

Histopathological Patterns of Breast Carcinomas with Molecular Profile (ER & PR Status)

Kishan Bookya¹, Kanya Kumari²

¹Associate Prof., Department of Pathology, ASCR Govt. Medical College, Nellore.

²Assistant Prof., Department of Pathology, MediCiti Institute of Medical Sciences, Medchal, Ranga Reddy, India.

Corresponding Author: Kanya Kumari

Received: 28/05/2015

Revised: 23/06/2015

Accepted: 30/06/2015

ABSTRACT

Introduction: Breast carcinoma is the most common malignant tumor and the leading cause of carcinoma death in women the high mortality associated with breast cancer is linked to the aggressiveness of the tumor which depends to a large extent on the histopathological subtypes. Different histological subtypes of infiltrating breast tumors have variable prognosis. Histological subtype largely influences further treatment strategy.

Aim: The aim is to study the histopathological patterns of breast and to assess ER and PR status.

Materials and methods: This was a retrospective analysis of all consecutive breast cancer specimens submitted to the histopathology department of Kakatiya Medical College Warangal and private hospital, Warangal (St. Anns hospital) for duration of 3 yrs. i.e. from March 2011 to April 2014.

Results: A total of 190 cases of breast carcinoma were reviewed, 184 (96.8%) were in females and about 6(3.1%) were in males. Maximum number of cases belonged to age group of 41-60 years i.e. 92.1% (175/190). On histopathological examination invasive ductal carcinoma -No special type (NST) was the predominant morphological type reported, constituting 77.3%(147/190), among special types included: Medullary carcinoma and Mucinous variant was common each constituting about 4.2%(8/190), 3.6% (7/190) Papillary carcinoma, 2.1%(4/190) tubular carcinoma, infiltrating lobular carcinoma occupied 5.7%(11/190), metastases about 1.5% (3/190) and least was anaplastic carcinoma about 1.05%(2/190). In our series 41.7% (71/170) cases aged 41-60 years found to be ER+/PR- and 18.7%(32/170) aged 41-60 years are both ER+/PR+. According to Modified Bloom-Richardson Grading 76.3% (145/190) cases were grade II followed by 14.2% (17/190) cases grade III.

Conclusion: Invasive ductal carcinoma (NST) was the most common histopathological pattern in our study followed by Medullary carcinoma, mucinous, Papillary carcinoma, tubular carcinoma, infiltrating lobular carcinoma and anaplastic carcinoma. Histopathological subtypes like medullary, mucinous and tubular variants have a better prognosis.

Key words: Invasive ductal carcinoma, No special type (NST), Histopathological subtypes.

INTRODUCTION

The mammary gland tumors are very heterogeneous in terms of morphology and biological behavior. [1] Based on the

histological and biological criteria, this can be estimated that about almost half of surgically removed breast tumors are malignant. [2] Breast carcinoma is the most

common malignant tumor and the leading cause of carcinoma death in women, with more than 10,00,000 cases occurring worldwide annually. [3] In India, cancer of the breast is the most common cancer among women in many regions and has overtaken cervix cancer, which was the most frequent cancer a decade ago. [4]

Breast cancer is still a major cause of death in women worldwide and represents an etiologically heterogeneous disease, with an intrinsic complexity in cellular–biomolecular profile and diversity in its responsiveness to treatment. Family history brings together genetic and environmental factors that may cause cancer. [5] Clinical evidence and large epidemiological studies have shown that up to 5%–10% of all breast carcinoma may be attributed to germ line mutations in well-studied breast cancer susceptibility genes.

