

Is Carcinoma Breast A Different Disease in Pakistani Population?

Pages with reference to book, From 114 To 116

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Abstract

Carcinoma of the breast tends to be different in coloured and white races. Is this pattern also expressed in Pakistani population? To answer this query we carried out a retrospective study of breast cancer on 193 cases who were divided into 2 groups i.e. less than and more than 50 years age groups. In the former group, 93% tumours were of grades II or III and approximately 51% were estrogen receptors negative. In more than 50 years age group, 75% tumors were in grade II and III, with almost 37% being estrogen negative tumors. Majority (75%) of the patients had over 5 cms lump with equal number having positive lymph node status, All these factors point to the fact that besides presenting late, our population has additional unfavourable prognostic factors (JPMA 47:114,1997).

Introduction

Breast carcinoma tends to have a different process in white and black races¹⁻⁴. Initially, this was attributed to the stage of the disease at presentation. However, there were still residual differences in the survival rates, even where the differences in the stages were controlled. Although there are exceptions⁵, the survival rates of breast cancer in blacks are lower than in whites and other ethnic races^{6,7}. We carried out a retrospective analysis of breast cancer cases submitted to our laboratory which caters to a large group of local Pakistani female population belonging to all economic strata. The purpose was to observe the different disease patterns in local population. This was an uncontrolled study, accompanson can be made with existing data in the world literature.

Materials and Methods

Two hundred and one cases of breast cancer tissues received during 1991, were included inthe study. The material was from within the hospital (The Aga Khan University Medical Centre) and from other centres. Eight cases were excluded from the study due to reasons mentioned in the result section. Both formalin fixed and fresh tissue were included in the study. After being received the material was transferred to 10% buffered formalin and allowed to stand overnight. Sections were then taken, of 3-4u routinely processed and stained withHematoxylinand Eosin. They were studied under the light microscope and graded according to the Bloom and Richardson grading system⁸, taking into account tubule formation, nuclear pleomorphism and mitosis.

Thbule formation

When definitive tubule formation was seen in more than 75% of the tumors, it was scored as 1, less than 10% of the tumor, was 3 and the intennediate category had a score of 2.

Nuclear pleomorphism

If there was little variation in size and shape of the nuclei and they appeared regular, 1 point was given, marked

variation, particularly whenvery large and bizarre nuclei were seen, 3 points were given. The nuclei intermediate between the two extremes were scored as 2.

Mitotic rate

Here only clearly identifiable mitotic figures were counted. Less than 10 mitotic figures/10 HPF were scored 1, more than 20 mitosis/10 HPF scored 3, and a score of 2 was assigned for the intermediate category. After all three parameters were scored, the combined grade was assigned. Grade I was given to the tumors having combined score of 3,4 or5, Grade 2 was assigned if the combined score was 6 or7 and Grade 3 was given to cases which scored total 8 or 9 points. Estrogen receptor studies were performed on all tumours using immuno-histochemical method. The tissue received in formalin was stained with Signet universal immuno-peroxidase staining kit by PAP (peroxidase anti-peroxidase) method. The kit used for frozen tissue was Abbot ERA- ICA monoclonal kit. The positivity for human estrogen receptors appeared as brown stain within the nuclei. The immuno- histochemical localization of the estrogen receptors was scored in the semi-qualitative fashion, incorporating both the intensity and distribution of the specific staining. The evaluations were recorded as percentages of positively stained target cells in each of the four intensity categories^{7,8} ; 0 = no staining, +1= Weak but detectable staining, +2= Mildly distinct staining, +3= Moderately distinct staining, +4= Strong staining. For each tissue, a value designated as H score derived by summing the percentage of cells stained at each intensity was multiplied by the weighted intensity of staining. A H-score of 0-74 was established as negative, 75-99 as weak positive, 100-119 as intermediate positive, 120 and above as strongly positive.

Results

A total of 201 patient samples were included in the study but 8 were not suitable for further analysis because specimen was too small for comparative Hematoxylin and Eosin and Estrogenic receptor staining (4 patients). The specimen was autolyzed or inadequately fixed, so interpretation of the histologic and receptor status was doubtful (2 patients). Only lymph nodes were received with metastatic tumor without the primary breast tumor (2 patients). Remaining 193 specimen were studied and interpreted.

One hundred and twenty-three patients (63.73%) were less than 50 years of age and remaining 70 (36.27%) were more than 50 years. The youngest was 16 years and oldest 81 years. The mean age was 47.8 and median age was 45 years. The grading of the tumours in the two age groups is shown in Table I.

Table I. Scatter of grades in two age groups.

	<50 years group	>50 years group
Grade I	7%	7%
Grade II	43%	59%
Grade III	50%	34%

It was observed that majority of patients in over 50 years age group had grade II carcinoma whereas half of the

The relationship between Estrogen Receptor positivity according to the tumour grade is presented in Table II.

Table II. Estrogen receptor positivity according to grade.

