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Original Article

Breast carcinoma in young females below the age of 35 years - histopathological and prognostic significance

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ABSTRACT

Background: Breast cancers rarely occur in young women but are known to have more aggressive behaviors and poorer outcome. We here compare the significance of breast carcinoma in female below the age of 35 to the age over 35 whose specimens were submitted to Manipal teaching hospital, Pokhara.

Materials and Methods: All cases of mastectomy with carcinoma from January 2000 to September 2011 were included in the study. Clinical and histopathological datas of all cases were reviewed and collated.

Results: A total of 148 mastectomy specimens were received, among which, 23 cases (16%) were below 35 years; whereas 125 cases (84%) were above 35 years of age. In both groups, Stage II was the commonest stage but stage III was much more common in older group (33% versus 9%) and stage I was more common in younger age group (39% versus 27%). Bloom Richardson grading showed that in the older age group, grade 1 is the commonest grade (50%) while in the younger group; grade 3 is the commonest (39%). Patients were followed for a varying period of 6 months to 5 years. Two cases (2% of followed up cases) in older group and 3 cases (15% of followed up cases) in the younger group showed recurrence.

Conclusion: Breast carcinoma in the patients younger than 35 years though presented at an early stage has higher grade tumor and poorer outcome.

INTRODUCTION

Breast cancers rarely occur in young women. About 2% of the patients with breast cancer are < 35 years.[1] Breast cancer at young age has been reported to have a more aggressive behavior and unfavorable prognosis compared to the older patients.[1,2]

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The aim of this study was to evaluate the implication and prognostic significance of diagnosis of breast carcinoma below the age of 35 in comparison to the age over 35 in Pokhara valley, Nepal.

MATERIALS AND METHODS

This was a retrospective and prospective study done from the period of January 2000 to September 2011. All the patients who were diagnosed as breast carcinoma and underwent mastectomy were included. All cases were reviewed and the relevant clinical data were collated and the

Table 1: Distribution of cases according to age

Age group	Number of cases	Percentage
20 – 25	6	23(16%)
>25 – 30	9	
>30 – 35	8	
>35 – 40	23	125(84%)
>40 – 45	46	
>45 – 50	41	
>50	15	

Table 2:Histological types in all cases

Types Of Carcinoma	Below 35 (n=23)	Above 35 (n=125)
Ductal	20 (87%)	113(90%)
Lobular	1(4%)	3(2%)
Medullary	2(8%)	3(2%)
Metaplstic	-	2(1.6%)
Secretory	-	1(0.8%)
Apocrine	-	1(0.8%)
Papillary	-	1(0.8%)
Mucinous	-	1(0.8%)

Table 3: Tumor size (T) and nodal status (N) in all cases below and above 35 years of age

Tumor & Lymph node		Below 35 (n= 23)	Above 35 (n=125)
T0	No palpable tumor	-	-
T1	≤2 cm	16 (70%)	54 (43%)
T2	>2 cm and ≤ 5 cm	6 (26%)	44 (35%)
T3	> 5 cm	1 (4%)	20 (16%)
T4	Chest wall / skin invasion	-	7 (6%)
N 0	No regional node	12 (52%)	45 (36%)
N 1	Movable ipsilateral axillary node	11 (48%)	80 (64%)

Table 4: TNM staging of all cases

TNM Stage	Below 35 (n=23)	Above 35 (n=125)
I	9 (39%)	34 (27%)
II	12 (52%)	50 (40%)
III	2 (9%)	41 (33%)

Table 5: Microscopic findings of tumors in both age groups

HISTOLOGICAL FINDING	Below 35 (n= 23)	Above 35 (n=125)
Tumor emboli	15 (65%)	83 (66%)
Dermal / nipple invasion	-	10 (8%)
Stromal inflammation	18(78%)	108 (86%)
Necrosis	18(78%)	90 (72%)

Table 6: Bloom Richardson Grading of all cases

Grade	Below 35 (n=23)	Above 35 (n=125)
1	6 (26%)	63 (50%)
2	8 (35%)	46 (37%)
3	9 (39%)	16 (13%)

histopathology slides were reviewed by two pathologists independently. Patients were grouped in two age groups as below and above 35 years. All data including family history, clinical presentations, pathological type and grade, TNM stages were compared. Follow up data with data on recurrence were analyzed. Exclusion criteria included (a) the patients who were diagnosed as Stage IV and did not undergo mastectomy and (b) patients who were diagnosed as breast carcinoma on fine needle aspiration cytology but were lost to follow up.

