (PR) expression ($p \leq 0.05$) and Ki-67 expression ($p \leq 0.05$).

Conclusion: These outcomes revealed that the stromal CD10 expression may serve as an independent prognostic indicator in the advancement and spread of breast cancer and may participate in the progression of novel therapies for breast carcinoma.

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Keywords: CD10; Invasive breast carcinoma; molecular classification; prognosis.

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INTRODUCTION

In 2015, breast cancer caused an estimated 570,000 fatalities, making it as one of the most prevalent malignancies affecting women globally [1]. It accounts for 15% of annual casualties globally and is the primary cause of cancer-related fatalities [2]. Invasive (infiltrating) cancer of the ducts is by far the most prevalent histologic profile of invasive breast carcinoma. According to the World Health Organization classification which is the most applied classification for invasive breast malignancies [3]. There is limited research regarding the predictive significance of innovative stromal markers like CD10. A prevalent severe lymphoblastic antigen, CD10 which is metalloproteinase dependent on zinc, is frequently observed in mature neutrophils, stem cells of bone marrow lymphocytes, pro B lymphoblasts, cancer of renal cell, stromal sarcomas of the endometrium, and different subtypes of lymphoma. There is evidence that stromal of CD10 expression corresponds to biologically aggressive behavior in range of epithelial cancers, including phyllode tumors [4]. This research aimed to appraise the expression of the stromal marker CD10 in cases of invasive breast carcinoma and estimate its correlation with various clinic-pathological parameters.

PATIENTS AND METHODS

This descriptive cross-sectional research included 60 breast specimens diagnosed with invasive breast carcinoma. The specimens from females aged 30 and 70 years were selected from those submitted to the histopathology laboratory at Al-Zahraa University Hospital according to the predetermined inclusion and exclusion criteria.

Inclusion criteria

1. Age: from 30 to 70 years.
2. Modified radical mastectomy specimens.
3. Complete hormonal status (ER, PR, and HER2 neu).

Exclusion criteria

1. Tru cut breast biopsy.
2. Post-chemotherapy mastectomy specimens.
3. Age less than 30 or more than 70.

4. Post radiotherapy.
5. Insufficient clinical data.

Different clinical and pathological parameters were collected for each case–including patient age, lymph node metastasis, tumor size, histological grade, the receptor for hormone, HER2 neu status, and ki-67 expression. Then, cases were classified according to molecular classification, into four groups depending on the immunohistochemical status of estrogen receptors (ER), progesterone receptors (PR), HER2, and Ki67 expression as defined by Goldhirsch et al. [5]: luminal A (ER+ and/or PR+, HER2 neu -, low Ki67), luminal B (ER+ and/or PR+, HER2 neu + and/or high Ki67), HER2 over-expressing (ER-, PR-, HER2 neu+), and triple-negative (ER-, PR-, HER2 neu -).

Analysis of CD10 expression

One section of the tumor was sliced and placed on positively charged slides for the subsequent immunohistochemical staining. The staining of CD10 in the stromal cells of the tumor was performed using the standard immune-peroxidase method with DAKO auto stainer link 48. A ready-to-use monoclonal mouse Anti-human CD10 clone 56C6 (Dako-Denmark) was utilized for this purpose. As a positive control for CD10, a section of normal breast tissue was included. To establish a negative control, the primary antibody was omitted from the staining process.

Evaluation of CD 10 expression

Two pathologists assessed the immunostaining outcomes in the cytoplasm of the stromal cells and scored in a semi-quantitative manner. The scoring system categorized staining as negative, weak (either weak or strong staining in less than 30% of stromal cells per slide), or strong (staining observed in more than 30% of stromal cells per slide) [6, 7]. Subsequently, the results were compared with various prognostic factors (patient age, lymph node status, tumor size, histological grade, the receptor for hormone, HER2 neu status, and ki-67 expression.

Statistical analysis

The gathered data were examined utilizing the statistical package for Social Sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). Furthermore, numbers and percentages were used to represent Qualitative variables. Qualitative data from groups were contrasted utilizing the Chi-square test and the Fisher's exact test in cases where the anticipated score in any given cell was below five. The margin of error = 5%, confidence level = 95% and the significance level was determined at p-value $\leq$ 0.05 was considered statistically significant, while a p-value > 0.05 was considered statistically insignificant.

