Metachronous Contralateral Breast Cancer in Ahmadu Bello University Teaching Hospital, Zaria, Northwestern Nigeria

Abstract

Background: Breast cancer is the most frequent cancer of women. Metachronous contralateral breast cancer (MCBC) is a cancer in the contralateral breast after 6 months of the initial diagnosis of the first breast cancer. It is an important public health issue because of an increased incidence of a primary breast cancer and improved survival. There is a paucity of data in the Northwestern region of the country. The study was to document the incidence, the method of detection, clinicopathological features, and the treatment of MCBC in our hospital. Patients and Methods: It was a 7-year prospective study from January 2011 to December 2017. Patients who had treatment for nonmetastatic breast cancer, American Joint Committee on Cancer (AJCC) Stages I–II, were followed up. Those that developed MCBC were studied. Age, the method of detection, stage at presentation, pathological types, hormone receptor status, and treatment were documented. Data obtained were analysed using SPSS version 21.0. Results were presented as simple percentages and charts. Results: Of 1285 women with nonmetastatic breast cancer, 47 had MCBC (incidence of 3.7%); 30 (63.8%) were aged 21–50 years; 23 (48.9%) detected by self-breast examination; 13 (27.7%) by clinical breast examination; seven (14.9%) by mammography; and four (8.5%) by breast ultrasound scan. Fourteen (29.8%) were AJCC stage I; 23 (48.9%), stage II; seven (14.9%), stage III; and three (6.4%), stage IV. Thirty-nine (83%) were invasive ductal carcinoma; 22 (50.0%) were estrogen receptor/progesterone receptor (ER/PR) positive, human epidermal receptor (HER)-2 neu negative; nine were (20.5%) ER/PR and HER-2 neu positive; six (13.6%) were ER/PR negative, HER-2 neu positive, whereas seven (15.9%) were triple negative. Forty-three (91.5%) had modified radical mastectomy and 19 (40.4%) had cytotoxics. Conclusion: With an average of six cases in a year, MCBC is common in our hospital. Majority (63.8%) were young. The commonest method of detection was self-breast examination. Majority (78.3%) presented at an early stage. Most (91.5%) still had modified radical mastectomy.

Keywords: Contralateral breast cancer, metachronous method of detection, treatment

Introduction

Breast cancer is the most common female malignancy in Nigeria.[1–3] It is also the most common malignancy of women in Denmark[4] as well as in Europe[5] and the United States.[6] A woman with a unilateral breast cancer is known to have an increased risk of developing contralateral breast cancer (CBC).[7] This CBC increases the agony brought about by the disease, complications from the ablative surgical treatment, and side effects from adjuvant chemotherapy and radiotherapy, all contributing to poor prognosis for such patients.[8] There are well-defined risk factors for developing unilateral breast cancer, but the risk factors for CBC are more uncertain. Young age at diagnosis, family history of breast cancer, and lobular histology have been associated with an increased risk of CBC,[9] whereas the use of adjuvant tamoxifen therapy has been shown to reduce the risk.[10] Furthermore, chemotherapy and oophorectomy, as well as prophylactic contralateral mastectomy in particular, have been associated with a decreased risk.[11]

For the purpose of this study, metachronous contralateral breast cancer (MCBC) is defined as a breast cancer in the contralateral breast after 6 months of the initial diagnosis of the first breast cancer. It is becoming an important public health issue because of the increased incidence of primary breast cancer and improved survival. Breast cancer incidence though known to be less in Sub-Saharan Africans appears to be on the increase from clinical and also laboratory experiences.[12–15] The incidence of bilateral breast cancer is known to have an increased risk in Sub-Saharan Africans. Furthermore, the incidence of primary breast cancer is known to have an increased risk in Sub-Saharan Africans. Breast cancer is the most common malignancy of women in Sub-Saharan Africa, with an increased risk of developing contralateral breast cancer. Breast cancer incidence in Sub-Saharan Africans is known to be less than in the Western world. Breast cancer incidence in Sub-Saharan Africans is known to be less than in the Western world. Breast cancer incidence in Sub-Saharan Africans is known to be less than in the Western world. Breast cancer incidence in Sub-Saharan Africans is known to be less than in the Western world.
breast cancer (BBC) has been reported to be 2.4% (Ilorin), 2% (Benin), 2.2% (Ife), and 4% (Lagos), all in Nigeria,\textsuperscript{[12,16-18]} whereas higher incidences of between 3.3% and 9.6% have been reported among the Caucasians.\textsuperscript{[8,19-22]} Despite being a centre for excellence for cancer treatment with a huge volume of breast cancer patients, there is no documentation on MCBC in our hospital, and there is a paucity of data in the whole Northwestern region of the country. The aim of this study was to document the incidence, the method of detection, clinicopathological features, and treatment of MCBC in our hospital.

