Metastatic Breast Cancer and Hormonal Receptor Status among a Group of Women in Sub Saharan Africa

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Abstract

Background: Breast cancer is the third commonest cancer in women in Uganda. The majority of breast cancer patients in Uganda present with advanced disease. Many studies show that metastatic lesions frequently lodge in bones, lung and liver. Tumour hormone receptor status correlates with site of metastatic lesions and survival among breast cancer patients.

Objective: To determine the sites of metastatic breast lesions and how they relate to the hormonal receptor status.

Methods: In this cross sectional descriptive study, 71 women with histologically confirmed incident breast cancer with metastases were analysed, their hormonal receptor status was determined. All patients underwent a chest X-ray, an abdominopelvic ultrasound scan and a bone scan. The χ^2 and t tests were used to compare variables for statistical differences.

Results: The mean age of participants was 45 years. Most metastases were to bone 56% (40/71), of these 45% (32/71) tumours were exclusive to bone and 94% of these (30/32) were ER+ . Of the 13 (18% of all patients) who had metastases to the liver, 7 were exclusive to the liver, and 1 (14.%) was ER positive. Of the 30 (42 %) patients with lung metastases, 23 patients were exclusive to lungs and 9/30 (39%) were ER+. In all 68% (48/71) were ER+, and bone metastases were associated with ER positivity and low grade tumors.

Conclusion: Breast metastases had a preponderance to bone in this largely premenopausal group of women and these tumors were mostly ER positive. In the absence of tests to determine ER status, empirical antihormonal therapy may be used.

Key words: Metastatic Breast Cancer, Hormonal Receptor Status

Introduction

Worldwide almost one third (32%) of all cancers diagnosed in women are breast cancer responsible for 18% of cancer deaths in women (1). Breast cancer in sub Sahara Africa present in relatively young women, mostly in late stage III and IV. It runs an aggressive course and carry a low 5 year survival rate (2). Breast cancer incidence in Uganda has nearly tripled from 11: 100,000 in 1961 to 31:100,000 in 2006 (3). Close to a third of the patients present with metastatic disease and thus the outcome of treatment is inevitably unsatisfactory (2).

Breast cancer metastases frequently occur in bones, lungs and the liver, and therefore, the investigations recommended include bone scan, chest X-ray and liver ultrasound other imaging studies such as computer tomography (CT) or magnetic resonance imaging (MRI) may be performed to confirm the presence of metastases (4).

It is widely recognized that tumour hormone receptor status correlates with overall survival in metastatic breast cancer but there is little focus on the potential correlation between tumour receptor status and patterns of disease spread among breast cancer patients (5).

The aim of this study therefore was to investigate the distribution of metastatic lesions and how they relate to hormonal receptor status.

Method

Study design

A cross sectional descriptive study

Study setting

It was conducted at the Mulago Breast clinic from November 2010 to June 2011. Mulago is the national referral and teaching Hospital for Makerere University. The hospital receives approximately 250 incident cases of breast cancer per year. It is situated 2km from Kampala city center and has a capacity of 1500 beds. The breast care services are available all week with an outpatient clinic operating once a week The patients are referred to the breast clinic from within and out of the hospital; from private clinics

and other hospitals country wide. Mulago is the only centre in Uganda that offers free and comprehensive specialist led breast cancer services

Study procedure

Upon presentation to the Breast unit a full history and clinical examination were performed. The physical examination included determining the primary tumour size and nodal involvement (axillary, infraclavicular and supraclavicular). A chest X-ray, abdominopelvic ultrasound scan and bone scan to determine the presence of metastases. Three core biopsies were taken and analysed for tumor type, grade by histology. The hormonal receptor status was determined by immunohistochemistry tests using a primary tumor sample.

The required sample size (n) was calculated using the formula developed by Kish and Leislie[6]. All 71 patients with confirmed invasive breast cancer with metastases were eligible. Patients with evidence of other concurrent cancers and or had started on any form of anti-cancer therapy were excluded.

Data collection

Data were collected using a structured and pretested questionnaire and entered using Epidata computer soft ware version 3.1 and transferred to SPSS version 16 for cleaning and analysis. We used the t-test to compare continuous variables. We evaluated associations between variables using the Pearson's χ^2 test. Differences between variables were considered statistically significant when the p-value of any statistical test used was < 0.05.

Ethical consideration

Written informed consent was obtained from each participant. Ethical approval was obtained from the School of Medicine Ethics and Research committee at the College of Health Sciences at Makerere University.

