Early Metastasis in Different Types of Breast Carcinoma - A Personal Experience

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ABSTRACT

Background: Carcinoma breast is one of the leading causes of death in woman today and is the most common cancer among women. More than 2.3 million of women are diagnosed breast cancer each year world-wide. Carcinoma breast may present from an extent of non-palpable lump to a fixed mass with distal metastasis. As presentation is highly variable, management strategy varies even in same stage of disease.

Objective: To identify early metastasis of different types of breast carcinoma and its management.

Materials and methods: This is a prospective type of observational study in 100 cases done in the different surgical units of Dhaka Medical College Hospital (DMCH), Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bashundhara Ad-din Medical College Hospital (BAMCH).Patients were selected clinically and by some standard investigation (FNAC and core biopsy) from January 2006 to December 2018.

Result: Patients at different age groups had suffered from different types of breast carcinoma. Early diagnosis by triple assessments and proper surgical and post-surgical managements reduced both loco- regional and distant metastasis and also reduced both morbidity as well as mortality. Results of treatment and histopathological reports were recorded. It was found that FNAC is cheap and minimally invasive diagnostic procedure with high sensitivity (100%) and specificity (95%).Core needle biopsy is more accurate tissue diagnostic in breast cancer. Down staging has profound symptomatic and cosmetic benefit. In renders inoperable tumors become operable and reduce morbidities.

Conclusion: Early diagnosis and treatment is the mainstay to achieve satisfactory outcome. Screening program especially Self-Breast Examination (SBE) is very much helpful in early diagnosis of disease in our social setting. Screening mammography has had the most substantial impact on the early diagnosis of, and subsequent decrease in mortality from breast carcinoma. Women of 20-40 years of age should have a breast examination every 2-3 yearly. Women of more than 40 years of age should have a breast examination every yearly.

Key Wards: Carcinoma breast,metastasis, FNAC, mammography, mastectomy, systemic therapy, neo adjuvant therapy.

Introduction

Breast cancer is the second leading cause of cancer deaths in women today (After lung cancer) and is the most common cancer among women, excluding non-melanoma of skin cancers. According to the World Health Organization (WHO) about 2.3 million women were diagnosed with breast cancer in 2020. The American cancer society estimates that 281,550 new cases of invasive breast cancer are expected to be diagnosed in women and about 2,650 in men in2021. About 43,600 women in the U.S. are expected to die in 2021. About 1 in 8 U.S.women (about 13%) will develop invasivebreast cancer in their lifetime. Any age may be affected but it is rare below the age of 30 years. One in 10 breast lumps referred to a breast clinic will prove to be malignant.2The above-mentioned information indicates the importance of early diagnosis and prompt adequate management in breast carcinoma. In Bangladesh breast cancer in not uncommon. Women at different age groups are presented commonly in advanced stage, with both

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local and systemic manifestation, due to variety of causes like poverty, ignorance, shame, religion, poor health knowledge, lack of social awareness, reluctant to attend a male doctor, and blind dependency on indigenous and non-scientific measures compels our patients to present in a stage beyond cure.

Common formsof breast carcinoma-invasive ductal carcinoma (IDC), invasive lobular carcinoma (ILC), ductal carcinoma in situ (DCIS) and Lobular carcinoma in situ (LCIS). Less common forms of breast carcinoma: medullary carcinoma, tubular carcinoma, inflammatory carcinoma, Paget's disease of the nipple, malignant phylloides tumors, papillary carcinoma and metaplastic carcinoma.[1,2]

Metastasis of breast carcinoma commonly occurs through lymphatic and hematogenous routes. The main lymph channels pass directly to the axillary and internal mammary lymph nodes. Later spread occurs to the supraclavicular, abdominal, mediastinal, groin and opposite axillary lymph nodes.[1,2] Hematogenous metastasis is most commonly to bones (at the sites of red bone marrow i.e. vertebrae, skull, pelvis, ribs, sternum, upper end of femur, upper end of humerus), liver, lung andbrain. The ovaries and suprarenal glands are also frequent of deposits.[1-2]

To determine a cancer's histologic grade, examine the breast cancer cells and their patterns under a microscope. A sample of breast cells may be taken from a breast biopsy; lumpectomy or mastectomy.[1-2] Diagnosis depends on clinical breast examination, ultrasound,mammography,biopsy, cancer marker and certain imaging test such as chest X-ray, CT scan, MRI and bone scan. Blood tests are needed to evaluate a patient's overall health and detect whether cancer has spread to certain organs.[1-2]

Introduction of mammogram and other imaging techniques has tremendous impact in developed countries. Many patients were diagnosed carcinoma breast at a stage when they were clinically impalpable 5 to 10 years disease free survival has improved to very satisfactory level.

