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Pathology

Evaluation of Breast Lumps in Females with Assessment of Estrogen Receptor, Progesterone Receptor and HER2/NEU Status in Patients with Breast Carcinoma

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Abstract: Breast lump is one of the most common surgical problems in females. Diagnosis of breast lesions is routinely performed by the triple assessment. Determination of hormone receptors and human epidermal growth factor receptor 2 (HER2/neu) is important for optimal management in breast cancer patients. The aim of this study is to evaluate the pattern of breast lumps in females with assessment of expression of estrogen, progesterone receptors and Her2/neu in breast carcinoma. This study included a total of 50 patients presenting with palpable breast lesions to Northern Railway Central Hospital (NRCH), New Delhi from May 2012 to June 2015. 50 patients presenting with a palpable breast lesion were included in this study. The breast lesions were classified into benign and malignant and were analyzed in various age groups. Out of 50 patients 25 (50 %) were diagnosed to have a benign aetiology and 25 patients (50 %) were given a diagnosis of malignancy. Highest incidences of benign breast lesions in our study (44%) were in the age group of 20 – 30 yrs and malignant lesions (40%) were between the age group of 50-60 years. Estrogen receptor and progesterone receptor status and HER-2/NEU status was evaluated by immunohistochemistry or supplemented by FISH. Out of 25 IDC cases, the receptor distribution was ER+/PR+ (32%), ER+/PR- (16%), ER-/PR+ (4%), ER+/PR+Her2+ (12%), ER-/PR-Her-2- (16%) and Her2+ 20%. It is recommended to effectively use these parameters to prognosticate and treat breast cancer patients.
Keywords: ER, PR, Her-2/neu, breast cancer.

INTRODUCTION

Lumps in breast may be due to benign or malignant lesions. 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 [1]. Despite increasing incidence rates, annual mortality rates from breast cancer have decreased over the last decade (1.9 percent per year from 2008 to 2012)[2].Various risk factors for breast carcinoma include age of menarche <12, nuliparity, family history of breast cancer in a first degree relative, genetic factors, the effect of endogenous and exogenous hormones in women etc. A benign proliferative breast lesion is an important risk factor for subsequent transformation to malignancy. Transition from normal to cancer begins by proliferation, then progresses to atypia & finally arrives at neoplasia [3]. Hormone receptors and human epidermal growth factor receptor-2 (Her2/neu) status play an important role in the diagnosis, management and prognosis of breast cancer. The determination of estrogen receptor(ER) and progesterone receptor (PR) status in breast cancer is a standard practice now days [4]. Low-grade cancers have positive ER and PR and have lower risks of mortality, compared to high-grade cancers that are negative for ER and PR and also have an overexpression or amplification of HER2[5]. Various clinical trials have shown that treatment with adjuvant hormonal and/or chemotherapeutic regimens increases the survival advantage for women with hormone receptor-positive tumors [6]. In breast cancer the average incidence of estrogen receptor and progesterone receptor positivity is 77% and 55% respectively as shown in the studies [7]. However, lower rates of positive estrogen and progesterone receptor breast cancers are found in Indian population from the western literature. The frequency of negative estrogen receptor and progesterone receptor is much more common in India (46.5%) than in the West (10%)[8]. HER-2 oncogene shares extensive homology with epidermal growth factor receptor (EGFR). It is overexpressed in 10- 35% of breast cancer patients and is considered one of the poor prognostic factors in breast cancer. Trastuzumab is a monoclonal antibody that targets HER-2/neu extracellular domain and helps in improving survival in patients with over expressed

HER-2 receptor [9]. This study was done to evaluate the pattern of breast lumps in females and to assess the status of hormone receptors (ER) and (PR) and Her-2/neu in patients with breast cancer.

