ORIGINAL RESEARCH PAPER

Pathology

CORRELATION OF APOPTOTIC INDEX WITH HISTOLOGICAL GRADING IN BREAST CARCINOMA PATEINTS

KEY WORDS: Carcinoma breast, Apoptotic Index, Histological Grade.

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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. Apoptotic index- a measure of the rate of death of cancer cells within a tumour, is an independent prognostic marker. Apoptotic index is usually low in benign breast lesions. It gradually increases with increasing grade and is highest in invasive carcinoma.

Methods: In all mastectomy cases, histological findings were noted along with assessment of grade and apoptotic index. The mean apoptotic index was compared with the grades.

Results: Grade II infiltrating ductal carcinoma was seen in most of the cases. Grade III tumours had a significantly higher mean apoptotic index (p-value =0.000).

Conclusion: Apoptotic index gradually increases with increasing grade in breast cancer.

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer in women and the second most common cause of cancer death in the world. The incidence of this disease has been fairly rising over the past several decades. It is seen that one in eight women have a life time risk of developing breast cancer.[1] Breast cancer is no longer seen as a single disease but rather a multifaceted disease comprising of distinct biological subtypes with diverse natural history, presenting a varied spectrum of clinical, pathological and molecular features with different prognostic and therapeutic implications.[2]

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.[3] In India, breast cancer is the second most common cancer among women after carcinoma cervix. The rising incidence of breast cancer in India is mainly attributed to the westernization of the country.[4]

The most common type of breast malignancy is adenocarcinoma, all other types (squamous cell carcinoma, phyllodes tumour, sarcoma and lymphoma) make up 5% of the total.[5] The pattern of invasive carcinoma are ductular, lobular, tubular, cribriform, mucinous, medullary, apocrine, juvenile (secretory) and carcinoma with neuro-endocrine features.[6]

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.[6] Histological grade is an important prognostic indicator that can predict overall and metastasis free survival for breast carcinoma patients.[7]

Apoptosis is a complex and finely regulated process linked to cellular proliferative activity. Apoptotic index is defined as a measure of the rate of death of cancer cells within a tumour. This is estimated by determining the proportion of dying or apoptotic cells per 100 cancerous cells.[8]

Apoptotic index is usually low in benign breast lesions and higher in in-situ carcinomas with a gradual increase from grade I to grade III. The apoptotic index is higher in invasive carcinoma and highest in recurrent carcinomas.[9] A high apoptotic index is seen to be associated with decreased survival of patients of breast carcinoma.[10]

AIM

To study the relation of apoptotic index with histological grading of breast carcinomas

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 may 2011. In each case, a detailed clinical history and histological findings were noted along with assessment of grade and apoptotic index.

Grading was done using the most widely used grading method, Modified Bloom and Richardson grading technique.[11] In this technique, 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, resulting in a total score of between 3 and 9 points.[12]

Apoptosis was assessed in light microscopy by using high magnification (oil immersion X 100 lens).[13] For calculation of apoptotic index, 10 high power fields were analyzed. Number of apoptotic bodies per 100 non apoptotic tumour cells was the apoptotic index for that tumour.[14] Areas of artefactual change, necrosis and inflammatory exudates along with luminal apoptotic bodies were excluded.[15]

The mean apoptotic index was calculated for all the three grades. ANOVA test was applied to find out whether or not the means of all the grades were equal by calculating p- value. Post-Hoc test was applied to find out which of the grades show significant difference in mean apoptotic index.[16]

RESULTS

The present study was conducted over a period of 4 years comprised a total of 61 mastectomy specimens. H&E sections were studied to determine the histological type, grade and apoptotic index. On basis of morphology, the cases were divided into various histological types (Table/Fig 1).