**Patients and Methods**

It was a 7-year prospective study from January 2011 to December 2017. Patients who had treatment for nonmetastatic breast cancer (American Joint Committee on Cancer [AJCC] stages I-III) were followed up in the outpatient surgical clinic. Patients were taught self-breast examination (SBE) to be carried out on the eighth day of the menstrual cycle for premenopausal women and the eighth day of the month for postmenopausal women. SBE was to be done monthly by the patients. Clinical breast examination (CBE) was conducted on patients 3 monthly for the first 2 years after treatment of the initial disease and thereafter every 6 months during clinic visits as per the protocol of the unit. Patients also had breast ultrasonography every 6 months for the first 2 years and thereafter yearly for women less than 35 years. Mammography was done for patients who were 35 years and above on a yearly basis. Those that developed MCBC were then studied. Information documented included age, the time of occurrence, the method of detection, stage at presentation, pathological types, hormone receptor status, and treatment. Patients were followed up for an average of 4 years after treatment. The information obtained was analysed using SPSS version 21.0 (IBM 2012, Armonk, New York, USA). The results were presented as simple percentages and charts.

**Results**

In total, 1285 women had nonmetastatic breast cancer in the study. Forty-seven had MCBC (incidence of 3.7%); 30 (63.8%) patients were between the ages of 21 and 50 years. See Table 1 for the age distribution of patients with MCBC. Twenty-eight (59.6%) patients developed MCBC within 2–4 years of the initial breast cancer. See Table 2 for the time of occurrence of MCBC. Twenty-three (48.9%) patients detected MCBC by SBE, 13 (27.7%) by CBE, seven (14.9%) by mammography, and four (8.5%) by breast ultrasound scan. Mammography was done for patients who were 35 years and above on a yearly basis. Those that developed MCBC were then studied. Information documented included age, the time of occurrence, the method of detection, stage at presentation, pathological types, hormone receptor status, and treatment. Patients were followed up for an average of 4 years after treatment. The information obtained was analysed using SPSS version 21.0 (IBM 2012, Armonk, New York, USA). The results were presented as simple percentages and charts.

| Table 1: Age distribution of MCBC |
|----------------------------------|
| Age (years) | Frequency | % |
| 21–30 | 4 | 8.5 |
| 31–40 | 11 | 23.4 |
| 41–50 | 15 | 31.9 |
| 51–60 | 8 | 17.0 |
| 61–70 | 7 | 14.9 |
| >70 | 2 | 4.3 |
| Total | 47 | 100.0 |

| Table 2: Time of occurrence of MCBC |
|----------------------------------|
| Time (years) | Frequency | % |
| 6 months–1 | 1 | 2.1 |
| 1–2 | 2 | 4.3 |
| 2–3 | 10 | 21.3 |
| 3–4 | 18 | 38.3 |
| 4–5 | 9 | 19.1 |
| 5–6 | 4 | 8.5 |
| >6 | 3 | 6.4 |
| Total | 47 | 100.0 |

| Table 3: Treatment received by patients with MCBC |
|----------------------------------|
| Treatment | Frequency | % |
| Modified radical mastectomy | 43 | 91.5 |
| BCS | 4 | 8.5 |
| Radiotherapy | 8 | 17.0 |
| Cytotoxics (cyclophosphamide, Adriamycin, and Paclitaxel) | |
| Neoadjuvant | 7 | 14.9 |
| Adjuvant | 12 | 25.5 |
| Hormonal therapy (tamoxifen/letrozole) | 34 | 72.3 |
| Trastuzumab | 0 | 0.0 |

receptor/progesterone receptor (ER/PR) positive and human epidermal receptor-2 (HER-2) neu negative; nine (20.5%) were ER/PR and HER-2 neu positive; six (13.6%) were ER/PR negative, HER-2 neu positive, whereas seven (15.9%) were triple negative. Forty-three (91.5%) had modified radical mastectomy. See Table 3 for the treatment of MCBC. The mortality at the end of the study was 12 (25.5%) patients.

