RESEARCH ARTICLE

Locally Advanced Breast Cancer in Jamaica: Prevalence, Disease Characteristics and Response to Preoperative Therapy

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Abstract

Breast cancer is the most common cancer in Jamaican women. Locally advanced breast cancer (LABC) is associated with aggressive biology and poor prognosis, and has a predilection for African-American women. In this retrospective review, we assessed the prevalence of LABC as a breast cancer presentation in a population of mainly Afro-centric ethnicity, and determined disease characteristics and response to pre-operative chemotherapy. LABC was prevalent (20%), and had a low pathological response rate to pre-operative chemotherapy, with a high risk of disease recurrence. Increased utilization of breast cancer screening may help detect cancer at less advanced stages, and optimizing pre-operative chemotherapy is recommended to improve response rates and ultimately survival.

Keywords: Breast cancer - locally advanced breast cancer - neoadjuvant chemotherapy - preoperative chemotherapy

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Introduction

Breast cancer is the most common cancer in Jamaican women (Gibson et al., 2010). Locally advanced breast cancer (LABC) is an advanced presentation associated with a poor prognosis (Hortobagyi et al., 1998) and traditionally includes Stage IIB and Stage III disease (Edge and Compton, 2010). These tumours are typically large and may extend beyond the breast tissue into the surrounding skin, muscle or chest wall, with clinical involvement of ipsilateral lymph nodes (axillary, internal mammary, supraclavicular or infraclavicular). In North America, around 5-10% of women newly diagnosed with breast cancer will have LABC (Newman, 2004; Kaufmann, 2006). Based on data from the large-scale, population-based Surveillance, Epidemiology and End Results database from the United States, LABC comprised 5.9% of all female breast carcinomas (Anderson et al., 2003). However, in non-industrialized nations worldwide, the incidence of LABC is greater (Sant et al., 2004; Parkin et al., 2005).

There is a predilection of LABC for African-American women, usually diagnosed at an earlier age than other ethnicities, with later stage at disease presentation and more aggressive biology (Elledge et al., 1994). There are no published reports of the prevalence of LABC as a presentation of breast cancer in Jamaican women. Given the primarily Afro-centric ethnicity of the population, one might expect a significant proportion of newly diagnosed breast cancer to be LABC. We retrospectively reviewed the prevalence and characteristics of LABC as a presentation amongst newly diagnosed breast cancer patients seen in the Haematology/Oncology clinic at the University Hospital of the West Indies (UHWI), a tertiary care hospital in Kingston, Jamaica. We also assessed the clinical and pathological tumour response to pre-operative chemotherapy, and patient outcomes during post-therapy surveillance.

Materials and Methods

After approval from the UHWI/UWI/Faculty of Medical Sciences Ethics Committee, a list of all new-patient consultations booked for the Haematology/Oncology Clinic for the 2-year period 2006 to 2007 was obtained from the Medical Records Department, UHWI. Retrievable medical charts were reviewed to identify patients with a diagnosis of breast cancer. We performed data extraction using a standardized extraction template to collect data for all breast cancer patients including: patient age, sex, parish of residence, reason for investigation for breast cancer (including palpable breast lump, abnormal mammogram, physician-detected abnormality) and any history of prior screening mammograms (mammograms performed as part of investigation of current diagnosis were excluded). Charts were reviewed for results of investigations to exclude metastases (including bone scan, Chest X-ray, Abdominal Ultrasound, CT scan chest/abdomen) and histopathology reports reviewed for tumour size and nodal status; TNM stage was then

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determined for each patient. We reviewed available immunohistochemistry test results to determine the oestrogen (ER) and Her-2-neu (Her2) receptor status. Immunohistochemistry testing for progesterone receptor was not being performed during the period under study. We documented the reason for referral to the clinic including: for post-operative therapy, for pre-operative therapy (for LABC) or for management for metastatic breast cancer. For patients referred for pre-operative therapy, we reviewed treatment and follow-up records to ascertain chemotherapy regimens used, clinical and pathologic response rates and patient outcomes at last follow-up. Based on the descriptive nature of the study, univariate analyses with descriptive summary statistics are presented. Statistical tests were performed with Statistical Package for Social Sciences® v 12.0.

Results

There were 626 new patient referrals to the Haematology/Oncology clinic during the 2-year study period. We were able to retrieve medical records for 395, for a retrieval rate of 63%. Breast cancer was the most common cancer diagnosis seen in the clinic, accounting for 68% of cancers seen (121 of 177).