HISTOLOGICAL TYPE OF BREAST CANCER. (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

Grading was done on all breast carcinoma cases (58 cases) on H&E stained slides. Maximum (44.7%) cases were of grade II i.e. moderately differentiated. 36.2% and 19% cases belonged to grade I and grade II category. (Table/Fig 2)

GRADE WISE DISTRIBUTION (Table/Fig 2)

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

Apoptotic index was calculated for all the cases in percentage. Mean apoptotic index was calculated for all the three grades along with the standard deviation. The mean apoptotic index was maximum for grade III tumours i.e. 3.0±0.99 while it was minimum for grade I tumours i.e. 0.7± 0.77. (Table/Fig 3)

GRADE Vs. APOPTOTIC INDEX (Table/Fig 3)

GRADE	NUMBER OF CASES (N)	MEAN APOPTOTIC INDEX	STANDARD DEVIATION
I	21	.7443	.077934
II	26	1.2615	.77309
III	11	3.0182	.99178
TOTAL	58	1.4074	1.14901

ANOVA test was applied to determine whether or not the means of the three groups are equal or not. The p- value was 0.000 (<0.05), suggesting mean apoptotic index for at least one of the grades is significantly different from others. In order to determine "which of the grades have significantly different mean?", Post Hoc tests were applied and it was found out that grade I and II tumours have same apoptotic index (p-value =0.089, insignificant) but grade III tumours had a significantly higher apoptotic index (p-value =0.000)

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. (17)

The histological typing of all the cases in the present study was done and 88.5% cases of infiltrating ductal carcinoma were noted. The second most common category was invasive lobular carcinoma (6.5%). Almost similar results were noted in other studies. (Table/Fig 4)

COMPARISON OF RESULTS OF HISTOLOGICAL TYPING (Table/Fig 4)

STUDY	IDC - most common (%)	ILC -second most common (%)
Grethe Albrektsen et al[18].	81.4	6.3
R. Yerushalmi et al[19].	78	6
Mohamed B Satti[20]	90.6	5.9
Azizun-Nisa et al[21]	85.3	7
PRESENT STUDY	88.5	6.5

Grading of breast carcinoma cases was done and cases were divided into 3 grades- I, II & III depending upon the score. In the present study, maximum (44.7%) cases were of grade II category. 36.2% and 19% cases belonged to grade I and grade III category, respectively.

Mean apoptotic index was calculated for all the three grades. The mean apoptotic index was maximum for grade III tumours i.e. 3.0±0.99 while it was minimum for grade I tumours i.e. 0.7± 0.77. ANOVA test and Post Hoc tests concluded that grade III tumours had a significantly higher apoptotic index. Similar findings were noted by Jingxiang Huang et al[22] and M. Mustonen et al.[23] (Table/Fig 5)

COMPARISON OF RESULTS OF CORRELATION OF GRADE WITH MEAN APOPTOTIC INDEX (Table/Fig 5)

STUDY	GRADE	Mean apoptotic index (%) ± S.D	p- value
Jingxiang Huang et al[23]	I	0.97 ± 0.17	0.029
	II	0.97 ± 0.17	
	III	1.62 ± 0.23	
M. Mustonen et al[24]	I	0.52	0.0004
	II	0.72	
	III	1.17	
PRESENT STUDY	I	0.7± 0.77	0.000
	II	1.26 ± 0.77	
	III	3.0±0.99	

Similarly Zhang GJ et al[24] also concluded that apoptotic index gradually increases in extent from grade I to III invasive carcinoma.

CONCLUSION

Thus, apoptotic index increases with the increasing grade in breast carcinoma. It is a useful parameter to assess the prognosis in carcinoma breast.

Table/Fig 6- H&E – Infiltrating Ductal Carcinoma- Grade III with high apoptotic index
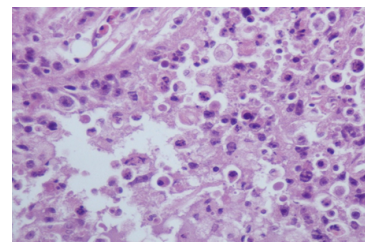
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