Treatment depends upon clinical stage of the disease at presentation and other tumor characteristics such as tumor grade. Treatment of early breast cancer will usually involve surgery with or without radiotherapy. Systemic therapy such as chemotherapy and hormone therapy are added if there are adverse prognostic factors such as lymph node invasion including metastatic relapse. Advanced or metastatic breast cancer is usually treated by systemic therapy to relieve symptoms and extend a women's life time. Fortunately, the mortality rate of breast cancer has reduced in recent years with an increased emphasis on early detection and more effective treatment.[3] It is observed that breast cancer survival rate has greatly increased over the past 20 years due to early detection and improved multidisciplinary approach in the form of neo-adjuvant therapy and per operative radiotherapy.[3] The cycle started with Beatson in 1896 and is currently resting with ATAC trial 2002.[5] Considering various case reports, Breast Conserving Surgery (BCS) is getting popular as 5 years survival rate is almost equal with mastectomy alone[1]. Additionally psychological trauma of losing breast will be reduced from BSC. Recent advances like BRCA-1, BRCA-2 and other (chromosomal) genetic factors, newer drugs and advances in targeted radiotherapy all added to hopes in successful management of breast cancer patient, only when disease is diagnosed early.

Materials and methods:

Type of study: Prospective study.

Study place: The study was conducted in the admitted patients of different surgical units ofDhaka Medical College Hospital (DMCH), Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bashundhara Ad-din Medical College Hospital (BAMCH).

Study period: From January 2006 to December 2018.

Selection of cases: Patients presenting with clinical features of carcinoma breast and only who volunteered after proper explanation were selected finally for the study.

Inclusion criteria: All clinically diagnosed cases of carcinoma breast irrespective of age & sex.

Exclusion criteria:

1. Patients who had a history of mastectomy and recurrence.

2. Sarcoma and malignancies other than carcinoma.

3. Patients who willingly withdrawn themselves from the study.

Sample size: Total 100 patients.

Management:

Breast carcinoma should be managed by multidisciplinary approach of general surgeon and reconstructive surgeon.[1] Great dispute is present regarding the management of carcinoma breast since the history of treatment available. To reach a consensus is very difficult as the management depends upon the patient status, modalities available and other different factors. Two methods of treatment are accepted till date. One is systemic therapy in the form of chemotherapy and hormone therapy. Another is local therapy, which includes surgery and radiotherapy.[1]

Early breast cancers are managed by surgery and radiotherapy. On the other hand, locally advanced or metastatic cases are usually treated by systemic therapy to palliate symptoms and surgery playing a much smaller role. Treatment of breast carcinoma is highly variable in different centers. Roughly stage I and stage II diseases are managed by curative surgery. Patients in stage I and II can be managed by breast conserving surgery followed by local radiotherapy to the breast. Intra operative radiotherapy may help. Axillary sampling can be done by separate incision in the axilla. Sentinel lymph node biopsy can help in the management of axilla in negative cases. If properly evaluated it can avoid extensive axillary dissection and reduce ultimate morbidity. Stage II cases can be managed by Patey's mastectomy effectively. In stage III disease down staging may avoid radical surgery and breast conserving surgery still might be possible in those cases after appropriate neo-adjuvant therapy. In stage IV diseases there is no scope of curative surgery. Various palliative measures may help. Patients with fungating or necrosed lesions are managed by toilet mastectomy. Pre-menopausal women respond to chemotherapy and post-menopausal women respond to hormone therapy significantly.[9] Irrespective of age estrogen receptor positive cases respond well to hormone therapy.[9]

Observations & Results:

After data collection, individual cases were analyzed and the presented in this section by tables and pictures.

