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Research Article

Inflammatory breast cancer: features and outcomes in a breast unit in Dakar, Senegal

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ABSTRACT

Background: The aim of this study was to determine clinical features and outcomes of patients with inflammatory breast cancer (IBC) treated in our breast unit.
Methods: This study was performed at Gynaecologic and Obstetric Clinic of Dakar Teaching Hospital, in which a breast unit was created since 2007. All women with diagnosis of inflammatory breast cancer in our Breast Unit between January 2010 and December 2013 were included in this study. The diagnosis of IBC was made clinically using the American Joint Committee on Cancer (AJCC) and confirmed histologically. The follow-up cut-off for this data set was December 31st, 2014. All analyses for this study were performed using SPSS software (version 20.0).
Results: Between 2010 and 2013, 22 women with breast cancer who met eligibility criteria were included out of 161 patients followed for breast cancer leading to a frequency of 13.6%. The median age at diagnosis was 43.4 years (26-79 years). Mean time to diagnosis was 4 months. The mean time to recurrence was 11.2 months. This recurrence was observed in 45.5% of cases. The median overall survival was 13.3 months (CI 95% 8.576-18.526), the survival rate was 31.8%.
Conclusions: This series shows a high frequency of inflammatory breast cancer. These tumours are very aggressive with a very poor prognosis.

Keywords: Inflammatory breast cancer, Outcome, Senegal

INTRODUCTION

Inflammatory breast cancer (IBC) is a rare subtype of locally advanced breast cancer according to the tumour-node-metastasis (TNM) breast cancer staging system. IBC is classified as T4d and clinically characterized by diffuse induration of the skin with an erysipeloid edge, usually with no underlying mass.[1]

Inflammatory breast cancer comprises 2.5% of all breast cancers.[2] The median overall survival among women with IBC is less than 4 years even with multimodality treatment options.[3]

Several studies have reported that IBC constitutes a larger proportion of breast cancers in low income countries than Western countries.[4] Managing IBC in low-income countries poses a different set of challenges including access to screening, stage at presentation, adequacy of multidisciplinary management and availability of therapeutic interventions.

The aim of this study was to determine clinical features and outcomes of patients with inflammatory breast cancer (IBC) treated in our Breast Unit.

METHODS

This study was performed at Gynaecologic and Obstetric Clinic of Dakar Teaching Hospital, in which a Breast Unit was created since 2007. All women with diagnosis of IBC between January 2010 and December 2013 were included.

The diagnosis of IBC was made clinically using the American Joint Committee on Cancer (AJCC) and confirmed histologically. Inflammatory breast cancer is defined under the current AJCC manual for staging of cancer as T4d N0-2, stage IIIb, carcinoma of the breast.[5] These criteria are the basis of the definition of IBC set forth by the American Joint Committee on Cancer (AJCC) as "a clinicopathological entity characterised by diffuse erythema and oedema of the breast, often without an underlying palpable mass".

The follow-up cut-off for this dataset was December 31, 2014.

Overall survival was calculated from the time of diagnosis to the time of death or the time of last follow-up. Patients still alive at the time of last follow-up were censored. The Kaplan-Meier method was used for survival rates.

All analyses for this study were performed using SPSS software (version 20.0).

RESULTS

Patients and tumour characteristics

Between 2010 and 2013, 22 women with breast cancer who met eligibility criteria were included out of 161 patients followed for breast cancer leading to a frequency of 13.6%. The median age at diagnosis was 43.4 years (26-79 years). Mean time to diagnosis was 4 months. Table 1 and 2 summarize patient and tumour characteristics.

Management

All patients underwent neoadjuvant chemotherapy with anthracyclin-based regimens. Modified Patey mastectomy with axillary dissection was performed in 17 patients while 5 patients deceased during the time of chemotherapy. Endocrine therapy with Tamoxifen was given while appropriate. Radiation therapy was not used.

Outcome

The mean time to recurrence was 11.2 months. This recurrence was observed in 45.5% of cases. The median overall survival was 13.3 months (CI 95% 8.576-18.526) as shown in figure 1 where the outcome is compared to other types of breast cancer during the same period. Survival rate was 31.8%.

Table 1: Patient characteristics diagnosed for Inflammatory Breast Cancer (N = 22).