**Discussion**

An increase in the incidence of breast cancer worldwide has been reported by several authors.\textsuperscript{[6,12,15]} It will therefore not be a surprise if the same trend holds true for MCBC, as authors have noted that cancer in one breast raises the risk of subsequent cancer in the contralateral breast.\textsuperscript{[7]} The incidence of MCBC in our hospital was 3.7%. This is similar to the incidence of BBC (4.26%) in a study by Oguntuola et al.,\textsuperscript{[8]} among women in Nigeria. With an average of six cases diagnosed in 1 year, MCBC is common in our hospital. However, figures from studies in Caucasian

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populations showed lower rates of MCBC.\textsuperscript{[12,23]} This disparity may be related to the fact that populations in such developed countries are privileged to enjoy screening programmes for breast cancer such that the initial tumour is seen at an earlier stage than in patients in our hospital with consequent poor survival rate noted in our patients. The biologic behaviour of the respective breast cancers may also have played a role in creating this disparity with breast cancer in our patients and indeed other black women said to be more aggressive than Caucasian women.\textsuperscript{[9,13,15,16]}

A majority of the patients (63.8\%) in this study were 50 years or younger. This is similar to what was noted by Oguntola \textit{et al.},\textsuperscript{[9]} among patients in Osogbo, Southwestern Nigeria, as well as Gogas \textit{et al.}\textsuperscript{[22]} and Finney Jr. \textit{et al.}\textsuperscript{[23]} among Caucasian populations. This finding may be explained by the fact that patients presenting at a younger age have a higher risk of developing MCBC after surviving the initial lesion.\textsuperscript{[9,22,23]}

In this study, the highest number of patients with MCBC (31.9\%) was in the 41–50-year-old age group. This is similar to the mean age (47 years) for the diagnosis of BBC reported by Adeniji\textsuperscript{[24]} and Bailey \textit{et al.}\textsuperscript{[24]} (48 years) but is slightly higher than 39.1 years reported by Oguntola \textit{et al.}\textsuperscript{[9]}. In this study, a majority of the patients (38.3\%) developed MCBC between the third and fourth year following the initial primary breast cancer diagnosis. This is lower than the 117-month (9.75 years) and the 144-month (12 years) interval reported by Gogas \textit{et al.}\textsuperscript{[22]} and Finney Jr. \textit{et al.}\textsuperscript{[23]} respectively, among Caucasian populations. This difference in time interval may be explained by the fact that breast cancer in Nigerian (and other Sub-Saharan) populations is thought to be biologically more aggressive tumours.\textsuperscript{[9,13,15,16]}

The current guidelines recommend that after the completion of therapy for a primary breast cancer, women should undergo annual surveillance mammography to detect metachronous contralateral cancers.\textsuperscript{[22]} However, in breast cancer screening trials and programmes for the general population, the sensitivity of mammography is lower for women in their 40s than for women more than 50 years of age\textsuperscript{[20]}; it would therefore follow that, for surveillance, mammography may be less effective in breast cancer survivors younger than 50 years of age than in older women. In this study, only 14.9\% of the patients had their MCBC diagnosed through surveillance mammography, and this may be explained by the fact that a majority of the patients were younger than 50 years rendering mammography less effective. Another reason could be related to the quality of the mammogram because it was film mammography that was used in the study. In contrast, 48.9\% of the patients in this study detected the MCBC through SBE. This can be explained by the fact that SBE was more frequently performed during surveillance of these patients after treatment as it was done on a monthly basis. In poor-resource countries where digital mammography and tomosynthesis may not readily be available, SBE may be an effective surveillance tool in detecting MCBC in a predominantly younger population of less than 50 years.

A majority of the patients with MCBC (78.7\%) presented with early breast cancer AJCC stages I and II. In spite of the fact that they presented at an early stage, most of these patients (91.5\%) still had modified radical mastectomy. This was as a result of patient’s preference and the epileptic nature of radiotherapy services in our hospital and in the Northwestern region of the country making breast conservative surgery (BCS) + radiotherapy a more difficult option for the patients. The government should provide radiotherapy machines in all the centres of excellence for cancer treatment so that patients could easily have BCS and radiotherapy.

Despite the fact that a significant percentage was HER-2 neu positive, none of the patients received trastuzumab because patients could not afford the drug. This emphasises the need for near-universal health insurance coverage so that patients could benefit from the more expensive but potent drugs.

**Conclusion**

With an average of six cases diagnosed in 1 year, MCBC is common in our hospital. A majority of the patients were young (63.8\%), ≤50 years. SBE was the most common method of detection of the disease. Despite a majority of the patients with MCBC presenting at an early stage, most of the patients still had modified radical mastectomy. The government should provide radiotherapy machines in all centres of excellence for cancer treatment so that patients could easily have BCS and radiotherapy. There is a need for near-universal health insurance coverage so that breast cancer patients could benefit from the more expensive but potent drugs.

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**Conflict of interest**

There are no conflicts of interest.