Table-01: Age distribution of patients

Age	Number	Percentage (%)
20-29	04	04
30-39	10	10
40-49	14	14
50-59	22	22
60-69	42	42
70-79	06	06
80-89	02	02
Total	100	100

The above table shows distribution of patients according to age group. It shows majority of patients 42 (42%) were between the ages of 60-69 years. Next highest percentage of patients 22 (22%) were in the age range of 50-59 years and a quiet number of patients 14 (14%) were below 40 years; among them maximum 10 (10%) were between 30-39 years. Mean age is 46.19 years and age range from 25-80 years. It indicates that younger age group is not escaped from developing malignancy.

Table-02: Side of breast involvement

Side	Number	Percentage (%)
Right	64	64
Left	34	34
Both	02	02
Total	100	100

The above table shows right breast was mostly involved in 64 (64%) cases. Both breasts were involved only in 02 (04%) cases. Left sided breast was involved in 34(34%) cases.

Table-03: Area of breast involved in malignancy

Quadrant	Number	Percentage
Upper outer	40	40
Upper inner	32	32
Central	08	08
Lower outer	12	12
Lower inner	04	04
Multiple	04	04
Total	100	100

This table summarizes the area of involvement. It shows that in majority of patients, 40 (40%) there was involvement of upper outer quadrant. This indicates maximum patients presented in early stage. Upper inner quadrant was involved in 32 (32%) cases. 12 (12%) patients were presented with lower outer quadrant lump. Eight (08%) patients had involvement of the central part and lower inner part was involved in four (04%) cases.

Table-04: Associated signs found during examination

Sign	Number	Total
Peau-d-orange	04	
Oedema	00	
Skin infiltration	10	
Ulcer	02	
Nipple retraction	08	44
Puckering	04	
Satellite nodules	16	

Skin infiltration was involved in 10 (10%) of which 02 (02%) had ulceration of different sizes. Nipple retraction was found in eight (08%) patients. Sixteen (16%) had satellite nodule away from the tumour site. All these figures are tabulated in table 04. Clinical features documented above were present singly or in combination. So the incidence of symptoms does not correlate with total numbers of patients.

Table-05: Lymph node status (Axillary)

Clinical Examination			Classification based on preoperative findings					
Trait	Number	(%)	N_0		N_1		N_2	
			Number	(%)	Number	(%)	Number	(%)
N_0	42	42	22	22	20	20	00	00
N_1	18	18	00	00	10	10	08	08
N_2	40	40	00	00	06	06	34	34
Total	100	100	22	22	36	36	42	42

The above table (table-05) indicates lymph node status and accuracy of clinical examination. Clinically forty-two (42%) cases were in N0. Among them per operative N0 was only 22 (22%) and rest of the twenty (20%) cases had N1. It indicates though axillary lymph nodes were assumed clinically impalpable, per operatively they were found enlarged. In the same way 18 (18%) patients had mobile axillary lymph nodes clinically i.e. N1. Among them 10(10%) were mobile and 08 cases (08%) had fixed lymph nodes (N2)per operatively. Again 40 patients (40%) showed fixed lymph nodes (N2)clinically. Six (06%) of them were mobile (N1) per operatively and 34 (34%) cases had fixed lymph nodes actually. Sensitivity of clinical examination was calculated as 42%. This table also unfolds the inaccuracy rate of clinical examination.

Table-06: Types of breast carcinoma (invasive)

Types of breast carcinoma (Invasive)	Number	Percentage (%)
Invasive ductal Ca	80	80
Invasive lobular Ca	16	16
Medullary Ca	02	02
Mucinous Ca	02	02
Others	00	00
Total	100	100

This table was shown 80 patients (80%), most of the patients suffered frominvasive ductalCa, 16 patients (16%), suffered from invasive ductal lobular Ca. Only 02patients (02%) suffered from both medullary and mucinous Ca of breast. Others type not found.