RESULT

Out of total 148 mastectomy specimens, 125 cases (84%) were above 35 years and 23 cases (16%) were below 35 years (Table 1). Ductal carcinoma was the most common tumor in both age groups. Table 2 enumerates all the histological subtypes in both age groups. Tumor size and regional node involvement are shown in Table 3. Majority of the patients in younger age group presented in T1 stage (70% vs 43%) and 48% of younger patients had nodal metastasis in contrast to 64% in older age groups with nodal metastasis. Among those patients with nodal metastasis, older patients had lesser number of nodes. In younger patients with positive lymph nodes (11 cases), 6 cases (54.5%) had ≥4 lymph nodes involved; whereas among the older patients with positive lymph nodes (80 cases), 54 (67.5%) had ≤ 3 lymph node metastasis.

TNM stages in both age groups are compared in Table 4. In the microscopic findings, tumor emboli, stromal inflammation and necrosis were seen in both age groups but dermal/ nipple invasion (T4) was more common in older age groups as shown in Table 5. According to Modified Bloom Richardson grading (Table 6), grade 3 (fig. 1) was the commonest below 35 years age group (39%) followed by grade 2 (35%; fig. 2). In contrast, older age group showed lower grade with 50% being grade 1 (fig. 3) followed by grade 2 (37%). More positive family history (39% vs. 9.6%) and higher recurrence rate (87% vs. 74%) among the followed up cases were seen in younger age group.

DISCUSSION

Breast cancer in adolescence and early adulthood is a rare condition.[1] The estimated incidence is less than 0.1 per 100,000 women below the age of 20 years, increasing to 1.4 for women 20–24 years, 8.1 for women 25–29 years and 24.8 for women 30–34 years old.[2] In our study 4.05% women were of 20-25 years, 6.08% women were of 26-30 years and 5.4% were of 31-35 years were having breast cancer. Childhood breast cancer accounts for less than 1% of childhood cancers and less than 0.1% of all breast cancers.[3-5]

Breast masses in young women are mostly benign.[6-8] A population-based study over a period of 70 years confirms

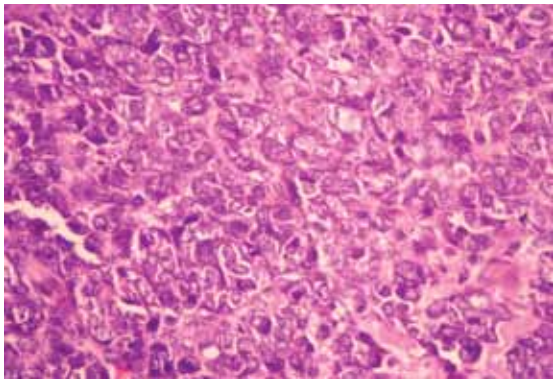

Figure 1: Tumor cells showing Bloom Richardson Grade 3 features (HE stain, X400).

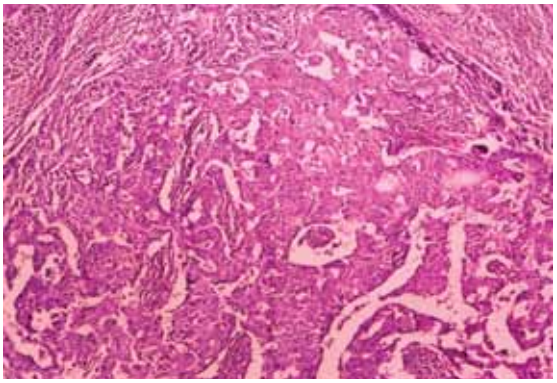

Figure 2: Tumor cells showing Bloom Richardson Grade 2 features (HE stain, X400).

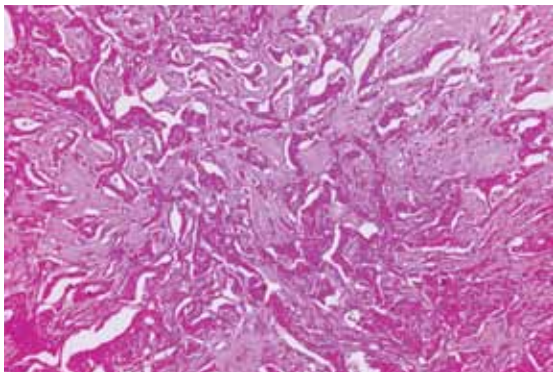

Figure 3: Tumor cells showing Bloom Richardson Grade 1 features (HE stain, X100).

