Immunohistochemical localization of Transferrin in breast lesions

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Citation

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Abstract

This study was conducted to evaluate staining pattern of transferrin in benign and malignant lesion of breast. Sixty cases of breast lesions including 30 cases each of benign lesions and infiltrating ductal carcinoma breast formed the material for study. Immuno staining for transferrin was done by standard streptavidin biotin peroxidase method. Majority of benign lesions showed either negative or weak staining pattern while majority of malignant lesions gave consistent reaction with transferrin. Staining pattern of transferrin is more of prognostic significance in breast tumors than diagnostic value and may facilitate the decision making process in the treatment of individual cases of carcinoma breast.

INTRODUCTION

Breast lesions are broadly divided into three categories namely benign breast lesions, carcinoma in situ and carcinoma of breast. Benign breast lesions include three broad categories of lesions namely non-proliferative, proliferative without atypia and atypical hyperplasia.[1] Majority (70-80%) of carcinomas are of invasive ductal type.[2]

Transferrin is the major iron transporting protein in plasma. It is a potential marker for identification of dividing cell detected by routine immunohistochemistry. Its expression correlates with the cellular proliferation being highest in rapidly dividing cells and much lower in resting and terminally differentiated cells.[3]

The study was conducted to assess the pattern of transferrin localization in benign and malignant lesions along with the correlation between transferrin expression and histological grading of infiltrating ductal carcinoma breast.

MATERIAL AND METHODS

Sixty cases of breast lesions were taken up for present study. Formalin fixed, paraffin embedded sections stained with conventional method of hematoxylin and eosin (H & E) were examined for histological typing/grading. Grading of infiltrating ductal carcinoma was done by modified Richardson and Bloom method.[4,5]

Immunohistochemistry was performed on 3-4 microns thick sections on Poly-L-lysine coated slides. Antigen retrieval was done in microwave with sodium citrate solution (PH=6). Primary antibody DAKO code no.: A0061 (Rabbit Anti-Human transferrin antigen) detection was done by standard streptavidin biotin peroxidase method using DAKO LSAB-2 system Kit (K-0673).

Positive reaction was in the form of fine granules in cytoplasmic membrane as well as in the cytoplasm. The extent of staining reaction was determined by semiquantitative grading as consistent, moderate and weak.

1. Consistent: Lesions with majority of cells (>50%) showing positive staining.

2. Moderate: Lesions in which approximately 50% of cells were positive for transferrin (>10% & <50%)

3. Weak Only few cells were reactive.

Statistical analysis of the data was performed using Chi-square test with Yates correction. ‘P’ value of <0.05 was taken as statistically significant.

OBSERVATIONS

A total of 60 cases were taken up for the study including 30 cases each of benign and malignant breast lesions.

BENIGN LESIONS

Most of the benign lesions showed either negative or weak staining for transferrin, seen mainly in myoepithelial cells

and a few stromal histiocytes. Only 4 cases including 2 fibroadenoma, 1 each of fibroadenosis and fibrocystic disease showed moderate staining. None of the benign lesions gave consistent staining with transferrin (Table 1). Fourteen cases of fibroadenoma included in the study showed variable pattern of transferrin positivity. 7 cases showed negative staining, 5 cases gave weak positivity and 2 cases showed moderate positivity.

MALIGNANT LESIONS

Histological grading of infiltrating carcinoma was done according to modified Richardson and Bloom grading system[4] (Table 2). All cases of carcinoma breast were positive for transferrin however consistency of reaction was different for different grades. 12 cases (40%) included in the study were of grade I, 11 cases (36.66%) were of grade II and 7 (33.33%) were of grade III. Majority of grade I carcinoma showed either weak or moderate staining for transferrin (Fig. 1) while most of the grade II and all grade III tumours gave consistent reaction with transferrin (Fig. 2).

Figure 1

Figure 1: Photomicrograph of grade I infiltrating duct carcinoma breast revealing moderate immuno reaction for transferrin (400x).

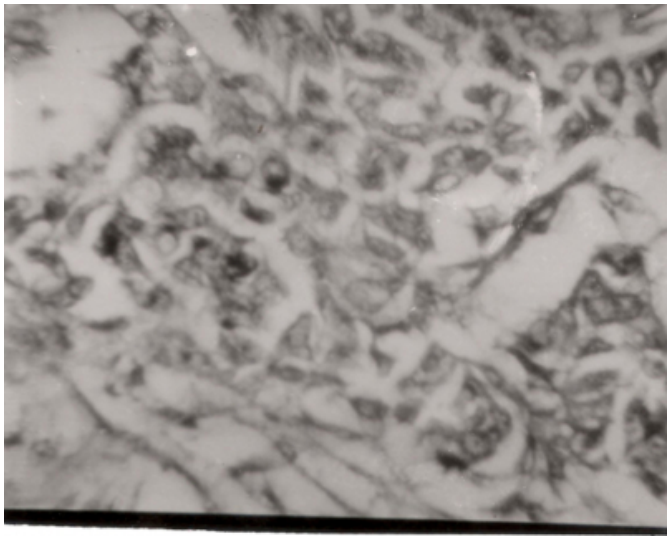
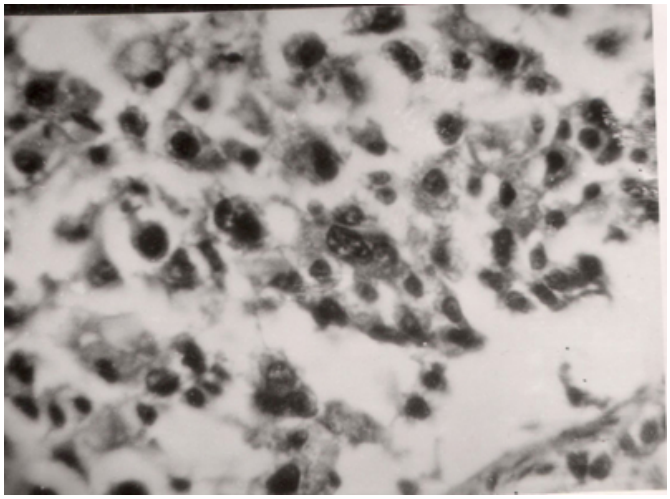


