Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/14483
DOI URL: http://dx.doi.org/10.21474/IJAR01/14483

RESEARCH ARTICLE

THE RELEVANCE AND IMPORTANCE OF TUMOR INFILTRATING LYMPHOCYTES (TILS) IN BREAST CANCER

Dr. U. Suganya[1], Dr. R. Manibarathi[2] and Dr. C. Suganthi[3]

1. Assistant Professor Of Pathology, Govt. Mohan Kumaramangalam Medical College, Salem.
2. Assistant Professor Of Pathology, Govt. Karur Medical College, Karur.
3. Assistant Profeesor Of Pathology ,Govt. Dharmapuri Medical College, Dharmapuri.

Manuscript Info

Manuscript History
Received: 25 January 2022
Final Accepted: 28 February 2022
Published: March 2022

Key words:-
Breast Cancer, Neo Adjuvant Chemotherapy, Tumor Infiltrating Lymphocytes

Abstract

Tumor infiltrating lymphocytes (TILs) were evaluated in many cancers like ovarian tumors, endometrial tumors, colon cancer and melanoma. Now there is increasing trend in evaluating TILs in breast cancer. Tumor infiltrating lymphocytes gives the patients immune response to the tumor. 100 cases of Modified radical mastectomy specimen were chosen from surgical pathology records. The representative formalin fixed paraffin embedded tissue samples were collected. Detailed history regarding Patients age, sex, side of the breast involved , Grade and neoadjuvant chemotherapy were assessed for 100 cases. Tumor Infiltrating Lymphocytes are evaluated with Immuno HistoChemistry CD45 and CD3 for 100 cases , in which 93% cases were Infiltrating Ductal carcinoma-NOS cases and 07 % cases are of special types like Mucinous, Metaplastic, Apocrine, and Medullary carcinoma. Results: In our study, Highest incidence of breast carcinoma occur in the age group of 41-50 years. Infiltrating Ductal Carcinoma NOS is the most common primary malignant neoplasm of breast constituting 93% of cases. Most of the malignant tumors are left sided. Forty seven percent of cancers are presented in the size range of 2-5cms. Majority of the tumors are of Grade II accounting for 63.5% of all cases. TILs were evaluated with three variables 0- 10 % 20- 40 % and 50- 90 %.Younger the age, more the TILs. Neo adjuvant chemotherapy had significant correlation with TILs (P= 0.05).

Introduction:-

Carcinoma of breast is the most common malignancy in women. It can occur at any age but is uncommon in women less than 25 years and over 80 years. Women with early menarche, nulliparity, late age at first birth, and late menopause have increased risk of developing breast cancer[4,7]. Familial breast cancers accounts for 5 to 10% [9].

In cancer, alteration in the structure of neoplastic tissues induces immune responses which eliminates transformed cells. When there is incomplete elimination of transformed cells, it escapes immune control. This process is known as cancer immunoediting and many experiments and clinical evidence shows that cancer can be prevented and controlled through effective immune responses[6].

Corresponding Author:- Dr. U. Suganya
Address:- Assistant Professor Of Pathology, Govt. Mohan Kumaramangalam Medical College, Salem, Tamilnadu, India.

For instance, a subtype of breast cancer, medullary carcinoma that exhibits stromal lymphocytic infiltrate with high histological grade and axillary lymphnode metastates has better prognosis after local treatment [2].

The adaptive immune response to breast cancer can be seen in benign breast atypia and in invasive malignancy and the density of the response increases with infiltrating malignancy.

Using the recommendations of Denkert et al. [1], stromal TILs should be scored as a percentage of only the stromal areas and not the areas occupied by carcinoma cells in the total assessed surface area. For example,A score of 50% stromal TILs include 50% of the stromal area and not the stromal nuclei.

Percentage of TILs are evaluated and classified as 0-10%, 20-40% and 50-90% as per the evaluation of tumor-infiltrating lymphocytes (TILs) in breast cancer: recommendations by an International TILs Working Group 2014.

Aims and objectives:-

To correlate histological grade of invasive carcinoma and neoadjuvant chemotherapy with Tumor Infiltrating Lymphocytes using immunohistochemical stain CD45 and CD3.

