

Correlation Of Histological Grade With Immunohistochemistry In Breast Carcinoma

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Abstract:

Background: Carcinoma breast is globally the most common cancer in women and second most common cause of cancer death worldwide. Tumour grade is an important prognostic indicator in breast cancer patients that helps in predicting overall and metastasis free survival for the patient. In addition to traditional tumour/nodal/ metastasis staging variables, assessment of estrogen and progesterone receptors is an important prognostic factor to predict survival and response to hormonal therapy. This is now-a-days being done exclusively by immunohistochemistry.

Methods: In all mastectomy cases, histological findings were noted along with assessment of grade. Immunohistochemical staining was done and ER/PR status was compared with the histological grading.

Results: infiltrating ductal carcinoma (88.5%) constituted maximum number of cases with Grade II seen in most of the cases. Immunohistochemical staining revealed maximum cases (31%) of ER-/PR- category. Stastitital analysis revealed a significant association between grading and ER/PR status.

Conclusion: Histological grade shows a significant association with ER/PR status. A higher grade is associated with ER/PR- tumours.

Keywords: Carcinoma breast, Histological Grade, esterogen receptors, progesterone receptors.

I. INTRODUCTION

Malignant lesions of breast are a major concern and are of one of the leading cancers in females, comprising 22% of all female cancer. At the same time, it is also the principal cause of death in women globally. Breast cancer is the second most common type of cancer after lung cancer worldwide. Incidence of breast cancer is about 10.4% of all cancers (both sexes counted). The global burden of breast cancer in women as measured by incidence, mortality and economic costs is strikingly on increase. Worldwide, more than 1 million women are diagnosed with breast cancer every year and more than 4,10,000 die from this disease.

In India, breast cancer, though less common than in western population, has become the leading cancer in females in metropolitan cities overtaking carcinoma cervix, which was number one cancer in the past. India faces a potential breast cancer epidemic risk over the next decade as women adopt

western lifestyles by marrying and bearing children later. The rising incidence of breast cancer in India is mainly attributed to the westernization of the country.

Breast cancer is the predominant malignancy where oncologists use predictive markers clinically to select treatment options. Tumour grade is an important prognostic indicator in breast cancer patients that helps in predicting overall and metastasis free survival for the patient. Grade is based on the histological qualities of the primary tumour. This is an important determinant of prognosis that allows risk stratification within a given tumour stage. The microscopic grading system for breast carcinoma is the "Modified Bloom-Richardson grading system". This system takes into account tubule formation, nuclear pleomorphism and mitotic count. Histological grade is an important prognostic indicator that can predict overall and metastasis free survival for breast carcinoma patients.

Decisions for treatment of patients with breast carcinoma are made based on various prognostic as well as predictive factors. In addition to traditional tumour/nodal/ metastasis staging variables, assessment of estrogen and progesterone receptors is an important prognostic factor to predict survival and response to hormonal therapy. This is now-a-days being done exclusively by immunohistochemistry (IHC). This helps in increasing the accuracy of selecting or rejecting patients for hormonal therapy. Positive estrogen receptor (ER) status was found to be significantly associated with high nuclear and low histologic grades, absence of tumour necrosis, presence of marked tumour elastosis, and older patients. These pathologic parameters enumerated are either directly or indirectly related to tumour differentiation suggesting that ER represents another index of tumour differentiation. Breast cancer patients whose lesions contain both ER and PR have the best possibility of remission following hormonal therapy (approaching 70%) than the group of patients whose lesions contain either receptor alone (approximately 30%) or very low levels of both receptors (approximately 10%).

AIM

To study the relation between histological grade and ER/PR status in carcinoma breast

II. MATERIALS AND METHODS

A retrospective study was conducted in the Department of pathology, Subharti Medical College, Meerut on the mastectomy specimens obtained from June 2007 to August 2011. In each case, histological findings were noted along with assessment of grade. Immunohistochemical analysis for ER and PR was performed on fresh sections taken from the retrieved block.

Grading of breast tumours on H&E stained slides was done by using the Modified Bloom and Richardson grading technique. In this technique, the grade was obtained by adding up the scores for tubule formation, nuclear pleomorphism and mitotic count, each of which was given 1, 2 or 3 points. This resulted in a total score of between 3 and 9 points.

Immunohistochemistry was done using peroxidase antiperoxidase (PAP) technique. Positive and negative control was used with every batch of staining. Cases showing nuclear positivity were taken as positive. The results were divided into 4 categories- ER+/PR+, ER+/PR-, ER-/PR+ and ER-/PR-.

III. OBSERVATIONS AND RESULTS

The present study over a period of 4 years and comprised a total of 61 mastectomy specimens. Age of the patients in the present study ranged from 19 to 73 yrs. Mean age in the present study was 51 yrs.