The various systems for histopathological classification of breast cancers in use at present are descriptive, based on histological or cytological appearance, or both, of the tumors. While it has been claimed that tumor histology is of significance in some cases, in that some histological types behave less aggressively than others the usefulness of the different classification systems in evaluating individual patient prognosis and in selecting treatment has been questioned. [6-8]

Grading of breast carcinomas: The WHO system adds to tumor classification a system of grading based on a suggestion by Bloom and Richardson." This is based on the number of hyper chromatic nuclei and mitoses per high power field of vision (1, 2 or 3 points: few, moderate, many), irregularity of size, shape and staining of nuclei (1, 2 or 3 points) and tubule formation (1, 2 or 3 points: many, moderate, none). These points are added together and 3-5 = grade I; 6-7 = grade II; 8-9 = grade III. [9]

- Immunohistochemistry(IHC) has an expanding role in distinguishing usual ductal hyperplasia from atypical ductal hyperplasia/low-grade carcinoma in situ, subtyping a lesion as ductal versus lobular or basal versus luminal, helping distinguish true micro invasion from mimics (pseudo invasion), predicting the likelihood of response to anti hormonal and other therapeutic agents, improving sentinel node staging, and finally, helping recognize metastatic carcinoma of unknown primary site as originating in the breast. [10]

Aims and Objectives: The objectives of this study are:

- To study the histopathological patterns of breast carcinomas
- To assess ER and PR status.

MATERIALS AND METHODS

After obtaining the institutions ethical permission, a 3 year retrospective study was carried out from March 2011 to April 2014 on 190 patients in the department of pathology, Kakatiya Medical College, Warangal and private hospital (St. Anns hospital) Warangal. Patient's data were accessed through central records department. Case histories were obtained from the department of surgery.

Histopathologically confirmed invasive carcinoma cases were included in the study. Benign, in-situ lesions were excluded.

Patient's complete clinical data was recorded and the specimens received were fixed by keeping them in 10% formalin overnight. The specimens were received in different forms such as lumpectomy and modified radical mastectomies specimens.

After fixing, gross examination of the specimen was done and findings were recorded. Tumor size is measured in the

surgical specimens .Tumors are subsequently classified into three groups according to size (< 2 cm, 2–5 cm, >5 cm). Tissue sections about 1 cm apart were taken, labeled and processed. The sections were stained routinely with Haematoxylin and Eosin and examined under the microscope.

Microscopically they were classified according to histological grades into Grade I (well differentiated), Grade II (moderately differentiated), Grade III (poorly differentiated) and histological types according to modified Bloom-Richardson Grading System.

IHC was performed by using the avidin-biotin complex peroxidase technique with the chromogen diaminobenzidine and antigen retrieval. ER (Estrogen) and PR (Progesterone) reactivity of invasive tumors was assessed. IHC (ER/PR) is performed by standard method.

RESULTS AND OBSERVATION

This study includes 190 cases of breast malignancies reported during the period of 3 years. All the biopsy specimens were received in histopathology section. The specimens were analyzed grossly and microscopically. The observations of the present study were analyzed and recorded with respect to age, sex, quadrant involvement, and histopathological examination and lymph node metastases. The invasive carcinomas were further graded according to Bloom and Richardson grading system.

The age of the patients ranged from 20– 80 years. Average age of patients was 55 years. Maximum number of patients belonged to age group of 41-60 years i.e. 92.1% (175/190), 5.7% (11/190) in 61-80 yrs. and 2.1%(4/190) were in 20-40 age

group. The youngest breast carcinoma of our series reported was in a 32 year female and oldest was 65 yrs. age.

Out of the 190 cases of breast cancers analyzed only 3.1% (6/190) were in males and all males were in age group 61 to 80 years and remaining 96.8% (184/190) were in females.

Clinical presentation of breast carcinomas were observed to occur more on the upper and outer quadrant accounting for 82.6%(157/190) followed by Lower outer 5.7%(11/190), upper and inner quadrant 5.2 % (10/190), Lower inner quadrant 3.6% (7/190), central 1.5%(3/190).Majority of the patients about 63.6% (121/190) presented with axillary lymph node metastases level I and level II.

In the present study 78.9% (150/190) cases underwent Modified Radical Mastectomies and 21% (40/190) lumpectomy specimens, with right breast involved in 89.4% (170/190) of the cases and 5.7% (11/190) involved the left breast and 4.7% (9/190) showed bilateral involvement .