MATERIALS AND METHODS

This prospective study was done at Northern Railway Central Hospital (NRCH) from May 2012 to June 2015, involving 50 patients with breast lump(s) who gave their consent to take part. After detailed history, physical examination, and both FNAC and core needle biopsy were performed in an outpatient setting. Later on all of them had excision biopsy or mastectomy (MRM) according to their final diagnosis. Mastectomy or lumpectomy specimens were fixed in 10% formalin for 24 hours and then grossed in histopathology department. After paraffin embedding 5 µ sections were obtained, followed by detailed histopathological analysis of the specimen, including immunohistochemically (IHC) staining for ER, PR and HER-2 receptors were included. A Hercep test score of 3+ was considered as positive and score less than this (0+, 1+, 2+) was taken as negative for HER-2 receptor.

STATISTICAL METHODS

According to the objectives of the study, the collected data were compiled and tabulated. Data analysis was done by using SPSS-10.0, student t-test and chi-square tests wherever applicable.

RESULTS

50 patients presenting with a palpable breast lesion were included in this study. Out of 50 patients 25 (50 %) were diagnosed to have a benign aetiology and 25 patients (50 %) were given a diagnosis of malignancy. The age range of patients for benign lesions was 16–70 years with mean of 27.80±13.74. Maximum number of patients 11 (44%) were between the age 20-30 years. The age range of patients for malignant lesions was 30–80 years with mean of 55.44±9.92. Maximum number of patients 10 (40%) were between the age 50-60 years.

Table-1: Age distribution of cases overall

Age interval	N	Percentage
<20	7	14%
20-30	11	22%
30-40	4	8%
40-50	9	18%
50-60	11	22%
60-70	6	12%
>70	2	4%
Total	50	100%

Table-2: Age distribution of cases with benign breast disease

Age interval	N	%
<20	7	28%
20-30	11	44%
30-40	2	8%
40-50	3	12%
50-60	1	4%
60-70	1	4%
>70	0	0%
Total	25	100%

Table-3: Age distribution of cases with malignant breast disease

Age interval	N	%
<20	0	0%
20-30	0	0%
30-40	2	8%
40-50	6	24%
50-60	10	40%
60-70	5	20%
>70	2	8%
Total	25	100%

Table-4: Mean age of cases overall

Age	Mean	Std. dev
Benign	27.80	13.74
Malignant	55.44	9.92
TOTAL	41.62	18.32

The patients with palpable breast lumps were included in the study. Out of them 52% involved the left breast and 48% involved the right breast. The mean size of the breast lumps was 3.45 ± 1.43 cm in diameter with a range of 2-10 cm.

Table-5: Site distribution of breast lump

Site	N	%
Left	26	52%
Right	24	48%
TOTAL	50	100%

Out of 50 patients 17 were diagnosed as fibroadenoma, 3 were reported as fibrocystic disease, 3 as gynecomastia, 1 as phyllodes tumor,1 as intaductal papilloma while 25 were given a diagnosis of malignancy i.e infiltrating ductal carcinoma unspecified.

Table-6: Final histopath report

Cases	Histopath report
Fibroadenoma	17
Fibrocystic ds	3
Gynecomastia	3
Phyllodes tumor	1
Intaductal papilloma	1
IDC	25

Out of 25 IDC cases, the receptor distribution was as given in Table 19. ER+/PR+ (32%), ER+/PR- (16%), ER-/PR+ (4%), ER+/PR+Her2+ (12%), ER-/PR-Her-2- (16%) and Her2+ 20%. According to ER, PR and HER-2 status, maximum (48%) tumors were luminal-A (ER+, PR+/-,HER2-), 12% luminal-B (ER+, PR+/-, HER2+), 20% HER-2 + and 16% basal-like (ER-, PR-, HER2-) subtypes.