RESULTS

CD10 expression was identified within the stromal cells' cytoplasm as weak staining in 46.7% of all cases (Figure 1) while 31.7% displayed strong cytoplasmic staining of stromal cells, as illustrated in (Figure 2), and showed brownish staining in the myoepithelial cells of normal ducts, but no expression in tumor cells as shown in Figure 3.

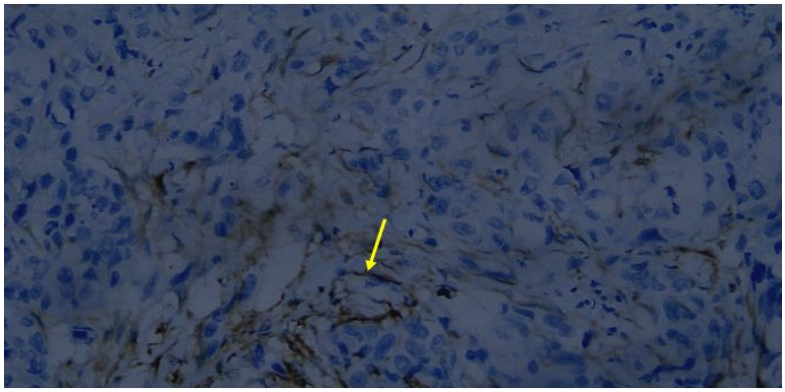

Figure (1): CD10 weak positive staining in stromal cells (The yellow arrow revealed the brownish cytoplasm in stromal cells of cancer (less than 30% percent of all tumor cells in the slide (magnification power x200).

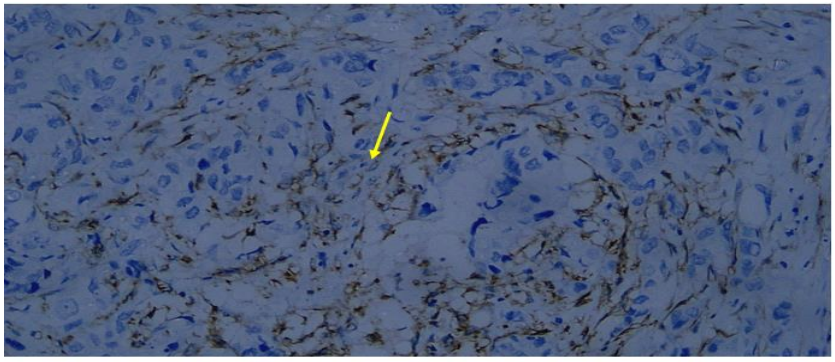

Figure (2): CD10 strong positive staining in stromal cells around the malignant cells (The yellow arrow demonstrates brownish cytoplasm in stromal cells of cancer (in all stromal cells around tumor cells in the slide (magnification power x200).

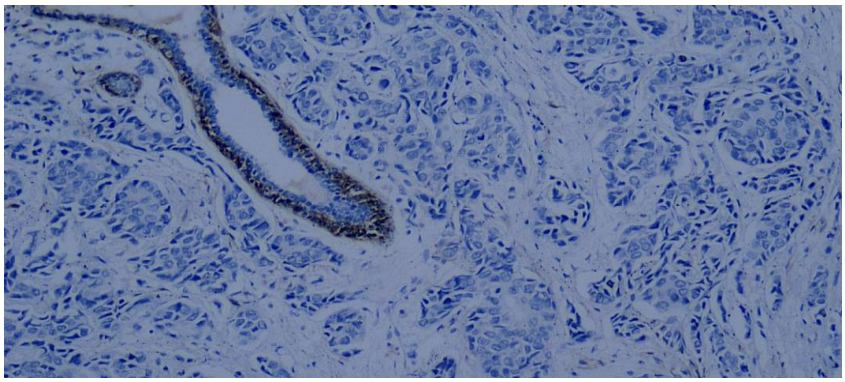

Figure (3): CD10 showed negative staining in stromal cells but strong in myoepithelial cells (x100). Stromal CD10 positivity was observed with greater frequency in cases of invasive duct carcinoma accompanied by lymph node metastasis, larger tumor size, and higher histological grade.

