



## Case Series

# Bilateral Breast Cancer

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Article history: Received 10 March 2024, Reviewed 31 May 2024, Accepted for publication 14 June 2024

## Abstract

**Background:** Synchronous bilateral breast cancer is not so common a phenomenon, so also is the findings in the same patient, of different histologic types with differences in receptor status and or tumour grades. We are beginning to encounter this phenomenon in our centre, hence this series. This case-series reported observed bilateral breast cancer in patients seen at our centre in Nigeria over a 11-year period (from 2008 to 2019), to further enrich the literature on this phenomenon.

**Case Presentation:** Case 1 was a 44-year-old hypertensive diabetic who presented to the surgical out-patient clinic with bilateral breast mass and a history of right breast fall-off before presentation to hospital. Case 2 was a 48-year-old woman who presented as emergency with difficulty in breathing with two-year history of breast disease. Case 3, a 60-year-old businesswoman with bilateral breast disease of 4 years interval.

**Conclusion:** Late presentation, preference for alternative therapy and delay in commencement of conventional treatment of breast cancer, and consequent increase in morbidity are witnessed in this case series. This is occasioned by ignorance and inability to afford breast cancer care requiring action.

**Keywords:** Bilateral Breast Cancer, Case series, Port Harcourt, Nigeria.



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## How to cite this article:

Elenwo SN, Ijah RF. Bilateral Breast Cancer. The Nigerian Health Journal 2024; 24(3):1602-1608.  
<https://doi.org/10.60787/tnhj.v24i3.799>

## Introduction

William Nisbet reported the first recorded case of bilateral breast cancer<sup>1</sup> and the literature has been growing since then. Globally, breast cancer is the most common cancer among women<sup>2</sup> and the West African sub-region is no exception.<sup>3</sup> It is also known that women with breast cancer have two-fold higher risk of developing a second breast cancer in the other breast than the general population.<sup>4-6</sup> There have been reports of bilateral breast cancer among patients, defined as synchronous when the diagnosis of bilaterality is made not more than one month apart,<sup>7</sup> with a reported incidence of approximately 1%.<sup>7,8</sup> However, some authors reported that synchronous bilateral invasive breast cancer is not uncommon, with a quoted incidence ranging from 0.3 to 12%.<sup>9-11</sup> There appear to be differences in opinion as regards the timing in the definition of synchronous bilateral breast cancer. While some consider a timing of one month apart,<sup>7</sup> some others report six months or less,<sup>12-14</sup> and yet some state a simultaneous occurrence.<sup>15,16</sup> In a ten-year study of mastectomy specimen, an overall incidence of 4.2% bilateral breast cancer was reported (66 out of 1578).<sup>17</sup>

In a study of hereditary breast cancer among Tunisian population<sup>18</sup> in Africa, genetic bilateral breast cancer was reported in a patient in whom other family members had breast cancer. BRCA gene mutations were reported to be more common among patients with bilateral breast cancer.<sup>19,20</sup> William et al.<sup>21</sup> stressed on the beneficial effect of Tamoxifen in reducing recurrence and contralateral breast cancer in patients with BRCA1 genes.

Cases of bilateral breast cancer have been reported among our patients in Nigeria. In a ten year-review, Anyanwu<sup>22</sup> reported that 5% of the cases had bilateral breast cancer. Another researcher<sup>23</sup> documented 0.8% in a 12-year review. A Nigerian study reported 12 women having bilateral Burkitt's lymphoma out of 18 patients in that series.<sup>24</sup> A rare case in the list of the uncommon occurrence was a report of bilateral male breast cancer in Oshogbo.<sup>25</sup> In Maiduguri, 4 out of 490 breast biopsy specimens were reported to be bilateral breast cancer.<sup>26</sup> In yet another study in Benin<sup>27</sup> 12.5% bilateral (metachronous) breast cancer was reported out of a review of 16 male breast cancer cases.

Synchronous bilateral breast cancer is not so common a phenomenon,<sup>7</sup> so also is the findings in

the same patient, of different histologic types with differences in receptor status and or tumor grades. The status of the second tumor is a subject of concern, considered independent when there is variation from the first tumor<sup>15,28</sup> with attendant challenges in patient management.<sup>7</sup> This phenomenon has previously been reported in Nigeria but not in our center, and we are beginning to encounter this occurrence hence this study. This case-series reported observed bilateral breast cancer in patients seen at the breast unit of the Department of Surgery of the University of Port Harcourt Teaching Hospital, Nigeria over an 11-year period (2008 and 2019), to further enrich the literature on this phenomenon.