On gross examination 94.2% (179/190) tumors were of the size >5 cm followed by 2-5cm about 4.2% (8/190) and less than 5cm about 1.5% (3/190). (fig.1)

TABLE 1: HISTOPATHOLOGIC PATTERNS

Type	No. Of cases	Percentage
INVASIVE:		
Infiltrating ductal carcinoma	147	77.3
Lobular carcinoma	11	5.7
SPECIAL TYPES:		
Tubular	4	2.1
Medullary	8	4.2
Papillary	7	3.6
Mucinous	8	4.2
Anaplastic carcinoma	2	1.05
Metastases	3	1.5
TOTAL	190	99.6

TABLE2: DISTRIBUTION OF PATIENTS ACCORDING TO AND RECEPTOR STATUS.

Age in yrs	No. of cases	ER+/PR+	ER+/PR-	ER-/PR+	ER-/PR-
21-40	5	1(20%)	3(60%)	0	1(20%)
41-60	170	32(18.7%)	71(41.7%)	53(31.1%)	14(8.2%)
61-80	15	4(26.6%)	0	6(40%)	1(33.3%)

Note: ER-Estrogen, PR- Progesterone

TABLE 3: HISTOPATHOLOGIC PATTERNS OF VARIOUS STUDIES [11-14]

Histopathologic patterns	AM Dauda et al	Vishal G. et al	Godwin A. EbugheI et al	Naila Nazir et al	Present study
Infiltrating ductal carcinoma	137(79.6%)	110(88%)	69(85.%)	40(80%)	147 (77.3%)
Lobular carcinoma	11(6.7%)	1(.75%)	1(1.2%)	1(2%)	11(5.7%)
Tubular	-	-	-	-	4(2.1%)
Medullary	6 (3.6%)	1(.75%)	3(3.7%)	2(4%)	8(4.2%)
Papillary	7 (4.2%)	1(.75%)	-	-	7(3.6%)
Mucinous	4 (2.4%)	2(1.5%)	2(2.5%)	1(2%)	8(4.2%)
Anaplastic	4 (2.4%)	-	-	-	2(1.05%)
malignant phyllodes	3(1.8%)	2(1.5%)	-	-	-
Metastases	-	-	-	-	3(1.5%)
Others	-	8(6.45)	6(7.4%)	6(12%)	-
TOTAL	172	125	81	50	

TABLE4:COMPARATIVE STUDY OF DISTRIBUTION OF RECEPTOR STATUS IN AGE GROUP 41- 60 YRS

41-60 yrs age group	No. of cases	ER+/PR+	ER+/PR-	ER-/PR+	ER-/PR-
Naila Nazir et al [14]	13	5 (38.5%)	5 (38.5%)	0	7 (53.8%)
Present study	170	32(18.7%)	71(41.7%)	53(31.1%)	14(8.2%)

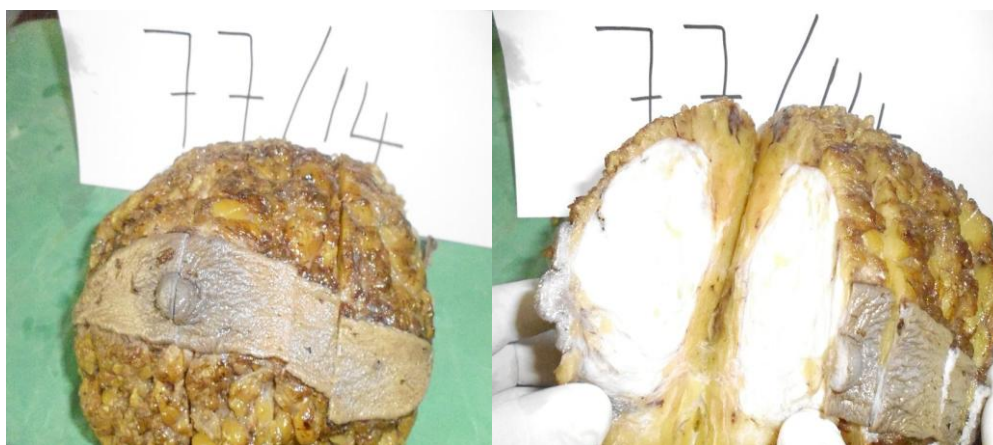


Fig.1 On gross examination: radical mastectomy specimen measuring 18x16x14cm On cut section grey white tumor areas measuring 7x6x5 cm invading into skin and under surface.