Table (1): Correlation of CD10 with different clinic-pathological parameters

Clinic-pathological Parameter	Total cases n= 60 no. (%)	CD10 expression			p-value
		Negative n=13 (21.7%) no. (%)	Weak n=28 (46.6%) no. (%)	Strong n=19 (31.7%) no. (%)	
Age distribution					
30-40 years	10(16.7%)	3 (23.1%)	5 (17.8%)	2 (10.5%)	>0.05
>40-50 years	22(36.7%)	8 (%)	10 (35.7%)	4 (21.0%)	
>50-60 years	13(21.6%)	0 (0.0%)	7 (25%)	6 (31.6%)	
>60-70 years	15(25%)	2 (15.4%)	6 (21.%)	7 (36.8%)	
Tumor size					
T1	6(10%)	3 (23.1%)	3 (10.7%)	0 (0.0%)	<0.05*
T2	31(51.6)	9 (69.2%)	15 (53.6%)	7 (36.8%)	
T3	23(38.4%)	1 (7.7%)	10 (35.7%)	12 (63.1%)	
Tumor grade					
I	9(15%)	7 (53.4%)	2 (7.1%)	0 (0.0%)	<0.05*
II	26(43%)	6 (46.1%)	15 (53.6%)	5 (26.3%)	
III	25(41.6%)	0 (0.0%)	11 (39.3%)	14 (73.7%)	
LN					
Negative	16(26.6%)	5 (38.4%)	10 (35.7%)	1 (5.3%)	<0.05*
Positive	44(73.3%)	8 (61.4%)	18 (64.3%)	18 (94.7%)	
ER					
Negative	29(48.3%)	(0.0%)	13 (46.4%)	16 (84.2%)	<0.05*
Positive	31(51.6%)	13 (100%)	15 (53.6%)	3 (15.8%)	
PR					
Negative	29(48.3%)	(0.0%)	13 (46.4%)	16 (84.2%)	<0.05*
Positive	31(51.6%)	13 (100%)	15 (53.6%)	3 (15.8%)	
Her2					
HER2 (-ve) Score 0 or 1	40(66.6%)	10 (76.9%)	20 (71.4%)	10 (52.6%)	>0.05
HER2 (+ve) Score 2 or 3	20(33.3%)	3 (23.1%)	8 (%)	9 (74.4%)	
Ki-67					
<20%	22(36.6%)	10 (76.9%)	10 (35.7%)	2 (10.5%)	<0.05 *
>20%	38 (63.3%)	3 (23.1%)	18 (64.3%)	17 (89.5%)	
Molecular sub type					
Her2+	13 (21.7%)	(0.0%)	4 (14.3%)	9 (74.4%)	<0.05 *
Luminal A	19 (31.7%)	10 (76.9%)	7 (25%)	2 (10.5%)	
Luminal B	13 (21.7%)	3 (23.1%)	9 (32.1%)	1 (5.3%)	
TN	15 (25.0%)	0 (0.0%)	8 (28.6%)	7 (36.8%)	

LN: Lymph node, ER: Estrogen receptor, PR: Progesterone receptor, TN: Triple negative, Using: x^2: Chi-square test & FE: Fisher's Exact test for number (%), *: Significant p-value (<0.05).

The results revealed that CD10 expression was high in stromal cells of tumors with the negativity of hormonal status and without HER2expressions. Furthermore, it demonstrated weak expression with a high KI-67 expression. All hormonal status is statistically significant with CD10 expression, estrogen receptor expression ($p < 0.05$), progesterone receptor expression ($p < 0.05$).

Among the 60 invasive breast carcinoma cases investigated, nineteen cases (31.7%) were classified as luminal A, 13 cases (21.7%) as luminal B, 13 cases (21.7%) as HER2 neu overexpression, and 15 cases (25%) as triple negative. The investigation of CD10 expression in stromal cells following molecular subtypes portrayed strong expression of CD10 with HER2 neu overexpression in and weak and strong CD10expression with triple-negative subtypes.