Results

We recruited 98 patients with metastatic breast cancer, 8 patients were excluded because they did not return to the breast clinic to complete data gathering, and 19 were dropped due to incomplete or inconclusive investigation results. Analysis was therefore done for 71 women with histologically confirmed invasive breast cancer and had metastases.

Tables 1 showing metastatic sites and tumour characteristics

Organ (site)	Frequency		Mean age (SD)	Hormonal status		Histology		Grade			Stage	
	Total	Exclusive		ER^+	PR^+	Invasive ductal	Others	1	2	3	III	IV
Bone	40	32	45 (14)	30*	23†	28	4	6	17	9	10	22
Lungs	30	23	45 (11)	9	5	15	8	5	10	8	7	16
Liver	13	7	44 (13)	1	1	6	1	2	4	1	4	3
Multiple sites	9	-	45	8	7	5	4	1	7	1	4	5

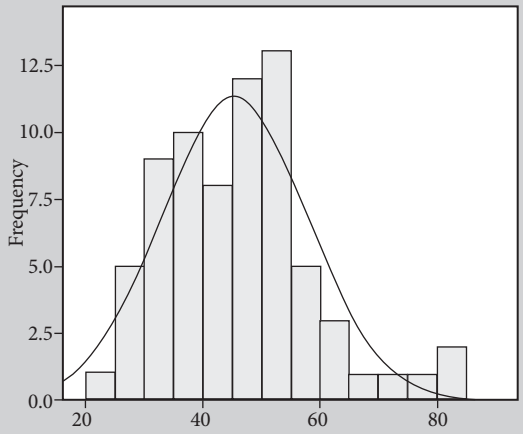
* ER- and PR- combined were 23 (32%) and ER+ and PR- 13 (18%).

Out of 71 patients 48 (68%) were ER+, 23 (32%) were ER negative and 35 (49.3%) had PR positive tumours. Table 1 shows the receptor status distribution

Age distribution

The age distribution of the patients is shown in figure 1. The age range of the patients was 23-81 years, with a mean age of 45years (SD 13 years) and a median age of 45years. Women ≤ 45 years comprised the majority 36/71 (51%). Out of 71 patients, 21 (30%) were postmenopausal whereas 50 patients (70%) were premenopausal.

Figure 1: shows age distribution of patients with metastatic breast cancer stage



Age at diagnosis

Metastatic sites and histological type

The most common histological tumour type was invasive ductal cancer. Patients with bone metastases had more of invasive ductal carcinoma than other histological types. On the contrary patients with lung metastases had more of the other histological types when compared to patients with metastases to other sites (p = 0.040) (Table2).

Table 2: Shows association of bone or lung metastases and clinico-pathological characteristics of breast cancer

Variable	Bone n=32 (%)	Other sites n=30 (%)	p-value	Lung n = 23(%	Other sites N= 39 (%)	P value
Age						
< 45 years	14 (47)	16 (53)	0.450	12 (40)	18 (60)	0.647
≥ 45 Years	18 (56)	14 (44)		11 (32)	21 (66)	
Histological type						
Invasive ductal Ca	28 (57)	21 (43)	0.910	15 (31)	34 (69)	
Others	4 (30)	9 (69)		8 (62)	5 (39)	0.040
Tumour grade						
Grade 1	6 (46)	7 (54)	0.859	5 (39)	8 (62)	0.691
Grade 2	17 (55)	14 (45)		10 (32)	21 (68)	
Grade 3	9 (50)	9 (50)		8 (44)	10 (56)	

Metastatic sites and hormonal receptors

Out of the 32 patients (80%) who had exclusive bone metastases 30 (94%) had ER positive tumours, (p≤0.001) and 23 (71.9%) were PR positive (p ≤ 0.001; OR =8).

Table 2 shows the comparison of distribution of exclusive metastatic sites by hormonal receptors. Patients with bone metastases were more likely to have ER positive tumours than negative compared to patients with metastases to other sites (χ^2 = 24.7; OR = 30 (95% CI 6-151; p≤ 0.001).