Characteristics	Number	Percentage (%)
Age		
< 50 years	14	63.6
≥ 50 years	8	36.4
Marital status		
Married	16	72.7
Not married	6	27.3
School level		
Not instructed	10	45.4
Primary level	6	27.3
High school and above	6	27.3
Socioeconomic status (income)		
Low income	19	84.4
Mid and high income	3	13.6
Body mass index		
Overweight	13	55.5
Normal	9	54.5
Menopausal status		
Premenopausal	16	72.7
Menopausal	6	27.3
Familial history of breast cancer		
Yes	5	22.7
No	17	77.3

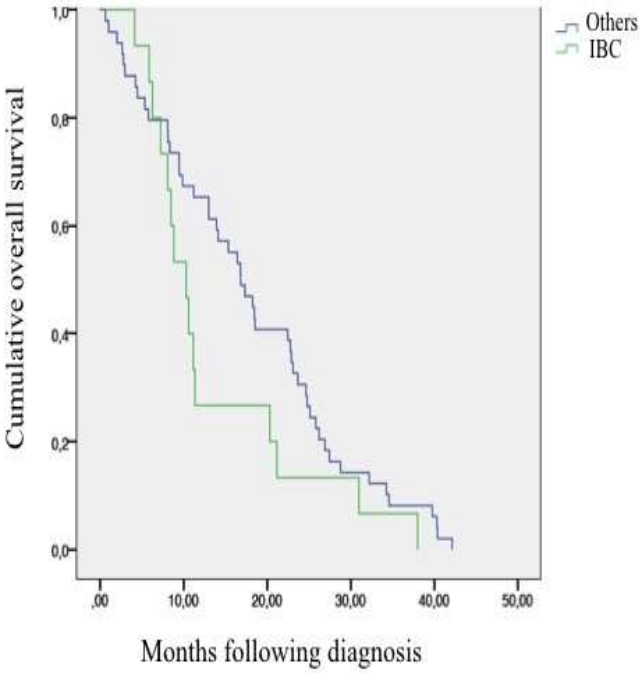

Figure 1: Survival curve using the Kaplan Meier method.

Table 2: Characteristics of patients and tumour.

Case	Age	Inflammatory signs	Breast mass	Evolution	Side	T	N	M	HR	HER-2	Time to relapse	Status	OS (months)
1	20	Yes	Yes	6	L	T4d	N3	M1	Unavailable	Unavailable		Deceased	11,4
2	53	Yes	Yes	2,5	R	T4d	N2	M1	Negative	Negative		Deceased	8,5
3	42	Yes	Yes	3	L	T4d	N2	Mx	Negative	Positive	11	Deceased	11,2
4	51	Yes	Yes	1	R	T4d	N0	Mx	Positive	Negative		Alive	
5	41	Yes	Yes	11	R	T4d	N1	Mx	Unavailable	Unavailable	30	Deceased	31,0
6	63	Yes	Yes	4	R	T4d	N2	M0	Negative	Negative	13,87	Deceased	20,3
7	42	Yes	Yes	1	L	T4d	N2	M1	Positive	Negative		Deceased	38,1
8	30	Yes	Yes	1	L	T4d	N2	M1	Unavailable	Unavailable		Alive	
9	56	Yes	No	6	B	T4d	N3	M1	Unavailable	Unavailable		Deceased	5,9
10	28	Yes	No	2	L	T4d	N2	M1	Negative	Negative		Deceased	4,2
11	53	Yes	Yes	6	R	T4d	N3	M1	Unavailable	Unavailable		Alive	
12	56	Yes	Yes	6	R	T4d	N3	M1	Negative	Positive	7	Deceased	7,3
13	43	Yes	Yes	4	L	T4d	N2	Mx	Unavailable	Unavailable	10	Deceased	10,3
14	42	Yes	Yes	2	R	T4d	N1	M0	Unavailable	Unavailable	5,33	Deceased	8,1
15	30	Yes	Yes	6	L	T4d	N1	M0	Unavailable	Unavailable	8,67	Deceased	10,6
16	39	Yes	Yes	6	R	T4d	N2	M0	Positive	Positive	14,03	Deceased	21,2
17	43	Yes	Yes	3	L	T4d	N2	Mx	Unavailable	Unavailable		Alive	
18	51	Yes	Yes	1	L	T4d	N0	Mx	Unavailable	Unavailable		Alive	
19	38	Yes	Yes	3	R	T4d	N0	M0	Negative	Negative		Alive	
20	30	Yes	Yes	4	R	T4d	N1	Mx	Unavailable	Unavailable	5	Deceased	6,3
21	42	Yes	No	12	R	T4d	N1	M0	Unavailable	Unavailable	7,5	Deceased	8,9
22	63	Yes	No	0,5	L	T4d	N1	M0	Unavailable	Unavailable		Alive	

Abbreviation: HER-2, human epidermal growth factor receptor-2. HR, Hormone receptor, R, Right breast. L, Left breast. T, Clinical tumor stage. N, Clinical nodal stage. OS, Overall surviv

DISCUSSION

Inflammatory breast cancer (IBC) in our setting is not a rare situation and has a poor outcome.