## Case 1

**Clinical History:** A 44-year-old businesswoman who presented at the surgical out-patient clinic with a lump in the left breast of 7 months duration and a wound over the right breast of 3 months duration. She had an associated history of cough, significant weight loss, and a fast and difficult breathing. Two years earlier she was diagnosed with cancer of the right breast following a biopsy. She declined the offer of treatment. At presentation in the facility, she claimed that a portion of the right breast had fallen off. There was no history of yellowness of the eyes or seizures. She was a hypertensive diabetic mother of three children (all breastfed) with no family history of cancer, no history of excessive alcohol consumption or tobacco usage, and no significant hormonal risk factors.

**Physical Examination:** A middle-aged woman, who was conscious and alert, pale, and had no other significant findings on general examination of the patient. The vital signs were stable except for an increased respiratory rate of 32 cycles per minute. There was gross breast asymmetry, with the left breast bigger than the right. The right breast had a residual breast tissue (from auto-breast amputation) underlying a central ulcerated area with surrounding hyperpigmented skin and nodules at the upper area. The residual breast tissue was fixed to the chest wall, and there were multiple matted right axillary lymph nodes, with enlarged right infra and supra-clavicular lymph nodes. The left breast had peau d'orange with no obvious palpable mass. Left axillary lymph nodes were not enlarged. There were signs of fluid collection in the pleural cavity bilaterally, and thoraco-centesis yielded free flowing serosanguinous exudates from both sides. The findings from other systems were not significant.

**Investigations:** The incisional biopsy of the right breast (and Tru-cut biopsy of the left breast) result showed invasive ductal carcinoma. Immunohistochemistry could not be done. The haemoglobin concentration was 11.3g/dl and the full blood count values were normal. Serum electrolytes, urea and creatinine were normal. The total protein and albumin were within normal limits. Liver function test revealed normal bilirubin and alkaline phosphatase, but the aspartate, alanine transferase and gamma glutamyl transferase were elevated above normal values. Chest radiograph showed widespread patchy opacities with bilateral pleural effusion, sparing the apical region. Abdominopelvic ultrasound scan result showed normal findings. Also, serology done for HIV and Hepatitis were seronegative.

**Treatment:** The pleural effusion was drained with bilateral tube thoracostomies, and patient was commenced on neoadjuvant chemotherapy comprising Paclitaxel, Epirubicin and Xeloda.

**Outcome:** Some improvement as evidenced by reduction in the elevated respiratory rate and improvement in breathing.

## Case 2

**Clinical History:** A 48-year-old businesswoman who was admitted through the emergency department with a history of difficulty in breathing of 4 days duration. She had been on treatment at a peripheral centre for a left breast lump of two years duration associated with bloody nipple discharge and for which a biopsy revealed breast cancer. She had declined surgery and chemotherapy in favour of herbal treatment for two years and subsequently developed soreness of the left breast with another lump being noticed in the right breast. She had two cycles of chemotherapy in a peripheral hospital, the last cycle being about a month before presenting in our emergency department. There was no history of yellowness of the eyes or seizures. She was a widow with two children (all breastfed) with no family history of cancer, no history of alcohol consumption or tobacco usage, and no significant hormonal risk factors.

**Physical Examination:** She was a chronically ill-looking middle-aged woman with alopecia, dyspnoeic, and bilateral enlarged and matted axillary lymph nodes. There was gross breast asymmetry (left > right), with hyperpigmented excoriations on

the right breast and a fungating ulcer spanning the whole left breast. Both breasts had cancer en cuirasse. There was also bilateral upper limb lymphoedema (left more than right). Other system's examinations were not significant.

**Investigations:** Biopsy histopathology/ immunohistochemistry results revealed triple negative invasive ductal carcinoma in both breasts. Chest radiograph showed right pleural effusion with bilateral patchy opacities in both lung zones. The result of full blood count was normal with a haemoglobin value of 11.5g/dl.

**Treatment:** She had oxygen by nasal catheter with right tube thoracostomy for drainage of right pleural effusion. She was also placed on triple drug chemotherapy with Paclitaxel, Carboplatin, and Doxorubicin.

**Outcome:** This patient also had some improvement as evidenced by reduction in the elevated respiratory rate and improvement in breathing.

## Case 3

**Clinical History:** A 60-year-old businesswoman with primary level of education who presented through the surgical out-patient clinic with recurrent right breast lump of 4 years duration whose biopsy result done showed breast cancer. She had declined conventional treatment offered 4 years ago following the biopsy. There was significant weight loss, but no history of cough, yellowness of the eyes, bone pain or seizures. Patient was a widow with five children (all breastfed) with no family history of cancer, no social or hormonal risk factors.

**Physical Examination:** On examination she was an elderly woman with a hard, non-tender right breast lump with right axillary lymph node enlargement. The mass was ill-defined and measured 10cm in its widest diameter. There was nipple deviation and displacement with a scar at the upper outer quadrant of the right breast overlying the mass. There was also a mobile lump in the upper outer quadrant of the left breast measuring 6cm by 5cm. There were no palpable nodes in the axilla. The examination of other systems revealed no significant findings.