Table-7: Receptor status (ER, PR, Her2 neu) distribution

Receptor	N	%
ER- PR- Her-2-	4	16%
ER+ PR+ Her-2+	3	12%
ER+ PR+	8	32%
ER+	4	16%
PR+	1	4%
Her-2+	5	20%

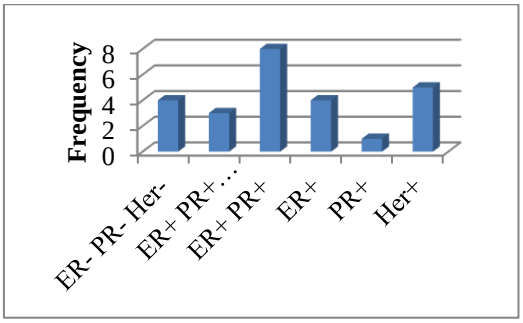

Fig-1: Receptor status (ER, PR, Her2 neu) distribution

DISCUSSION

Breast lesions can be detected at a very early stage by efficient breast screening methods including self-examination by the woman or by her doctor during clinical examination or by mammography. The triple test is the recommended approach for the investigation of palpable or impalpable breast lesions detected by imaging. It comprises the following components: clinical breast examination and medical history, imaging-mammography and/or ultrasound, and non-excision biopsy, i.e. Fine needle aspiration cytology (FNAC) and/or core needle biopsy (CNB) to determine the nature of the lesion. Breast lump of 50 female patients were analyzed in our study, each of them underwent fine-needle cytology of lump and core needle biopsy followed by either lumpectomy or a definitive surgical procedure like modified radical mastectomy (MRM), depending on the final diagnosis. The breast lesions were analyzed according to age wise distribution. Out of 50 patients selected for study, the age ranged from 16–80 years with a mean age of 41.62 years (table-1). The highest incidences of benign breast lesions in our study (44%) were in the age group of 20 – 30 yrs (table-2) and malignant lesions (40%) were between the age group of 50-60 years (table-3). Studies done by Homesh *et al.* [10] and Ariga *et al*. [11] showed similar age patterns. Various studies have reported that primary breast carcinoma arising before 40 years age are far more aggressive, metastatic and have high mortality rates compared to those arising in older patients, regardless of hormone receptor status [12]. Out of 25 benign cases the most common pathology found in our patients was fibroadenoma in 17 (68.2%) patients (table-6). Khemka *et al*.[13] and Tiwari M[14] also reported fibroadenoma as the commonest benign pathology. Infiltrating ductal carcinoma was the most common malignant lesion. Studies have shown that benign diseases of the breast are an important risk factor for breast cancer and the relationship is preferentially associated with atypical parenchymal lesions [15]. In breast cancer patient's assessment of hormone receptor (ER) and (PR) and HER-2/neu status is routinely done nowadays for prognosis and to select patients who are candidates of hormonal and anti- her2/neu therapy. Hormones receptors in our study were found as follows (table-7): ER+ve/PR+ve (32%), ER+ve/PR-ve (16%), ER+ve/PR+veHer+ve (12%), ER-ve/PR-ve/Her-ve (16%), ER-/PR+ (4%). Study by Hussain G A *et al.* [16] also showed similar results. The frequency of overall ER+ve cases was 48% and PR+ve cases were 36%. Studies done by Desai *et al*. [17] and Redkar *et al*. [18] found ER positivity to be 50.5% and 43.9% respectively similar to our study. Her-2/neu expression can be detected by immunohistochemically analysis and fluorescence in situ hybridization techniques in biopsy specimen. Trastuzumab, also called Herceptin is used for targeted therapy in patients with HER-2/neu positive tumours, improving survival and thus making it necessary to assess HER-2/neu status in patients with breast cancer [19]. Her-2/neu positivity in our study was 20%. Studies done by Huang HJ *et al*. [20] showed 17.7% positivity, Moses Ambroise *et al*. [21] showed 27.10% positivity respectively in their study which correlated with our study.

CONCLUSION

Our study has shown that benign proliferative lesions are common in the younger age and incidence of malignant lesions is higher in the elderly age group. A benign proliferative breast lesion is an important risk factor for subsequent transformation to malignancy. Therefore regular screening for breast lumps is required in young women for detecting breast cancer at a very early stage. Hormone receptors expressed i.e ER, PR and HER2/neu play an important role in diagnosis, management, prognosis and determination of treatment outcome in breast cancer patients. Routine testing for hormone receptors and HER-2/neu receptor expression is recommended in all patients of breast cancer because of their prognostic significance and impact on further management with targeted hormonal therapy, herceptin and anthracyclines based chemotherapeutic agents.

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