Patient and disease characteristics

The median age of breast cancer diagnosis was 52 years (range 22-84, IQR 20). One male was diagnosed during the study period. Most patients presented with a palpable breast lump (89%); other reasons were an abnormal mammogram (6.5%) and physician-detected finding (5%). With regard to screening, 5.8% of breast cancer patients gave a history of previous screening mammograms. The majority of breast cancer patients (65%) were referred for assessment for adjuvant therapy after breast cancer surgery. Twenty percent of patients were referred for pre-operative systemic therapy (for LABC), and 15% for management of metastatic disease. At presentation, the TNM Stage was I, II, III and IV in 8, 44, 26 and 21 percent respectively (Table 1). Most breast cancers were ER-positive (60%), while 20% were Her2-positive; 31% were negative for both ER and Her2.

Table 1. Patient and Disease Characteristics for All Newly Diagnosed Breast Cancer Patients

Characteristic		No.	(%)
Sex, Female		120	(99.2)
Median Age, years (range) (IQR=20)		52	(22-84)
Reason for referral,			
For post-operative therapy		78	(65)
For pre-operative therapy		24	(20)
For palliative therapy (metastatic disease)		18	(15)
TNM Stage, (n=84)	I	7	(8)
	II	37	(44)
	III	22	(26)
	IV	18	(21)
ER/Her2 Status, (n=97)	ER+/Her2-	48	(49.5)
	ER-/Her2-	30	(30.9)
	ER+/Her2+	11	(11.3)
	ER-/Her2+	8	(8.2)

LABC population

Of the patients referred for pre-operative systemic therapy (all female), 46% had cT3 tumours (Singletary et al., 2002) and 41% had tumours with direct extension to chest wall or skin (cT4) (Table 2). Inflammatory breast cancer (T4d) was the clinical diagnosis in 9%. Thirty-six percent of women with LABC presented with Stage IIIB disease. ER/Her2 status was unknown for 7 patients. For those with known receptor status, 41% were negative for ER and 12% were Her-2 positive.

The most commonly utilized neo-adjuvant chemotherapy regimen was adriamycin/cyclophosphamide with sequential taxane (paclitaxel) (59%); 41% of patients did not receive a taxane. One patient received up-front radiation for a large fungating tumour for local control. All other patients were referred for assessment for radiation post-surgery, but details of therapy actually received were not recorded. All patients with ER positive disease were prescribed endocrine therapy upon completion of chemotherapy. The two patients with Her2 positive disease were prescribed adjuvant trastuzumab but were unable to receive the recommended course due to financial reasons.

Assessment of response to pre-operative chemotherapy was possible for 19 patients, and is summarized in Table 3. Most patients (17 of 19) had a clinical response however only 2 (11%) had a pathological complete response (pCR). Disease recurrences were diagnosed in 9 of 19 patients (47%) within a median period of 11 months (range 8-18). Six of these (67%) occurred in patients who had ER-negative LABC. The 2 patients who had pCRs had no breast cancer recurrences and remained disease free at 19 and 25 months follow-up. They were both ER

Table 2. Characteristics for LABC Patients Referred for Pre-operative Systemic Therapy

Characteristic		No.	(%)
Clinical tumour size	cT2	3	(13.6)
	cT3	10	(45.5)
	cT4	9	(40.9)
TNM stage	IIA	2	(9.1)
	IIB	6	(27.3)
	IIIA	6	(27.3)
	IIIB	8	(36.4)
Chemotherapy recommendations	AC/FAC	9	(41)
	AC/Paclitaxel	13	(59)
Estrogen receptor status (n=17)	Positive	10	(59)
	Negative	7	(41)
Her2 receptor status (n=17)	Positive	2	(11.7)
	Negative	15	(88.2)
ER/Her2 Status	ER+/Her2-	10	(59)
	ER-/ Her2-	5	(29)
	ER+/Her2+	0	(0)
	ER-/Her2+	2	(12)

Table 3. Response Characteristics for 19 of 24 Patients Referred for Pre-Operative Systemic Therapy

Characteristic	Result
Clinical response, No (%)	
Any reduction in tumour/nodes	17 (89.5)
Pathological complete response, No (%)	2 (10.5)
Disease recurrence, No (%)	9 (47)
Median time to disease recurrence (months)(range)	11 (8-18)
Median follow-up (months)(range)	13 (6-39)

positive/Her2 negative. One patient (of 19 assessable for response) had Her-2 positive breast cancer and had received anthracycline and taxane chemotherapy, without trastuzumab; she remained disease free at 18 months.