Materials and Methods:-

100 cases of Invasive breast carcinoma were randomly selected ,of which 93 cases were Invasive ductal carcinoma NOS and 07 cases were of special types such as metaplastic, mucinous, medullary, IDC- NST with papillary features and their slides were reviewed and graded. Their representative formalin fixed paraffin embedded tissue samples were subjected for analysis of Tumor Infiltrating Lymphocytes with H&E slides and with CD 45 And CD 3 expression

Observation and results:-

Total of 100 cases were studied, percentage of TILs classified as 0-10%, 20-40%,50-90% and the following results were obtained.

Table 1:- correlation of chemotherapy given with TILs.

			TILS			Total
			0-10	20-40	50-90	
chemotherapy	Not given	Count	4	24	20	48
		%	8.3%	50.0%	41.7%	48.0%
	Given	Count	12	29	11	52
		%	31.2%	43.4%	38.7%	52.0%
Total		Count	16	53	31	100
		%	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=6.94 P=0.05

In our study , P- value is statistically significant if neo-adjuvant chemotherapy given to the patient before Modified Radical Mastectomy.

Table 2:- Correlation of grading of tumor with TILS.

			TILS			Total
			0-10	20-40	50-90	
GRADE	1	Count	2	9	8	19
		% within GRADE	14.3%	17.3%	26.7%	19.8%
	2	Count	12	34	15	61
		% within GRADE	85.7%	65.4%	50.0%	63.5%
	3	Count	0	9	7	16
		% within GRADE	0.0%	17.3%	23.3%	16.7%
Total		Count	14	52	30	96
		% within GRADE	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=6.216 P=0.184

In this study, all the ranges of TILs (0-10%, 20-40%, 50-90%) are maximally seen in Grade 2 tumors. P- value is not statistically significant with the grading of tumor.

Table 3:- Correlating grading with TILs for neoadjuvant cases.

			TILs			Total
			0-10	20-40	50-90	
GRADE	1	Count	2	2	1	5
		% within GRADE	20.0%	7.1%	8.3%	10.0%
	2	Count	8	21	7	36
		% within GRADE	80.0%	75.0%	58.3%	72.0%
	3	Count	0	5	4	9
		% within GRADE	0.0%	17.9%	33.3%	18.0%
Total		Count	10	28	12	50
		% within GRADE	100.0%	100.0%	100.0%	100.0%

Pearson Chi-Square=3.828* P=0.05

When TILs are compared with grading for those cases in which neo-adjuvant chemotherapy given , then P- value is statistically significant

Discussion:-

This study shows 0-10 % of stromal TILs in 16% cases , 20-40 % stromal TILs in 53 % cases and 50-90 % Stromal TILs in 31% cases.[8]

In our study, neo-adjuvant chemotherapy given before Modified Radical Mastectomy has correlated with Tumor Infiltrating Lymphocytes (P value - 0.05).Chemotherapy induced cell death causes release of tumor antigens which is presented to T cells by antigen presenting cells, in turn destroy cancer cells and increase in tumor infiltrating lymphocytes[5]. In our study, Tumor Infiltrating Lymphocytes are maximally seen in grade II tumors. Grading of tumor does not correlate with Tumor Infiltrating Lymphocytes (P- Value : 0.184). H. Ohtani et al showed 0 % in grade I, 8.3 % in grade II tumors, 29 % in grade III tumors.[3] When grading of tumors are compared for those cases in which prior chemotherapy given in this present study have correlated with Tumor Infiltrating lymphocytes. (P value- 0.05).

Conclusion:-

Fifty two cases of neo-adjuvant chemotherapy were included in this study, neo-adjuvant chemotherapy was statistically significant with Tumor Infiltrating Lymphocytes. Grading of tumors does not correlate with TILs. But grading of tumors correlate with TILs when neo-adjuvant chemotherapy given cases are taken into consideration and are statistically significant.

Fig 1:- CD 45 expressed in 50-90 % of stromal cells(100 X).