History

First described in 1814 by Sir Charles Bell in ''A System of Operative Surgery'', he stated that ''when a purple colour is on the skin over the tumour accompanied by shooting pains, it is a very unpropitious beginning".[6] The term ''inflammatory'' was first introduced in 1924, by Lee and Tannenbaum.[7] They observed that inflammatory breast cancer appeared to be a distinct clinical entity, defined by striking features at presentation (skin erythema, peau d'orange) with rapid disease progression and poor prognosis but with no constant histopathological type, the only characteristic finding being diffuse invasion of dermal lymphatics by carcinoma cells. It should be noted therefore that the name ''inflammatory'' carcinoma is a misnomer as there is no inflammatory infiltrate present on histopathology in the breast.[7]

Epidemiology

Inflammatory breast cancer is the most aggressive form of breast cancer and accounts for 1-6% of all breast malignancies.[8] Wingo et al. identified 3626 (1%) women who had been diagnosed with inflammatory breast cancer between 1994 and 1998, out of a total of 363,801 breast cancer cases registered in the North American Association of Central Cancer Registries.[9] The mean age of women diagnosed with inflammatory breast cancer was 57.6 years, significantly younger than all histological types combined (62.1 years).[9] The median age at diagnosis in our study was 43.4 years which is 10 to 20 years younger than the age reported in the literature even if it is known that the incidence of inflammatory breast cancer varies by ethnicity and age and is higher among black women and those diagnosed before age 50 years.[9] Higher rates of inflammatory breast cancer as a proportion of all breast cancers were found amongst the black population in the SEER study (10.1% of black women with breast cancer had inflammatory breast cancer, compared with an overall incidence of inflammatory breast cancer of 6.4%).[9]

Definition criteria

The first diagnostic criteria for IBC were published in 1956 by Haagensen.[10] These criteria are the basis of the definition of IBC by the American Joint Committee on Cancer (AJCC) as "a clinicopathological entity characterised by diffuse erythema and oedema of the breast, often without an underlying palpable mass". The diagnosis of IBC remains a clinical diagnosis with pathological confirmation of invasive disease with no specific additional pathological criteria and has therefore been open to subjectivity. The standardization of diagnostic criteria is essential and will help minimize such subjectivity. The International guidelines and AJCC guidelines 7th edition state that erythema and oedema should be present in at least one-third of the breast. As outlined by Ria et al., we have not specified criteria for the proportion of breast involvement or size criteria for erythema (or oedema), as this was considered too subjective to include as a useful specific criterion. It is particularly difficult to assess erythema in pigmented skin.[11]

Taylor and Meltzer subsequently described two clinical varieties of inflammatory breast cancer: i) Primary inflammatory breast cancer, characterised by a sudden onset of the above symptoms in a breast which previously appears normal; ii) Secondary inflammatory breast cancer, defined by inflammatory symptoms and signs which appear in a breast with a previous mass, in the chest wall post mastectomy or in the contralateral breast.[12]

Stricter criteria for diagnosis were established by Haagensen: diffuse erythema (at least one-third of the skin overlying the breast), oedema involving more than two-thirds of the breast, peau d'orange, tenderness, induration, warmth, enlargement, and diffuseness of the tumour on palpation with rapid progression of symptoms. The mean time to diagnosis was 4 months.

Risk factors

Some risk factors are associated to IBC: younger age at menarche and at the time of first live birth compared to non-IBC, premenopausal state (higher proportion of IBC patients were premenopausal than their non-IBC, ethnicity (independent predictor of elevated risk for breast cancer mortality), socioeconomic status (independent predictors of advanced stage at diagnosis in breast cancer) and body mass index.[4]

Clinical features

In only 3 (14.2%) patients the disease was confined to the breast alone while 38% of patients presented with associated distant metastases.