On basis of morphology, the cases were divided into various histological types. Out of these, infiltrating ductal carcinoma (88.5%) constituted maximum number of cases followed by 3 cases (4.9%) of mixed morphology of both infiltrating ductal and lobular carcinoma. There was a single

case of infiltrating lobular carcinoma and 3 cases of sarcoma. (Table/Fig 1)

DIAGNOSIS	CASES	PERCENTAGE (%)
Infiltrating ductal carcinoma	54	88.5
Infiltrating ductal & lobular carcinoma	03	4.9
Infiltrating lobular carcinoma	01	1.6
Malignant Phyllodes	02	3.2
Angiosarcoma	01	1.6
TOTAL	61	100

Table/Fig 1: Histological Type Of Breast Cancer

Grading was done on all breast carcinoma cases (58 cases) by adding up the scores for tubule formation, nuclear pleomorphism and mitotic count. Cases were divided into 3 grades- I, II & III. Maximum (44.7%) cases were of grade II i.e. moderately differentiated. 36.2% cases belonged to grade I i.e. well differentiated variety. Only 19% of the cases were of grade III category i.e. poorly differentiated (Table/Fig 2).

GRADE	CASES	PERCENTAGE (%)
Grade I	21	36.2
Grade II	26	44.7
Grade III	11	19
TOTAL	58	100

Table/Fig 2: Grade Wise Distribution

Immunohistochemistry was performed on all the breast carcinoma cases (Infiltrating ductal and lobular carcinoma- 58 cases).The results were divided into 4 categories- ER+/PR+, ER+/PR-, ER-/PR+ and ER-/PR-. Maximum cases (31%) were of ER-/PR- category. 25.8% cases were of category ER-/PR+. Only 24.1% cases were ER+/PR+. 19% cases were ER+/PR- (Table/Fig 3)

STATUS	CASES	PERCENTAGE (%)
ER+/PR+	14	24.1
ER+/PR-	11	19
ER-/PR+	15	25.8
ER-/PR-	18	31
TOTAL	58	100

Table/Fig 3: ER/PR Immunostaining Distribution

Grade was compared to the ER/PR status using Chi-Square test (Table/Fig 4)

Grade	ER/PR STATUS				TOTAL
	ER+/PR+	ER+/PR-	ER-/PR+	ER-/PR-	
I	10	3	6	2	21
II	4	7	8	7	26
III	0	1	1	9	11
TOTAL	14	11	15	18	58

Table/Fig 4: Grade Vs Er/Pr Status Crosstabulation

The p-value was calculated using Chi-Square test which came out to be 0.001 (i.e.<0.05 thus, significant) which concludes that there is significant association between grade and ER/PR status (Table/Fig 5)

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	23.865 ^a	6	.001
Likelihood Ratio	24.339	6	.000
Linear-by-Linear Association	15.668	1	.000
N of Valid Cases	58		

a. 6 cells (50.0%) have expected count less than 5. The minimum expected count is 2.09.

Table/Fig 5: Chi-Square Test

IV. DISCUSSION

Breast cancer is the most common malignancy among women globally. It is the most frequently diagnosed cancer in women and the second most common cause of cancer death in the women globally. Breast cancer is also increasing in India at a very high pace. It the second most common cancer in India among women after carcinoma cervix. The peak incidence of breast cancer is seen in 45-60 years of age and is rare in patients younger than 20 years and above 80 years of age.

Grading of breast carcinoma cases was done by the Modified Bloom and Richardson grading technique. Maximum cases were of grade II (44.7%). Similar findings were noted in the study done by Azizun-Nisa et al in which majority of the lesions presented as grade II lesions accounting for 55.3% cases. Grade III lesions accounted for 20% of the cases.

Histological grade is significant predictor of overall mortality for node negative and node positive patients. It is found to increase with tumour size and advancing anatomic stage. The first formal study of the grading of histologic differentiation in breast cancer was undertaken by Greenhough. Despite the subjective nature of his method and paucity of clinical data, he showed a good correlation with prognosis. Since then a number of different methods have been devised. Many studies have demonstrated a significant association between grade and survival.

Immunohistochemistry was performed on all the breast carcinoma cases (58 cases). The results were in close agreement with Zhou LH et al and Rosenberg LU et al. Assessment of steroid hormone receptors in resected breast cancer tissues is essential to decide whether endocrine therapy is indicated and to select the best treatment for each patient on the basis of receptor status. Evaluation of hormone receptor expression in tumour cell nuclei is an integral part of routine breast cancer diagnosis and provides important information with relevance for prognosis and choice of therapeutic approach.

In the present study, a significant association between grade and ER/PR status was found. A higher grade was associated with ER-/PR- tumours. Dunnwald LK et al and Adedayo A et al also reported that ER+/PR+ tumours had a lower histological grade and lower mortality rate than compared to ER-/PR-, ER-/PR+, ER+/PR- tumours.

V. CONCLUSION

Histological grade shows a significant association with ER/PR status. A higher grade is associated with ER/PR-tumours.

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