On histopathological examination invasive ductal carcinoma (fig.2,3) -No special type (NST) was the predominant morphological type constituting 77.3% (147/190), Among special types included: Medullary carcinoma a (fig.4)and Mucinous variant (fig.5) was common each constituting about 4.2%(8/190), 3.6% (7/190). (Table1)

According to Modified Bloom-Richardson Grading , 9.4% (18/190) cases were grade I, 76.3% (145/190) cases were grade II and 14.2%((17/190) cases were grade III.

In our series 41.7 %(71/170) cases aged 41-60 years found to be ER+/PR- and 18.7%(32/170) aged 41-60 years are both ER+/PR+.(Table 2)

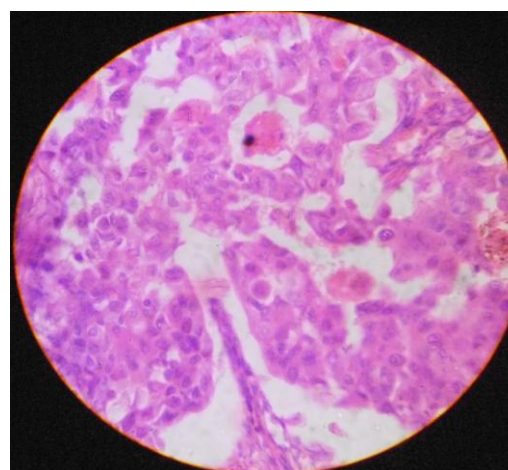


Fig.2 Invasive Ductal Carcinoma
On Microscopy: Sheets, nests, cords or individual cells, Tubular formations are prominent in well differentiated tumors but absent in poorly differentiated tumors, Tumor cells are pleomorphic and Stroma desmoplastic and obscure tumor cells, variable necrosis

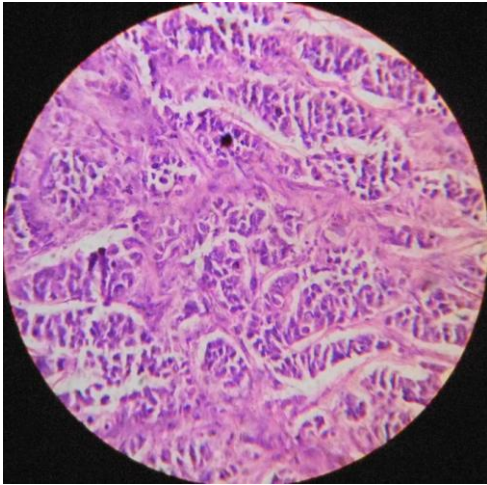


Fig.3 Lobular Carcinoma

On microscopy:

Tumor cells arranged in single file (linear, indian file) encircling ducts, loosely dispersed throughout fibrous matrix

Tumor cells are usually small, uniform, round with minimal pleomorphism, evenly distributed chromatin and no nucleoli.

Variable dense fibrous stroma with periductal and perivenous elastosis

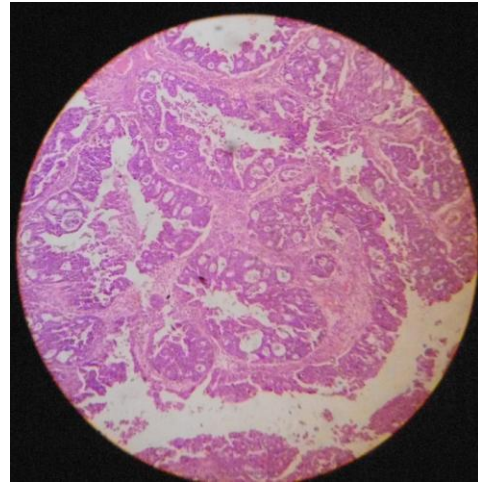


Fig.5 MUCINOUS VARIANT

On Microscopy: Well-differentiated (low grade) tumor cells

floating in a sea of lightly staining amorphous mucin.