Wingo et al. also found that in 2% or less of cases of inflammatory breast cancer the disease was confined to the breast alone, in approximately 70% to the breast and regional lymph nodes and the remainder presented with associated distant metastases.[9]

Management

The first proposed treatment for IBC was surgery with catastrophic results: less than 5 % survival at 2 years with rapid onset of permeation nodules on mastectomy scar signing local treatment failure.[13] The advent of radiotherapy had improved local control but overall survival remained very poor. The appearance for forty

years of systemic therapies has significantly changed the prognosis and patient survival.

The advent of neoadjuvant chemotherapy has greatly improved disease- free and overall survival for inflammatory breast cancer.[8] No substantial improvement in survival from hormone therapy for inflammatory breast cancer has been shown, which is not surprising given that patients with inflammatory breast cancers are more frequently oestrogen and progesterone receptor negative compared with other breast cancers.

Some older cytotoxic drugs are effective and affordable but we have any means to assess their efficiency before administration to patients. This situation leads to poor responses, which we can't bind to tumour resistance or drug inefficiency.

If the tumour is oestrogen receptor positive it is currently advised that patients receive 5 years of treatment with either tamoxifen or aromatase inhibitors.[8] In our low-income countries endocrine therapy with generic (low-cost) drugs such as tamoxifen provides effective post-surgical treatment for tumour that are positive for estrogen receptors (ERs). However, a tumour's ER status must be known before the drug can be used. In Senegal, ER and HER 2 (Human Epidermal Growth Factor Receptor 2) status are established in France needing sending tumour samples. The consequence of this situation is high costs of sample examination for patients and their families. When not affordable for the patient, the sample is analyzed by our pathologists, only the type of cancer is then available. Here is the explanation of unavailable ER and HER 2 in our patients.

Radiation therapy available in our country (1 machine) still uses Cobalt. Appointments are very far from surgery or chemotherapy and sometimes exceed 6 months.

Partnerships between industrialized and developing countries to build specialist capacity or to provide access to specialist care while local staffs are in training have been quite successful. A collaborative training programme between a pathology department in Tromsø, Norway, and the Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana, provides an example of how pathology diagnostic services can be made available to patients in low-income settings.[14] Problems observed in the Ghana laboratory, such as poor specimen quality and inadequate descriptions of macroscopic specimens, led to the development of new onsite guidelines for tissue fixation procedures, macroscopic examination and tissue block selection. Telepathology can also enhance training in some settings and has been used by doctors in the United Republic of Tanzania and other countries to consult with North American and European colleagues on challenging cases.[15]

Outcome

The mean time to recurrence was 11.2 months. This recurrence was observed in 45, 5% of cases. Two patients relapsed in a short time (5 months). Clinical observation and experience of the progression of inflammatory breast cancer had shown it to be a systemic process from an early stage, with wide dissemination of initially undetectable microfoci of disease. For example, Tabanne et al. describe metastases occurring within 2 months of loco-regional treatment, despite there being no evidence of metastatic spread on initial staging investigations. This led treatment to be focused on systemic therapy and in particular the use of neoadjuvant chemotherapy as primary treatment.[16]

The problem is much deeper and the solution is not at an individual level. It requires a radical reorganization of our health system. We cannot hope for cancer convincing results if drugs are in charge of patients. We have developed several social strategies. Indeed, a social worker in our department regularly approaches some persons who accept willingly to sponsor some patients. But the treatment is long and expensive; this approach has also shown the limits of its efficiency. The biggest challenges for low-income countries are little community awareness that breast cancer is treatable, adequate advanced pathology services for diagnosis and staging and full treatment options, especially for the administration of radiotherapy and the full range of systemic treatments.

Disparities in morbidity and mortality rates reflect the influence not only of biological and environmental factors, but also of social and cultural determinants linked to the question of fairness and social justice. Equity is an important aspect to consider in control efforts, which should be guided by special consideration for those who are more vulnerable to illness or less able to access health-care services because of social, economic or demographic factors beyond their control.

CONCLUSIONS

This series shows a high frequency of inflammatory breast cancer. These tumours are very aggressive with a very poor prognosis. Partnership with developed countries is needed to improve diagnosis, management and outcomes of patient with breast cancer. Partnership is not enough to create the opportunity for change, but can enhance such an opportunity when combined with the availability of proven interventions, results from on-going research and involvement of our health system, our pathologists and other care providers.

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