Table-07: Grading of breast carcinoma

Grade		Differentiation		Total	Percentage
Grade-I	00	Well	00	00	00
Grade-II	28	Moderate	28	28	28
Grade-III	72	Undifferentiated	72	72	72
Total				100	100

This table was showed all patients presented at Grade-II and Grade-III, on patient at Grade-I. There were 72% at grade-III and 24% at grade-II.

Table-08: Metastasis

Status	Number	Percentage (%)
M_0	86	86
M_1	14	14
Total	100	100

Above table indicates that only fourteen patients (14%) presented with metastasis at the time of diagnosis and 86 patients (86%) had no distal metastasis.

Table-09: Duration of distant metastasis in relation to histopathological types of breast Ca

| Types of breast carcinoma	Duration of distant metastasis (from history)	Site of metastasis
Invasive ductal carcinoma	1 month	Bone
	1 ½ months	Liver
	6 months	Bone
	4 months	Bone
Invasive lobular carcinoma	3 months	Lung
	2 ½ months	Lung
	6 months	Liver

This table showed more aggressiveness of breast carcinoma to the distant metastasis like bones, lungs and liver within 6 months.

Table-10: Comparison between FNAC and histopathology report

Report	FNAC		Positive for malignancy	
	Number	(%)	Number	(%)
Benign	06	06	00	00
Malignant	94	94	100	100
Total	100	100	100	100

Out of 100 patients six (06%) patients were reported benign and 94 (94%) patients were diagnosed as malignant by FNAC. In histopathology report all patients were diagnosed as malignant and no case as benign. Three cases were therefore false negative. Specificity of FNAC was calculated to be 100% and sensitivity was 96%.

Pie chart-1: Surgical treatment
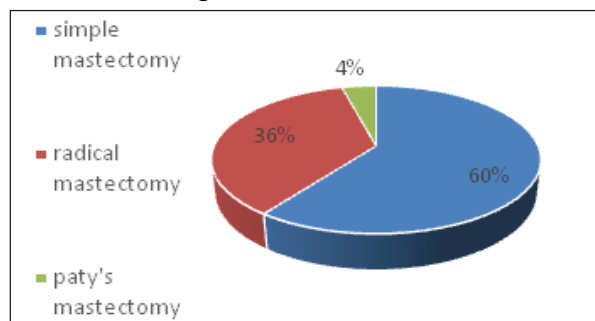
This pie chart shows the spectrum of surgical procedures 60 (60%) patients were managed by simple mastectomy with axillary dissection; 36 (36%) patients by radical mastectomy and only 04 (04%) patient by Patey's mastectomy.

Table-11: Site of distal metastasis

Site	Number	Percentage (%)
Bone	06	42.86%
Lung	04	28.58%
Liver	04	28.58%
Brain	00	00
Total	14	100

This table shows the site of distal metastasis with their frequency. In six (42.86%) i.e. most of the cases, bones were the site of involvement. In four (28.58%) cases, it involved lungs, and in only in four (28.58%) cases, liver was involved. These were documented from bone scan, Chest CT scan and Ultra sonogram of whole abdomen.

Discussion:

Breast cancer is nota disease of modern society; the ancient Egyptians recognized it as long as ago 1600 BC. However, breast cancer has become a major health problem over the last 50 years, affecting as many as one in twelve women during their lifetime.[1,2] The burden of breast cancer worldwide in both developed and developing countries are increasing and evidence suggests that unless action is taken it will continue to grow for the foreseeable future.

Breast cancer is a significant health problem in the industrialized western world, where it is the most common form of cancer among women in North America and almost all of Europe. It is estimated that

each year the disease is diagnosed in over 2.3 million women in worldwide and is the cause of death in over 400000 women.[16] The incidence and prevalence of breast cancer increases with increasing age. It is known that incidence rates for breast cancer is rare below the age of 20 years and then steadily rises so that by the age 90, 20% women are affected.[1] In our study it shows that majority if patients i.e. 42 (42%) were between the age of 60-69 years. Next highest percentage of patients i.e. 22 (22%) as in the age range of 50-59 years. Median age for carcinoma of breast is 60 years.[10] In our study median age was 46.19 years. This is alarming that earlier age groups are affected in comparison to western world in our country. In the USA, 75% of new diagnosed cases are women aged 50 years or older, and the lifetime risk of a diagnosis of breast cancer is approximately 12.5%.[1,2]