DISCUSSION

The markers of the carcinomatous stroma acquire more and more predictive interest in the study of several types of cancer. CD10 was recognized in leukemia as a prevalent acute lymphocytic leukemia antigen and has been extensively investigated for the last four decades. In addition, CD10 is expressed in many non-hematological malignancies, including genitourinary, gastrointestinal, female reproductive system, breast, lung, thyroid, and kidney cell cancers[8]. In certain types of breast cancer, stromal cells exhibit the expression of CD10. It is well established that the stromal expression of CD10 correlates with the aggressiveness of numerous epithelial cancers. Many studies have investigated the correlation between CD10 stromal expression and tumor prognosis[4]. This research was conducted to assess expression of the stromal marker CD10 in patients with invasive breast carcinomas and its relation to different clinic-pathological parameters.

The age group involved in the current research ranged 30-70 years. This research did not identify any statistically correlation between CD10 and patient age with a p-value >0.05. This agrees with the study conducted by Gaffoor et al.[9] (p=0.25), Sadaka et al. [10](p=0.99), Jana et al. [11] (p= 0.36), and Pradhan et al. [12] (p=0.988),which all demonstrated that the association of the CD10 expression with the increasing age was not statistically significant.

This research demonstrated a significant association between stromal CD10 expression and the size of malignant tumors ($p<0.05$); several studies have proven a positive correlation between stromal CD10 labeling and tumor size >20mm, as in the studies of Dhouha et al. [13] (p= 0.015), Devi et al. [14](p= 0.03), and Taghizadeh-Kermani et al. [15] ($p<0.05$).

This study demonstrated statistically significant higher frequency of LN metastasis in the positive, strong CD10 group than in either negative or weak CD10 group, with a p-value of <0.05. Several studies have demonstrated that the stromal expression of CD10 is significantly more common in patients with lymph node metastasis, as in our study such as Dhouha et al. [13] (p=0.009), Dhande et al. [4]($p<0.01$), Louhichi et al. [6]($p = 0.01$),Vo et al. [8]($p = 0.004$), and Devi et al. [14]($p<0.001$). Given the significant role that tumor size and nodal status play in determining the stage of breast carcinoma, these findings regarding the meaningful connection between the tumor size and stromal CD10 expression, and nodal involvement indicated that stromal CD10 expression strongly influences the aggressive behavior of breast carcinoma. Furthermore, this conclusion is reinforced by the significant relationship between tumor grade and stromal CD10 expression.

Several studies have demonstrated a statistically noteworthy correlation between the stromal expression of CD10 and the high grade of carcinoma in this research, illustrating statistically substantial association ($p>0.05$).This suggests that CD10 is an inadequate prognostic proxy, as in the studies of Gaffoor et al. [9],Dhouha et al.[13](p=0.002), Louhichi et al. [6],Sadaka et al. [10], and Girdhar et al. [16]. On the other hand, the investigations by Iwaya et al. [17], Puri et al. [18],and Vo et al. [8] showed the absence of a correlation between the tumor grade and the expression of CD10.

Concerning hormone receptors, several studies have demonstrated that the stromal expression of CD10 is correlated with ER negativity, as in this study ($p<0.05$) and additionally in the studies of Gaffoor et al.[9], Dhouha et al.[13], Rizk et al.[19], Sadaka et al.[10], Vo et al.[8], and Taghizadeh-Kermani et al. [15].

This study demonstrated a statistically significant higher frequency of PR negativity in the negative CD10 group than in the positive weak and robust groups, with a p-value <0.05 .Some studies have proven a substantial association between CD10 expression and PR negativity[8, 10, 19, 20].This result is inconsistent with those of Makretsovet al. [21]and those of our series (p=0.3)[7, 21].

The current study demonstrated no statistically significant association between CD10 and HER2 status, with a p-value of 0.275, in contrast to several studies that illustrated a significant relationship between CD10 expression and amplified HER2 status [10, 15, 22]. On the other hand, Makretsovet al. [21], Rizk et al. [19], Ziadiet al. [7], and Mohammadizadeh et al. [20] did not find any correlation between these two parameters, as in this study.