**Investigations:** Tru-cut biopsy result for the left breast lump showed mucinous carcinoma, while

that of the right breast showed invasive ductal carcinoma. Other laboratory investigation results were within normal limits.

**Treatment:** She had two cycles of neoadjuvant chemotherapy with paclitaxel and epirubicin and was offered bilateral modified radical mastectomy and adjuvant chemotherapy and radiotherapy.

**Outcome:** Patient felt better, satisfied with treatment, and was discharged home for out-patient follow-up and further care.

## Discussion

The age range of the cases presented was 44 – 60 years, being similar to findings described in the study by Gollamudi,<sup>7</sup> Intra,<sup>9</sup> and Huo.<sup>6</sup> Age has been linked to bilaterality when between 20 and 44 years,<sup>29</sup> and when less than 50 years.<sup>30-32</sup> Yet another researcher reported age as being significant only in metachronous tumours.<sup>33</sup> It is worthy of note that the interval between first diagnosis of cancer and a second cancer in the other breast was two years for the first two cases and 4 years for the last case. This range is longer compared to some reports,<sup>33-37</sup> and relatively shorter when compared to 5 year description by some authors.<sup>38, 39</sup>

The diagnosis of bilateral breast cancer was made after an interval of two years in cases 1 and 2-, and four-years interval for case 3. These were not synchronous cases, making this series different from earlier reported cases.<sup>11-15</sup> The histologic type of the tumor was the same for cases 1 and 2 (invasive ductal carcinoma), but different for case 3 (mucinous carcinoma in left breast and invasive ductal carcinoma in right). However, the immunochemical status of all tumors could not be ascertained due to inability of the patient to carry out the tests in cases 1 and 3. It has however been reported that bilateral (metachronous) breast cancers have more aggressive phenotypes,<sup>40, 41</sup> with associated worse prognosis.<sup>42</sup> An association between bilateral breast cancer and bone/visceral metastasis has also been reported.<sup>43</sup> Triple negative bilateral breast cancer has been reported,<sup>44</sup> but it appears that there is no direct link between triple negativity and bilaterality.

Early breast cancer diagnosis is desirable, however all the cases presented at advanced stages contrary to expectation with attendant increased morbidity. Abandonment of conventional care in preference for alternative therapy was seen in all cases. Patients

however returned for treatment with bilateral breast disease in a worse clinical state with attendant reduced chances of survival. The reasons for patients' line of action could be fear of losing one's breast (mastectomy), fear of chemotherapy, or lack of funds to support conventional treatment.

The first two cases had ulcerated breast lesions, with associated breast auto-amputation in the first case. Obviously, the cases presented were stage 4 diseases. It has been reported that initial tumor size and stage is strongly associated with contralateral tumor size and stage.<sup>45</sup> Only in case 2 was immunohistochemistry done. The reason for this experience is partly patient's inability to pay for the test.

Case 1 in this study revealed invasive ductal carcinoma in both breasts. This finding is similar to that of Padmanabhan et al.<sup>46</sup> in which about 70% of the cases described were invasive ductal cancer, though in this case 1 receptor status was not determined. There was also similarity in histologic characteristics in case 2, but different histology in case 3. This dissimilarity in histology also finds expression in studies done by other researchers.<sup>47-49</sup>

## Implications of the findings of this study

The implications of the occurrence of bilateral breast cancer as reported in this case series are far reaching and myriad. Advanced or late-stage breast cancer is a manifestation of the challenges inherent in our practice which include but not limited to diagnostic challenges (lack of awareness, cultural beliefs, poverty, and limited access to healthcare facilities), limited healthcare infrastructure (health facilities, personnel capacity building, research and data collection), treatment issues (resource constraints including treatment funding). Policy makers will therefore need to do more work to improved breast cancer screening and early detection, upgrading of treatment infrastructure, and enhance more research efforts to address the need our area of practice.

## Limitations of the Case Series

Although this study has provided further evidence of advance breast cancer in our environment, we are limited in our documentation of follow up details of the subsequent long-term outcome due to the nature of the report.

## Conclusion

Late presentation, preference for alternative therapy, delay in commencement of conventional treatment of breast cancer and consequent increase in morbidity are witnessed in this case series. Twin factors of ignorance and inability to afford breast cancer care also featured here. This calls for more effort in public education and governmental action to subsidize or entirely fund breast cancer care for patients in our sub-region.

#### Declarations

**Ethical Consideration:** Institutional Research Ethics approval was obtained, and a written consent of the patient was secured.

**Authors' Contribution:** Both authors were involved in the conceptualization, design and conduct of the study as well as gave their approval for the final draft of the report

**Conflict of interest:** None declared.

**Funding:** The research was self-funded by the authors.

**Acknowledgment:** We wish to acknowledge the three patients for their consent to present this case series.

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