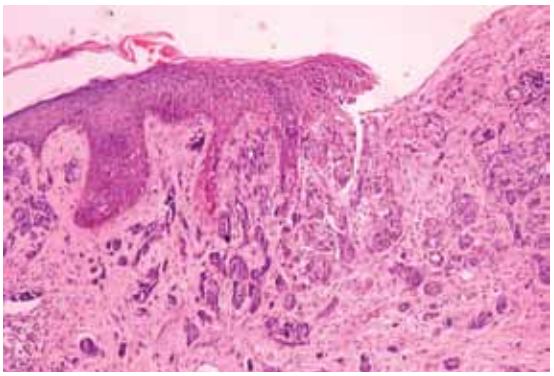

Figure 4: Tumor cells infiltrating into the nipple skin (HE stain, X100).

that breast carcinoma in young women is rare and more often caused by metastases or stromal malignancy such as malignant phyllodes tumor.[9] Breast masses in adolescence demonstrates that fibroadenomas are the most common breast masses[10] whereas malignancy was rare and more often caused by metastases or stromal malignancy such as malignant phyllodes tumor.[9] Breast carcinoma accounted for only 0.02% in surgically removed breast masses in girls and young women.[10] In a review of 357 patients aged 25 years or younger with a breast mass, 0.8% were benign phyllodes tumor, 0.3% had a breast carcinoma, and the rest had benign disease.[11]

In another study of 178 breast masses in patients aged 20 years or younger, no carcinomas were found.[3] Dehner et al[12] found only one case of breast cancer in a review of 374 breast masses in patients younger than 20 years of age. In our study there was no malignant case in younger than 20 years as the youngest patient with cancer was of 22 years-old.

Breast cancer occurring in very young patients are reported to have a aggressive biological behaviour leading to a unfavourable prognosis.[13,14] A review of the US National Cancer Database revealed that patients younger than 35 years had more advanced disease at diagnosis and a poorer 5-year survival rate than older premenopausal patients.[15] Similar findings have been reported in the past.[1,2,16] More positive axillary lymph nodes and higher incidence of local recurrences were detected in younger compared with older patients.[14] According to Ashley S et al[17], breast cancers in young age group tend to be larger when diagnosed and have a longer history of a palpable mass than tumours diagnosed in older women. However in our study, the tumor size in the younger group was smaller in size than the older group. T1 tumor was more frequently found in younger group (70% vs 43%) resulting in lower TNM stage in younger age group.

Immuno-markers and genetic studies also confirm that the breast carcinoma in young is different subset. Younger patients usually have ER/PR negative tumor and, those with ER-positive tumors had a significantly worse prognosis than those with ER-negative tumors.[1] There are specific subsets of young women who have a potential high-risk of developing breast cancer at a young age based on a genetic predisposition or having previously received irradiation.[18] Women diagnosed with breast cancer at the age of <35 years are likely to have germ-line BRCA1 or BRCA2 mutations in up to 15–30% of cases.[19-21] These mutations are more frequently associated with higher histological grade, lack of ERs, perivascular invasion and high proliferation rate.[1] The percentages of overexpression of HER2/neu in 'very

young' and 'less young' women were similar in the study done by Colleoni et al.[1]

A study of more than 1 million women with breast cancer recorded in the American College of Surgeons Cancer Database between 1998 and 2005 demonstrated that women younger than 40 years of age were more likely to present with more advanced (stage III or IV) disease (20% vs. 13.5%), and they were more likely to have infiltrating ductal carcinoma (76.9 vs. 67.9).[22]

In our 11 years study, 16% of all mastectomy cases were of < 35 years of age. Lymph node metastasis was seen more frequently in older age group (older 64% vs. younger 48%) but in those cases with nodal metastasis, younger patients showed more predilections to increased number of nodal involvement. In both groups TNM stage II was the commonest, but Stage I is seen to be more common in younger age group. Older age group showed more number of skin infiltration (10 cases, 8%) resulting in T4 stage (fig.4). But, on the contrary, histological grade clearly shows a more aggressive tumor in younger group.

The triple test (palpation, ultrasound examination and core needle biopsy) is currently considered the gold standard for evaluation of breast masses in women younger than 30 years.[18] Excisional biopsy is now reserved for the patient in whom the core needle is non-diagnostic; when there is discordance in pathological findings, physical examination, and radiologic appearance. There is growing evidence that core needle biopsy is not routinely required in evaluation of breast masses in young women, except where metastatic disease is suspected.[6,18]

Poorer survival, in young patients, could be related to reduced screening, more aggressive disease, and delayed diagnosis.[23] Corpron CA et al found that delayed diagnosis in young women results from delayed presentation and biopsy, similar to other reports.[23] Younger women still have significantly poorer survival even after adjusting for stage, histology and grade.[24] Prevention and early detection are vitally important in these women. At present, definitive data on effective screening and prevention of breast cancer in very young women are lacking, but there are a number of ongoing trials which would provide some evidence on which to base future recommendations.[18]

CONCLUSION

In our study we found that younger patients presented with higher grade, more positive family history and more recurrence rate. However, tumor size and TNM stage was lower in younger age group. So, age should be considered as an important factor in assessment of the prognosis and more regular follow up should be carried out after mastectomy in younger patients. Further studies including hormonal markers like ER/PR and genetic studies in this group of population may give more insight in future.

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