Figure 4

Table 2: Correlation between transferrin reactivity and histological grading of malignant lesions (infiltrating duct carcinoma)



DISCUSSION

Carcinoma breast is one of the most common malignancies in adult women. Non cancerous lesions of breast are far more common than cancer.[6]

Transferrin a glycoprotein, is a major iron transporting protein in plasma. It is a growth factor required for proliferating normal and malignant cells.[7]

Our study included 30 cases each of benign lesions and carcinoma breast. None of the benign lesions included in the study showed consistent staining for transferrin. Only 13.3% cases showed moderate staining while 33.3% gave weak staining. These findings are consistent with the study by other authors .[3,8,9]

50% cases of fibroadenoma were negative for transferrin reaction. 35.7% cases of fibroadenoma showed weak positivity while 14.28% cases showed moderate staining. These results were closer to results obtained by Aggarwal et al[3] and Fauk et al.[9]

75% cases of fibroadenosis and 50% of fibrocystic disease showed weak, positive staining consistent with the results of study conducted by Aggarwal et al.[3] All the cases of duct ectasia were negative for transferrin which is in accordance with study by Aggarwal et al[3].

Out of total 40% grade I cases of infiltrating ductal carcinoma, 6.66% cases showed consistent pattern of staining, 20% moderate while 13.33% showed weak staining for transferrin. In study conducted by Warba et al[10], 17.9%

cases of grade I showed consistent staining, 3.4% showed moderate and 5.6% gave weak positivity.

33.3% grade II carcinomas reveal consistent staining pattern, moderate staining in 3.33% and none of the grade II carcinomas showed weak staining. These results are close to findings of Warba et al.[10]

All the cases of grade III carcinoma gave consistent staining pattern of transferrin which is in accordance with study done by Warba et al[10] (Table 3 & 4).

Figure 3

Table 1: Correlation between transferrin intensity and histological typing in benign lesions

Diagnosis	No. of cases	- Negative staining	+ Weak staining	++ Moderate staining
Fibroadenoma	14	7(50.0%)	5(35.7%)	2(14.2%)
Fibroadenosis	6	3(50%)	2(33.3%)	1(16.6%)
Fibrocystic disease	4	2(50%)	1(25%)	1(25%)
Duct ectasia	3	3(100%)	-	-
Epithelial hyperplasia	1	-	1(100%)	-
Benign phyllodes tumour	2	1(50%)	1(50%)	-

Figure 5

Table 3: Comparative study of intensity of staining in malignant lesions

S. No.	Studies	Grade I				Grade II				Grade III			
		Total cases	Intensity of staining			Total cases	Intensity of staining			Total cases	Intensity of staining		
			C	M	C		C	M	C		C	M	W
1.	Warba et al (1986)[10]	14	6	3	5	34	26	6	2	30	27	3	0
2.	Aggarwal et al (2000)[3]	21	19	1	1	30	25	5	0	32	30	2	0
3.	Present study	12	2	6	4	11	10	1	0	7	7	0	0

Figure 6

Table 4: Comparative study of positive benign and malignant lesions in various studies

Sr. No.	Studies	Total no. of Benign	Positive cases	Total no. of malignant cases	Positive cases
1.	Fauk et al (1980)[9]	29	1	22	16
2.	Rosiello et al (1984)[8]	6	0	40	8
3.	Aggarwal et al (2000)[3]	63	18	90	83
4.	Present study	30	14	30	30

C - Consistent staining
M - Moderate staining
W - Weak staining

{image:6}

CONCLUSION

From the present study it can be concluded that Transferrin is a potential marker for identification of dividing cells, expression correlating with cellular proliferation, being highest in rapidly dividing cells. Transferrin shows an intense positive staining in malignant breast tumours as compared to benign breast lesions. Though evaluation of transferrin carries no diagnostic value, the study of transferrin is of prognostic significance in breast tumours and may facilitate the decision making process in the treatment of individual cases of carcinoma breast. Transferrin may be used as a carrier to target toxic therapy selectively to tumour tissue.

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