Table 3: Showing distribution of metastatic sites by receptor status

Variable	Receptor status				Oestrogen receptor			Progesterone receptor		
	ER+/PR+ n = 29 (%)	ER+/PR- n=11(%)	ER-/PR- n = 22(%)	p value	Positive n=40(%)	Negative n = 22 (%)	P value	Positive n=29(%)	Negative n= 33 (%)	p value
Pattern 1										
Bone only	23 (72)	7 (22)	2 (6)	<0.001	30 (94)	2 (6)	<0.001	23 (72)	9 (28)	<0.001
Others	6 (20)	4 (13)	20 (67)		10 (33)	20 (67)		6 (20)	24 (80)	
Pattern 2										
Liver only	1 (14)	0 (0)	6 (86)	0.012	1 (14)	6 (86)	0.003	1 (14)	6(86)	0.067
Others	28 (51)	11 (20)	16 (29)		39 (71)	16 (29)		28 (51)	27 (49)	
Pattern 3										
Lung only	5 (22)	4 (17)	14 (61)	0.003	9 (39)	14 (61)	0.001	5 (22)	18 (78)	0.002
Others	24 (62)	7 (18)	8 (21)		31 (80)	8 (21)		24 (62)	15 (39)	

Bone metastases and receptor status

Of the 32 patients who had exclusive bone metastases, 30 (94%) were ER+ whereas 23 (72%) were PR positive.

Majority of the patients with exclusive bone metastases 23 (72%) had ER+/PR+; 7 (13%) were ER+/PR- and 2 (6%) were ER-/PR-. Patients with bone metastases were more likely to have ER positive tumours than negative tumours compared to patients with metastases to other sites (χ^2 = 24.7; OR = 30 (95% CI 6-152; p< 0.001).

Lung metastases and receptor status

In all, 23 patients had exclusive lung metastases, 9 (39%) were ER+, 14 (61%) were ER− while 5 (3%) were PR positive.

Of those with lung metastases 14 (61%) had ER−/PR−, 5 (22%) were ER+/PR+ and 4 (17%) were ER+/PR−. Patients with lung metastases were more likely to have ER negative tumours than positive compared to patients with metastases to other sites (χ^2 = 10.293; OR = 6 (95% CI 2.0-19.0; p= 0.001).

Liver metastases and receptor status

Among the 7 patients that had exclusive liver metastases 1 (14) was ER positive while 6 (86%) were ER negative, 1 (14%) were PR positive while 6 (86%) were PR negative. Majority of the patients with exclusive liver metastases had ER−/PR− 6 (27%); 1 (3%) was ER+/PR+ and 0 was ER+/PR−.

Table 3: Showing distribution of metastatic sites by receptor status

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Patients with ER or PR positive tumours tended to develop bone metastases while ER or PR negative developed lung metastases.. The tumour receptor status was statistically significantly different among the three distribution sites ($p \leq 0.001$).

Discussion

In this study we describe the distribution of metastatic breast lesions among patients seen in Uganda's largest breast cancer treatment center, and how it relates to the hormonal receptor status. We found that most metastases occurred in bone and patients with bone metastases had significantly high frequency of ER/PR positive tumours ($p \leq 0.001$).

Those with lung metastases had mainly ER/PR negative tumors (p= 0.003). There was a significant difference between the hormonal receptor status of patients with lung metastases compared to patients with metastases to other sites.

These findings were in accordance with previous studies(2,7) done in Uganda; in addition these results show similar age distribution (mean 45 years and a range of 23 to 81 years) as earlier reported[2, 7], and the premenopausal status is similar to what has been reported before(2,7,8).

The majority of tumours (76%) in this study were invasive ductal cancer similar to what has been previously reported in both Africans and in whites (69%)(2,7,9,10); 54% of tumours were grade 2.

Most tumors (68%) were ER positive, this agrees with some studies that state a similar figure [7] although others have reported a much less ER positivity value(7,10-13).

Patients with bone metastases had predominance to ER positive tumors (68%) whereas those with lung metastases tended to be ER negative. These results agree with[14] previous reports which suggest that patients with ER+/PR+ primary tumors tend to

develop bone metastases. Bone metastases may have a worse prognosis compared to lung metastases[12, 15] though this hasn't be validated in the indigenous African population

These findings therefore suggest that a good proportion of the patients with metastatic breast disease would respond to anti-hormonal therapy (14).

Study limitations

A third of the patients who were enrolled were dropped, this may have had an influence on the results, although the analysis of age and tumor clinical stages were similar to the patients included in the study.
The numbers analyzed are rather small.

Conclusion

Breast metastases had a preponderance to bone in this largely premenopausal group of women and the tumors were mostly ER positive. Perhaps in the absence of tests to determine ER status, patients in resource poor environments with metastatic bone disease would benefit from empirical anti hormonal therapy.

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