Breast cancer presents with various features extending from non-palpable mass to invasive lesions. About 70% patients of breast cancer present with lump.[9] Our observation was 100%. Though there is no predilection to the right or left breast, in our study it revealed 64% in the right and 34% in left breast was involved. Less than 01% percent patient presents with bilateral breast involvement.[9] Our study shows it as 02%. This is not far from standard results. 60% of the lesions arise in the upper and outer quadrant.[1]In our study it was 40%. Most of the lesion occupied upper quadrants of the breast. This was due to the advanced stage of disease Males are affected 0.5% by carcinoma breast[1] but in our study we got no male patients. Family history of breast cancer may be present in 5% cases. 65 None of our patients had positive family history.

Although benign breast lump are six times more common than malignant. The persistence of any mass in the breast raises the suspicion of carcinoma, which are the most malignant lesion of breast and leading cause of death from cancer in women. Therefore, no mass is trivial to be investigated. There are various diagnostic tools among them FNAC is the cheapest and easiest to perform. False positive result of FNAC is extremely low (<1%) and false negative result is albeit higher (10%).[9]

In our study, FNAC gives sensitivity to 96% and specificity of 100%. Amin el Tahir et al[13] showed predictive values of 97.3% with sensitivity of 93.5% and specificity of 98.1%. our result is not far from others. So FNAC is an extremely reliable diagnostic tool. It appears that clinical examination of axilla remains incomplete so significant number of cases remains under staged pre operatively. One reason may be that patients are conservative in exposure and examination cannot be done freely specially in outpatient department and ward. All patients should be examined in a room with special arrangements for privacy and comfort. So that, patients can relax. Using examination gloves will also help examination in a clinical setup. There is 30% error rate in clinical evaluation of axillary lymph nodes and tumour size.[12] Physical examination is notoriously in accurate in lymph node assessment having false positive result in 25-31% cases and false negative result in 27-33% cases.[11] Another finding has quoted that clinical examination has 86% sensitivity and 90% specificity.[8] Sensitivity of clinical examination in our study in lymph node assessment was 55.75%. Lesions assuming malignant clinically proved benign in biopsy were 60% and 30% lesions assuming benign clinically proved malignant in biopsy.[9]

5% patients in UK present as locally advanced disease and 20% in developing countries. In 1980 American College of Surgeons showed that 85% first seen with stage-I or Stage-II disease. Positive lymph node was 40%. Average size presenting to doctor was less than 2cm.[7] In our study 40% patients were in Stage-III and 14% patients were in stage-IV at presentation. About 8% patients had distal metastasis at their first presetation.[10] Lack of awareness and aversion to male surgeon was the leading cause of this advanced presentation. Neo adjuvant therapy is an important modality of management which simultaneously down stage the disease and combats systemic disease. 70% cases responded to neo adjuvant therapy by tumor shrinkage.[8] Significant clinical response was observedin about 70-90% cases after neo adjuvant therapy but complete pathological response was observer in less than 15% cases.[6] In our study about 50% patients showed significant clinical improvement after neo adjuvant therapy and more cosmetic result was achieved. Cancer WG et al demonstrated 84% patients had significant clinical response to neo adjuvant therapy.[13] This difference might be due to inadequate use of chemotherapy agents.

Lymph node response after neo adjuvant therapy was 33% in our set up. Lisa A Newman MD et al showed the response as 33%.[14] In my study both tumor and lymph node responders were 12%. Lisa A Newman M D et al showed the response was 21%.[14] Our result is consistent with others observations. Neo adjuvant therapy has no role in long term survival of patients after management rather it aids in down staging with a view to make fit for breast conserving surgery and in advanced cases to make the dissection easy and limited.[7] So that primary closure after mastectomy would be possible avoiding skin grafting. Ideally stage-III patients are eligible for neo adjuvant therapy but in our study stage-IV patients were also included only to ease closure after toilet mastectomy or to control aggressive features like bleeding from lesion. Management of axillary lymph nodes became easier after neo adjuvant therapy.Newman M D et al shows that after completion of neo adjuvant therapy 59% patients were eligible for breast conserving surgery. Before completion it was 39%.[14]In our set up breast conserving surgery was not performed but surgery became easier and less invasive after completion of neo adjuvant therapy.