Discussion

Approximately 20% of breast cancer referrals to the Haematology/Oncology clinic were for pre-operative or neo-adjuvant systemic therapy (NST) for LABC. It must however be noted that not all women with LABC will be referred for NST (based on referral patterns, patient preference and surgeon preference). We previously reviewed the surgicopathological characteristics of breast cancer for women who presented for adjuvant systemic therapy after definitive surgery, and found that 33% had Stage III disease; if Stage IIB was included in the definition of LABC, then these accounted for the majority (62%) of pathologically staged breast cancer (Chin et al., 2014). In that study, the median tumour size was 3.5cm, with range of 0.4-13cm. Based on international recommendations some of these patients may have been candidates for NST (Kaufmann et al., 2012). This highlights the need for implementing national guidelines on the management of LABC, so that eligible patients may be considered for NST.

Compared with data from the Surveillance, Epidemiology and End Results database from the United States (Anderson et al., 2003), more of our patients with newly diagnosed breast cancer have LABC (33% versus 4.6% with Stage III disease). There are several possible reasons for this. Firstly, mammographic screening, which allows detection of earlier lesions, is under-utilized in our population. In populations that receive regular screening mammography, the percentage of patients with locally advanced disease is less than 5% (Seidman et al., 1987). Very few women in our review had mammographically detected tumors; in fact, most had tumours that were large enough to allow self-detection (median size 3.5cm). This is in keeping with findings from the largest series of breast cancer cases reported from Jamaica, with a mean tumour size of 4.1±2.7cm found in 641 specimens (Shirley et al., 2010). Increased utilization of screening mammography can be expected to reduce the proportion of patients presenting with locally advanced disease. Secondly, patients may present with advanced breast cancer due to delays in seeking health care. LABC encompasses not only rapidly progressing ER-negative disease, but also neglected low-grade ER-positive breast cancers (Chia et al., 2008). Late presentation of neglected primaries may be due to socio-cultural barriers to early health-care access including fear of treatment (Kobetz et al., 2010). Lastly, as seen in other black populations (Elledge et al., 1994; Furberg et al., 2001), Jamaican patients may have more aggressive tumour biology. These reasons for disparity in LABC rates merit further investigation.

Studies on breast cancer in East African women also support more advanced disease presentations with more ER and PR negative disease (Bird et al., 2008). We found an ER negative rate of 41%. As PR testing was not being done during the period of this review, we cannot comment on the prevalence of triple negative cancers, but found that 29% had ER-/Her2- breast cancer. The triple negative profile is the immunohistochemistry surrogate for basal-like breast cancer, and occurs at a higher prevalence among pre-menopausal African American patients (Carey et al., 2006). This aggressive subgroup has a worse prognosis with earlier recurrences (Dent et al., 2007). Future studies should be directed at estimating the prevalence of basal-like breast cancer in our breast cancer population, as we seek to improve knowledge on biology and prognosis.

Pathological complete response (pCR) rates of up to 19-31% have been found in large prospective studies (Smith et al., 2002; Bear et al., 2003). The pCR in this study was lower, and while small patient numbers makes its significance difficult to interpret, it is imperative to consider how our rates can be improved. This is crucial because pCR to neoadjuvant systemic therapy has been shown to be the best predictor of disease free survival (Montagna et al., 2010). In our study the 2 patients who had pCRs had no disease recurrences during follow-up. The addition of a taxane to anthracycline-based chemotherapy improves response rates (5), however 39% of our patients did not receive a taxane. A prospective study with all patients receiving standard chemotherapy drugs and protocols will help to clarify this issue.

Limitations to this study are inherent to the retrospective methodology, as treatment and clinical response were not meticulously documented in the clinical charts, making their assessment difficult, and also small sample size.

LABC is a common presentation of breast cancer, and carries a poor prognosis. Increased patient education and implementation of breast cancer screening programmes will help detect earlier lesions and increase the chance of favourable outcomes. Rationalization of pre-operative chemotherapy and national guidelines are recommended to provide optimal care.

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