Tumor cells are arranged in solid, and acinar pattern

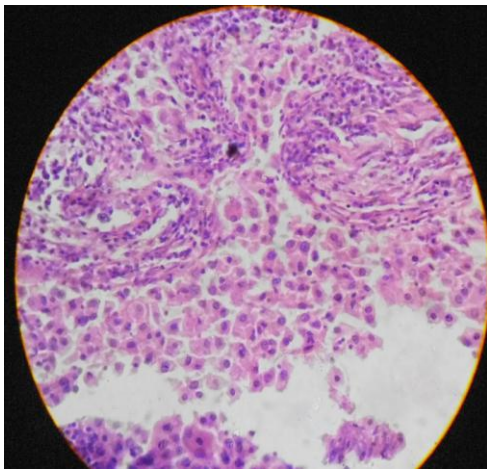


Fig.4 MEDULLARY CARCINOMA

On microscopy: indistinct cell borders (syncytial growth) making up 75%+ of tumor with large pleomorphic tumor cells containing large nuclei, prominent nucleoli, peripheral cells are more eosinophilic.

Prominent lymphoplasmacytic infiltrate at periphery

DISCUSSION

The most common histopathological type of breast cancer found in present study was invasive ductal carcinoma- no special type accounting for 77.3% (147/190), The least common histopathology type in our series was Anaplastic carcinoma 1.05% (2/190).

Histopathology patterns compared with various studies following (Table 3). [11-14]

In the present study age of the patients ranged from 20– 80 years. Average age of patients was 55 years. Maximum number of patients belonged to age group of 41-60 years 92.1% (175/190), this was compared with Naila Nazir et al study which included the age of the patients ranged from 27 – 85 years. Average age of patients was 49 years. maximum number of patients belonged to age group of 31 - 50 years (56%) , In Godwin A. Ebughe1 et al study the mean age of the patients was 45.06 years, ranging from 23 to 76 years, with most of the patients being less than 50 years old (69.1%) followed by 30-39 years (38.3%) and 40-49 years (27.2%). [13]

Present study showed out of the 190 cases of breast cancers analyzed 184(96.8%) were in females ,6(3.1%) were in males coinciding with Am Dauda et al study which was out of the 172 cases of breast cancers analyzed, 7(4%) were in males while the remaining 165(96%) were in females giving a male: female ratio of 1:24. [11]

In the present study out of the 190 cases of breast cancers analyzed only 3.1% (6/190) were in males and all were in age

group 61 to 80 years this was coinciding with Vishal G. Mudholkar et al study out of 125 malignant cases 2.4% (3/125) were males in the age range of 60 – 70 years. [12]

In the present study 78.9% (150/190) cases underwent modified radical mastectomies and 21% (40/190) lumpectomy specimens, with right breast involved in 89.4%(170/190) of the cases and 5.7%(11/190) involved the left breast this was compared to Nazir et al study where out of 50 cases 48 cases were modified radical mastectomies and 2 lumpectomy specimens, with left breast involved in 30(60%) of the cases and 20(40%) involved the right breast. [14]

76.3% (145/190) of patients presented with grade II followed by grade III 14.2%((17/190) and 9.4% (18/190) cases were grade I, this was compared with Godwin A. Ebughe et al study which showed 66.7% (54) of patients presented with grade 3 disease, followed by grade 2 disease (23.5%), with grade 1 disease being least commonly seen (9.9%). [13]

CONCLUSION

Invasive ductal carcinoma (NST) was the most common histopathological pattern in our study followed by medullary carcinoma, mucinous, papillary carcinoma, tubular carcinoma infiltrating lobular carcinoma and anaplastic carcinoma. Different histological subtypes of infiltrating breast tumors have variable prognosis. Histopathological subtypes like medullary, mucinous and tubular variants have a better prognosis.

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How to cite this article: Bookya K, Kumari K. Histopathological patterns of breast carcinomas with molecular profile (ER & pr status). Int J Health Sci Res. 2015; 5(7):122-128.

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