This study demonstrated a statistically significant higher association between Ki-67 and stromal labeling of CD10 with a p-value <0.05. Regarding the level of Ki-67, few studies have studied this parameter [8, 13, 18] and found that a level of Ki-67≥14% was significantly associated with stromal labeling of CD10 ($p = 0.001$), as in this study.

The results revealed a statistically significant higher frequency of HER2+ve and TN in the solid positive CD10 group than in the negative CD10 group, with a p-value <0.05. This agrees with the studies of Gaffoor et

al. [9] in which triple-negative cells exhibited substantially higher expression of CD10 (66.6%) and HER2 varieties (100%; p = 0.001), Dhouha et al.[13] (p=0.009)in triple-negative cases, Pradhan et al. [12], Jana et al. [11] (p=0.0004), Kandamuthan et al. [23], which were significantly associated with CD10 stromal overexpression in triple-negative cases. This was discordant with the research of Louhichi et al.[6], which portrayed that the relationship between CD10 expression and triple-negative tumors was not statistically significant (*>0.05*).

CONCLUSION

According to the results of this research, CD10 stromal expression was substantially correlated with tumor size, LN metastases, and high tumor grade but not with patient age. Concerning hormonal receptors, this study demonstrated a highly positive relationship between CD10 expression and ER/PR negativity; however, no association was detected between CD10 and HER2 status. In addition, it demonstrated a statistically significant higher association between the biochemical marker Ki-67 and the stromal labeling of CD10. CD10 could be recommended to be incorporated into routine histopathology reports, as it may serve as an independent prognostic indicator. Moreover, CD10 has the potential to serve as a target for further drug development. Further prospective clinical investigations, characterized by extended follow-up periods and survival analysis, are imperative to validate these results and facilitate the exploration of novel therapeutic approaches.

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الملخص العربي

دراسة هستوكيميائية مناعية عن ظهور(سي دي 10) في نسيج سرطان الثدي التوغلي : دراسة باثولوجية اكلينية

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ملخص البحث

الخلفية: اثبتت الداراسات السابقة وجود علاقة بين ظهور سي دي 10 وسرعة انتشار العديد من الاورام الخبيثة

الهدف: يهدف هذا البحث الي تقييم ظهور ســـي دي 10 في ســـرطان الثدي التوغلي وارتباطه بخصـــائص المريض

الطرق: شملت هذه الدراسة علي 60 مريضا تتراوح اعمارهم بين 30و70 سنة وهذه الحالات تم تشخيصها علي انها سرطان ثدي متوغل في معمل الباثولوجي بمستشفي الزهراء الجامعي وتم الكشف عن نسبة وجود سي دي 10 في نسيج سرطان الثدي المتوغل باستخدام الطرق الهستوكيميائية المناعية.

النتائج: قد ظهر ســـي دي 10 في ســـيتوبلازم الخلايا المغزلية المحيطة بالورم بين 78.4% من الحالات و قد تراوحت نسبه ظهور ال سي دي 10ما بين ظهور قوي فى 31.7% وظهورضعيف في46.7 % وقد كانت نسبة ظهور ال سي دي 10 اكثر احصـائيا في الاورام التي بها انتشـار للورم الرئيسـي الي الغدد اللمفاوية ($p\leq0.05$) والاورام ذات الحجم الكبير($p\leq0.05$) بالاضـــافة الي ارتباط ظهور ســـي دي 10بوجود مســـتقبلات لهرمون الاستروجين والبروجستون ونشاط الورم ($p\leq0.05$).

الإستنتاجات: كشفت نتائج هذة الدراسة الي ظهور سي دي 10 في الاورام ذات الحجم الكبير و الاورام المنتشرة الي الغدد اللمفاوية مما يعني وجود دور لظهور ســـي دي 10 في انتشـــار ســـرطان الثدي وايضـــا قد تؤدي الي اكتشاف علاج جديد لسرطان الثدي.

الكلمات المفتاحية : سي دي 10، سرطان الثدي المتوغل ،التصنيف الجزيئي ،مستقبل الورم.

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