	<50 years group	>50 years group
Grade I	100%	60%
Grade II	79%	66%
Grade III	16%	38%

It indicates that well differentiated tumors show Estrogen receptor positivity, whereas high grade tumours show a reverse phenomena. This is denoted by the fact that only 16% and 38% of the poorly differentiated tumors in two age groups were estrogen receptor positive. Size and nodal status could only be evaluated in 53 mastectomy samples as rest of specimen were lumpectomies or incisional biopsies.

Table III. Size of the lumps.

No. of patients	Size of lump
5%	<2 cms
19%	2-5 cms
55%	5-9 cms
21%	>10 cms

As shown in Table III almost 75% patients had lump size larger than 5 cms.

Out of 53 patients, 40 patients (75%) had positive axillary lymph nodal status with only 10 (approx. 19%) patients having less than 3 lymph nodes positive and 30 patients (approx. 56%) having involvement of more than 3 lymph nodes.

Discussion

Breast carcinoma tends to be a different disease process in coloured as compared to the white females⁷. The black patients tend to do worse than their white counterparts. European women tend to have a higher rate of estrogen receptor positivity as compared to the non-European females i.e., 29% and 8% respectively⁹. In American population, black females have a higher mortality (20% more) as compared to white American females⁴. This was attributed initially to the differences in the disease stages at the time of discovery⁶. However, there were residual differences in the survival rates even when the differences in stage were controlled. In a subsequent survey by the American College of Surgeons of

breast cancers, survival differences between the races continued to be observed⁶. Few reports since then have suggested the different socio-economic status to be a relevant factor, although how this factor is translated into poor survival is not fully understood¹⁰. Young et al reported a lower 5 year survival in blacks as compared to whites as well as other ethnic groups¹¹. It is possible that socio-economic status is not the only factor affecting survival in blacks adversely, some of the malignant diseases may be different between different races. This possibility is partially supported by small differences found in tumour types and frequency with positive estrogen receptor¹². The difference in receptor status has also been reported by Mohia et al¹³ who have attributed the difference in receptor status to the degree of tumour differentiation i.e., the estrogen negative tumours are more likely to be less differentiated. Reports from Pakistani population also showed significant differences between the tumour differentiation and simultaneously performed Estrogen receptor status in Pakistani population as compared to the white population^{14,15}. According to these reports, 75% of the breast cancer patients in our population belonged to grade II and III category. In our study, 93% patients had grade II and III tumours and simultaneously performed Estrogen receptor studies showed more breast cancers with Estrogen receptor negative status. In less than 50 years age group, 42% (63/123 approx) were either negative or weakly positive for human estrogen receptor. Whereas, other local study¹⁶ has reported 78% negativity in premenopausal group. In more than 50 years age group, 41% (29/70 approx) were either negative or weak positive for estrogen receptors. Overall 48% tumours were negative or weak positive for the receptors and 52% positive for the receptors. In contrast to the western studies, report as many as 61% positivity for Estrogen receptors¹⁷. Another Pakistani study reported 52% estrogen receptor positive tumors¹⁶. About 54% of patients in our series were between 31-50 years and 10% were less than 30 years of age. This indicates that 64% of our patients fall in premenopausal group, 10% patients were under 30 years as compared to 2% western figures 18-20. Survival in younger patients is dismal²¹, in spite of the similar treatment protocol as compared to the older patients. Five year disease free survival in the women aged 30 years and younger is 43%¹⁸ while in over 30 years it is 59%. Other factors important in the breast cancers are size and nodal status²², the size of the primary tumours is a valuable information contributory towards the prediction of early recurrence of the tumour^{17,23}. In our study, only 53 samples were assessed for this parameter and almost three quarters had lumps larger than 5 cms. It is thus inferred that our population besides having other bad prognostic factors, also has an added factor of larger size, that is probably related to late presentation by these patients.

Regarding nodal status it is the single most important prognostic factor in cancer of the breast^{17,22,23}. A careful recording of axillary lymph nodes involved is the most significant component in the assessment of the disease. Patient survival, recurrences, disease free intervals and response to the treatment are dependent on this factor alone²⁴. Lewis and Rice have reported 39% of the axillary lymph node positivity for breast cancer in their series²⁵. Almost 75% of our patients had positive lymph node at the time of tumour resection. In summary, all these preliminary studies show that the carcinoma of the breast, which is the leading malignancy in Pakistan²⁶ tends to have features which point to an unfavourable prognosis as compared to those in west. This fact is also consistently observed in the black population in the West as compared to the white, which is associated with poorer prognostic factors (differentiation, size, degree of Estrogen receptor positivity). Is this trend expressed in our population as well? Initial studies from local population draw a more pessimistic picture in Pakistani females. raising a big argument "Is breast cancer a different disease in our population from the very beginning? Further studies may be helpful to achieve the final aim of better understanding of the disease in Pakistani females and thus compel our experts to develop more effective/aggressive modalities of diagnosing and treating these patients suitable to our disease patterns.

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