**References**

1. Nggada HA, Yawe KD, Abdulazeez J, Khalil MA. Breast cancer burden in Maiduguri, North Eastern Nigeria. Breast J 2008;14:284-6.
2. Jedy-Agba E, Curado MP, Ogunbiyi O, Oga E, Fabowale T, Igbinoba F, \textit{et al.} Cancer incidence in Nigeria: A report from population-based cancer registries. Cancer Epidemiol 2012;36:e271-8.
3. Morouanke SG, Ayorinde JB, Benedict AO, Adedayo FF, Adewale FO, Oluwadamilare I, \textit{et al.} Epidemiology and incidence of common cancers in Nigeria. J Cancer Biol Res 2017;5:1105.
4. Ewertz M, Christensen K, Engholm G, Kejs AM, Lund L, Matzen LE, \textit{et al.}; Academy of Geriatric Cancer Research
Abur, et al.: Metachronous contralateral breast cancer

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55Journal of the West African College of Surgeons | Volume 12 | Issue 4 | October-December 2022

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55Journal of the West African College of Surgeons | Volume 12 | Issue 4 | October-December 2022

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5. Ferlay J, Colombet M, Soerjomataram I, Dyba T, Randi G, Bettio M, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. Eur J Cancer 2018;103:356-87.

6. American Cancer Society. Breast Cancer Facts & Figures 2015–2016. Atlanta: American Cancer Society, Inc.; 2015.

7. Hunt KK, Mittendorf EA. Diseases of the breast. In: Townsend CM, Evers BM, Beaucham RD, Mattox KL, editors. Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice. 20th ed. Philadelphia, PA: Elsevier Saunders; 2017. p. 820-64.

8. Abdalla I, Thisted RA, Heimann R. The impact of contralateral breast cancer on the outcome of breast cancer patients treated by mastectomy. Cancer J 2000;6:266-72.

9. Oguntola AS, Agodirin SO, Adeoti ML, Aderonmu AOA. Bilateral breast cancer: Experience in a poor resource black African setting. East Cent African J Surg 2010;15:28-34.

10. Early Breast Cancer Trialists’ Collaborative Group. Tamoxifen for early breast cancer: An overview of randomized trials. Lancet 1998;351:1451.

11. Garba ES. Contralateral breast cancer. Nig J Surg 2003;5:1-6.

12. Adeniji KA. Pathological appraisal of carcinoma of the female breast in Ilorin, Nigeria. Postgr Med J 1999;:6:56-9.

13. Adelusola KA, Fadiran OA, Adesunkami ARK, Odesanmi WO. Breast cancer in Nigerian women in Ile-Ife. Nig Med Pract 1996;31:17-20.

14. Otu AA, Ekanem IO, Khalil MI, Ekpo MD, Attah EB. Characterization of breast cancer subgroups in an African population. Br J Surg 1989;76:182-4.

15. Adebamowo CA, Ajayi OO. Breast cancer in Nigeria. West Afr J Med 2000;19:179-91.

16. Chiedozie LC. Breast cancer in Nigeria. Cancer 1989;55:653-7.

17. Oluwole SF, Fadiran OA, Odesanmi WO. Diseases of the breast in Nigeria. Br J Surg 1987;74:582-5.

18. Atoyebi OA, Atimomo CE, Adesanya AA, Beredugo BK, da Rocha-Afodu JT. An appraisal of 100 patients with breast cancer seen at Lagos University Teaching Hospital. Nig Qt J Hosp Med 1997;7:104-8.

19. Kollias J, Ellis IO, Elston CW, Blamey RW. Prognostic significance of synchronous and metachronous bilateral breast cancer. World J Surg 2001;25:1117-24.

20. Carmichael AR, Bendall S, Lockerbie L, Prescott R, Bates T. The long-term outcome of synchronous bilateral breast cancer is worse than metachronous or unilateral tumours. Eur J Surg Oncol 2002;28:388-91.

21. Mose S, Adamietz IA, Thilmann C, Saran F, Pahnke R, Bottcher HD. The prognosis of bilateral breast carcinoma compared to unilateral breast tumour. 5- and 10-year follow-up. Stachlenther Oncol 1995;171:207-13.

22. Gogas J, Markopoulos C, Skandalakis P, Gogas H. Bilateral breast cancer. Am Surg 1993;59:733-5.

23. Finney GG Jr, Finney GG, Montague AC, Stonesifer GL Jr, Brown CC. Bilateral breast cancer, clinical and pathological review. Ann Surg 1972;175:635-46.

24. Bailey MJ, Royce C, Sloane JP, Ford HT, Powles TJ, Gazet JC. Bilateral carcinoma of the breast. Br J Surg 1980; 67:514-6.

25. National Comprehensive Cancer Network (NCCN). Breast Cancer NCCN Practice Guidelines in Oncology. Fort Washington, PA: NCCN; 2011.

26. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L; U.S. Preventive Services Task Force. Screening for breast cancer: An update for the U.S. Preventive Services Task Force. Ann Intern Med 2009;151:727-37, W237-42.