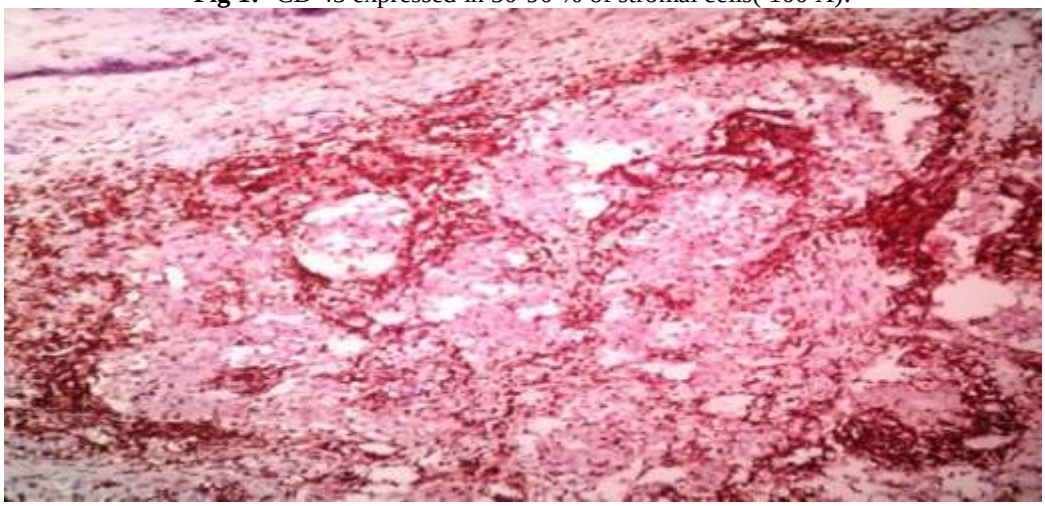


Fig 2:- CD 45 expressed in 20-40 % of stromal cells(100 X).