Local recurrence and distal metastasis are major problem in the management of carcinoma of breast. Dital metastasis will be found at local relapse in about 20% cases.[10] In our study distal metastasis was observed in 23.26% patients. Whereas Cance W G et al observed 31% in their study.[13] Our study reveals that distant is more in patients with advanced stage if disease and patients who didn't use adjuvant chemotherapy adequately.

Local recurrence after complete treatment is the main barrier of management outcome. Systemic micro metastasis causes it. Recurrence in breast, chest wall, axilla clinically found 80% cases within 2 years. So, in our study local recurrence occurred in 36.84% patient. Cancer W G et al showed in their study it was 14% only.[13] In the study by Scholl by et al the rate if local recurrence by neo adjuvant chemotherapy users group was 27%.[6] It was greater in our setup as majority of patients could not avail chemotherapeutic agents regularly and presented in advanced stage of disease and who didn't use adjuvant therapy regularly as per schedule.

Multidisciplinary approach with neo adjuvant therapy followed by local surgery and radiation therapy and chemotherapy has resulted on rates of local control

that exceeds 80% and 5 years survival rates exceeding 50% are not ususal.[15] Although clinically worth while the benefit of adjuvant systemic therapy for operable carcinoma breast are modest and in range of 20-30% reduction in the odds of recurrence or death.[7]

Management strategy depends upon stage of disease and modalities available. 75% treated with mastectomy and 25% with breast conserving surgery.[9] Despite an increasing trend toward breast conserving surgery up to 50% of women still require mastectomy.[1] Breast conserving surgery was not possible at all in our setup as about 93% patients were in stage-III and stage-IV. Other patients were not convinced for breast conserving surgery. So, it's outcome could not be assessed in my study. So, surgical management was Paty's mastectomy in 04 % of the cases.

Carcinoma of breast is more aggressive in younger than elderly. Local recurrence happened in the form of nodule, ulceration, local pain and swelling. Systemic spread may involve bones, lungs, brain, liver, spinal cord etc. Metastasis to bone observed in 49-60% cases, 15-20% cases in lungs, 10-15% to pleura, 7-15% to soft tissue and 5-15% to liver.[12] In our limited observation we found 42.86% bony metastasis, 28.58% pulmonary metastasis and 28.58% in hepatic metastasis. The low percentage of this prospective study is not very far from others. The low accuracy rate can be improved by increasing practice and number of cases.

Conclusion:

Breast cancer is an extremely emotional topic by virtue of its anatomical location and the importance of female breast in today's society. Breast is a common site of cancer in women and carcinoma breast is the leading cause of death among middle aged women in western countries.[1] Although it is common in western and affluent populations but it is not uncommon in our country. Early age groups are not escaped rather suffer more aggressive form of disease. Twelve years study was performed to observe early metastasis of different types of breast carcinoma. The aims of this study to identify different histopathological types of breast carcinoma in our country were more common, early diagnosis of metastasis and different modalities of treatment according to patient's condition. 100 diagnosed case of carcinoma breast were studied.

Preventive measures are not satisfactory except prophylactic mastectomy in high-risk cases, which is not feasible in all cases. Features are variable before the disease is advanced. So, it should not be missed clinically. Early staging showed better outcome after proper management. If adjuvant therapy is used adequately, local recurrence and distal metastasis is delayed. Chemotherapeutic agents should be cheap and easily available. Counselling should be performed to use full course of adjuvant therapy. Self-breast examination is a very effective tool of breast cancer screening. Vulnerable group should be encouraged to perform it as per schedule. Though it may raise anxious group, it will obviously reduce the burden of advanced disease. Man is not immortal. If horrors of carcinoma breast are hastened by modifiable factors that will be distressing and not acceptable. So, proper steps should be taken to raise awareness among the vulnerable group. Breast cancer awareness program should be taken at various levels to ensure early diagnosis and treatment with an aim to prevent metastasis and achieve good prognosis.

Conflict of interest: none.

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