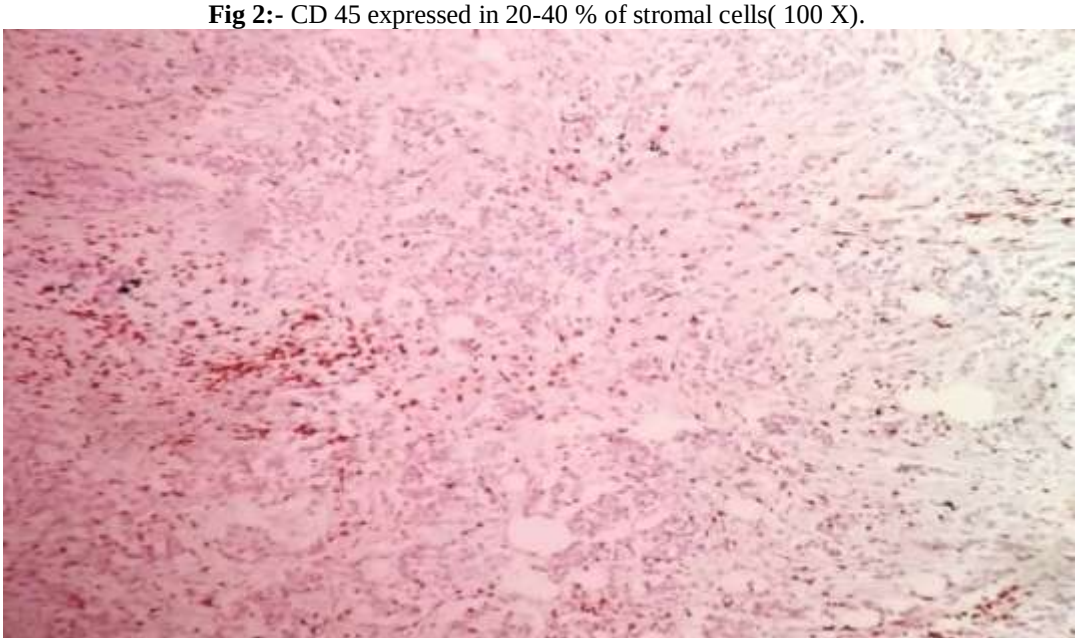
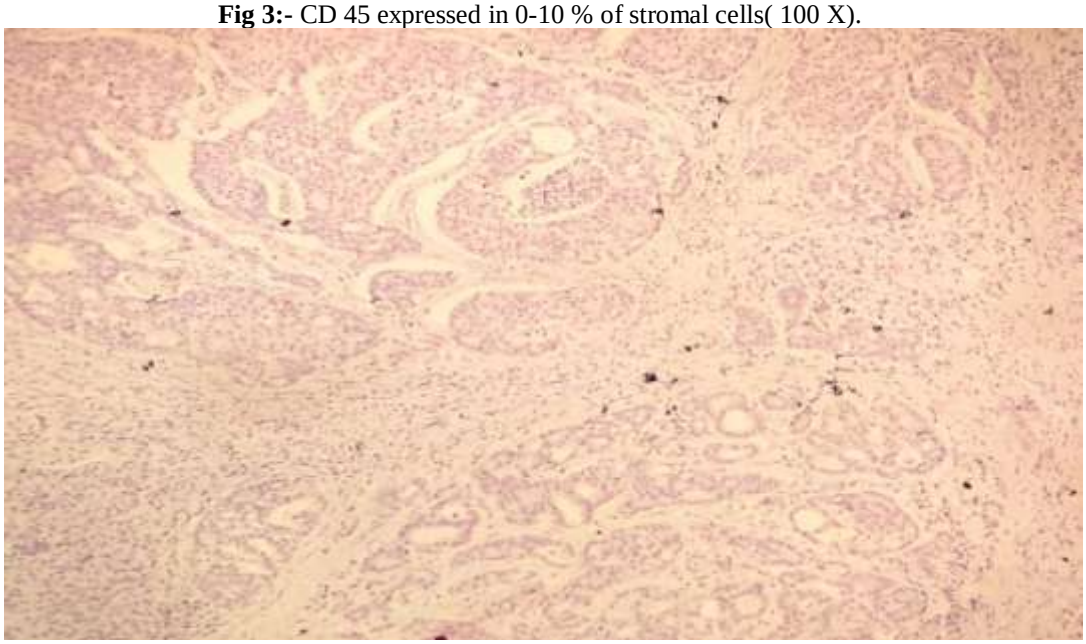


Fig 3:- CD 45 expressed in 0-10 % of stromal cells(100 X).



References:-

1. Denkert C, Loibl S, Noske A et al. Tumor-associated lymphocytes as an independent predictor of response to neoadjuvant chemotherapy in breast cancer. J Clin Oncol 2010; 28: 105–113.
2. doiWesolowski R and Carson WE (2014) Tumor Infiltrating Lymphocytes – The Next Step in Assessing Outcome and Response to Treatment in Patients with Breast Cancer. J Carcinog Mutagen 5: 199. doi:10.4172/2157-2518.1000199
3. H. Ohtani et al. Defining lymphocyte-predominant breast cancer by the proportion of lymphocyte-rich stroma and its significance in routine histopathological diagnosis. Pathology International 2015
4. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. Epidemiol Rev 1993, 15: 36–47.
5. Ke Wang, Jianjun Xu, Tao Zhang, Dan Xue Tumor-infiltrating lymphocytes in breast cancer predict the response to chemotherapy and survival outcome: A meta-analysis.

6. Mittal D, Gubin MM, Schreiber RD, Smyth MJ. New insights into cancer immunoediting and its three component phases–elimination, equilibrium and escape. Curr Opin Immunol. 2014;27:16–25.
7. Pathak DR, Osuch JR, He J. Breast carcinoma etiology: current knowledge and new insight into the effects of reproductive and hormonal risk factors in black and white populations. Cancer 2000, 88: 1230–1238.
8. Salgado et al The evaluation of tumor-infiltrating lymphocytes (TILs) in breast cancer: recommendations by an International TILsWorking Group 2014.
9. Tan DS, Marchio C, Reis-Filho JS. Hereditary breast cancer: from molecular pathology to tailored therapies. J Clin Pathol 2008, 61: 1073–1082.