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Clinic Pathological Profile of Bilateral Breast Cancer

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Abstract

Background: Bilateral Breast Cancer (BBC) is a rare entity, no definite guidelines in treatment depending on the diagnostic methods, nomenclatures and policies of treatment. Because the incidence of breast cancer is increasing and prognosis is improving, a growing number of women are at risk of developing bilateral disease. Bilateral Breast Cancer is either Synchronous (SBBC) when diagnosed within 6 months between the two sides and Metachronous (MBBC) when diagnosed more than 6 months.

Material and Methods: Retrospective study done at Tanta cancer center-Egypt between January 2013 to end of December 2014 to evaluate the cases of bilateral breast cancer.

Results: 46 patients were diagnosed with bilateral breast cancer out of 1454 cases with breast cancer with 3.12%, 30 cases synchronous and 16 cases metachronous, mean age of 50 years in both groups,18/46cases were premenopausal with 28/46 patients postmenopausal. SBBC group, 18/30 cases diagnosed at stage III, while in MBBC 8/16 diagnosed as stage III in primary tumor. 30/46 diagnosed by FNAC and 16/46 by true cut biopsy, 34/46 cases had infiltrating duct carcinoma. 24/46 cases treated surgically by bilateral Modified Radical Mastectomy (MRM). Most of cases are triple negative (ER, PR & her2/neu) in 26/46.

Conclusion: BBC is an uncommon clinical entity; these patients require individualized treatment based on the tumor and treatment factors of the lesion. Optimal results can be obtained by using Multimodal Treatment approach (MDT) for BBC.

Keywords: Bilateral Breast Cancer; Synchronous Breast Cancer; Metachronous Breast Cancer; Clinicopathological Profile

Abbreviations

BBC: Bilateral Breast Cancer; SBBC: Synchronous Bilateral Breast Cancer; MBBC: Metachronous Bilateral Breast Cancer; MRM: Modified Radical Mastectomy; CBS: Conservative Breast Surgery; ER: Estrogen Receptors; PR: Progesterone Receptors; HER2: Herceptin; IDC: Infiltrating Duct Carcinoma

Introduction

Breast cancer is the most common malignancy diagnosed in female [1]. Worldwide, it was estimated that new cancer cases and cancer deaths were 1.3 million and 327,000 every year [2]. With the development of the medical technology, early detection, early diagnosis and early adequate treatment may have led to prolonged survival and improved quality of life for breast cancer patients. Nevertheless, the long-term health of these patients will become a significant public health problem because the possibility of developing second primary cancers may be on rise; Bilateral Breast Cancer (BBC) is a rare entity, as compared to unilateral breast cancer, no definite guidelines in treatment depending on the diagnostic methods, nomenclatures and policies of treatment [3]. Because the incidence of breast cancer is increasing and prognosis is improving, a growing number of women are at high risk of developing bilateral disease with little is known about incidence trends and prognostic features of bilateral breast cancer [4]. Overall the incidence of BBC is 1.4%-12% of all breast cancer reported in various studies, The incidence of Synchronous Breast Cancer (SBBC) is 0.7%-3% whereas that of Metachronous Breast Cancer is (MBBC) 5%-10% [5]. Bilateral Breast Cancer is either Synchronous (SBBC) when diagnosed within 6 months between the 2 sides and Metachronous (MBBC) when diagnosed more than 6 months between the two sides, the origin of second cancer may be metastatic spread from the primary tumor or independent primary [6]. There is a two to six fold increased risk of developing contralateral breast cancer in women with first primary as compared to the general population, there is an increasing incidence of BBC due to improved diagnostic techniques, longer survival, and patient education [7,8]. The prognosis of BBC has been reported to be worse than that of Unilateral Breast Cancer (UBC) [9,10] and the biological aspects, as well as the optimum therapy, are still remains controversialm [11,12]. The present study was done to analyze the clinicopathological characteristics and treatment outcome at a tertiary cancer center in Tanta Cancer Center in Delta of Egypt.

Materials and Methods

This is a retrospective study carried out at a tertiary cancer center, Tanta cancer center in Egyptian delta, Egypt. All patients diagnosed for breast cancer were collected from start of January 2013 till end of December 2014, they found to be 1454 Patients in the department of surgical oncology, 46 (3.12%) patients diagnosed for bilateral breast cancer and taken up for the study with treatment outcomes

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as well as the follow-up data were recorded. Two tumors diagnosed within an interval of 6 months was defined as SBBC whereas MBBC as second cancer diagnosed after 6 months. The analysis of patient's characteristic including age, pre/post-menopausal status, family history of breast cancer, mode of detection, and histological features between the two breasts was done. Patients were followed up for treatment outcomes and disease recurrence. Those not on regular follow-up were contacted telephonically.

Results

During the period of start of January 2013 to the end of December 2014, total number of breast cancer diagnosed was 1454 cases, of them 46 (3.12%) patients diagnosed as Bilateral Breast Cancer (BBC), 30 (2.02%) patients diagnosed as Synchronous Breast Cancer (SBBC) while 16 (1.1%) patients diagnosed as Metachronous Bilateral Breast Cancer (MBBC), all patients diagnosed in this study are women with median age of 50years (range from 28-71) in synchronous group and (35-65) in metachronous group, 40 patients had previous breast feeding with 3 patients had positive family history of breast cancer for mothers. 6 cases diagnosed by mammographic exam and 24 cases by clinical examination in SBBC while in MBBC, 4 cases diagnosed by mammographic examination compared to 12 cases diagnosed clinically. Tumor size tend to be more larger in Synchronous than Metachronous group which start at right side in 10 cases and 6 cases started with left side with least period between the two of 12 months and longest is 108 months.

At the time of diagnosis there were 10 cases premenopausal and 20 postmenopausal at synchronous group while in metachronous group there were 8 and 8 pre and postmenopausal, average time of diagnosis of contralateral breast cancer is 5ys ranging from 12-108 months. Nine cases diagnosed with mammographic examination while 37 patients diagnosed clinically.

Pathologically 30 patients were diagnosed by FNAC 18 cases in SBBC and 12 cases in MBBC and 16 patients diagnosed with true cut needle biopsy 12 cases in SBBC and 4 cases in MBBC group, while out of 92 pathological examination there were 68 pathology diagnosed as infiltrating duct carcinoma, 12 pathology were lobular carcinoma, 4 pathology as mucoid carcinoma; 4 mixed lobular and ductal carcinoma, 4 were multifocal and duct carcinoma in situ diagnosed in 2 biopsies. Out of 92 tumors 48 tumors diagnosed at stage III while 23 tumors diagnosed as stage II and 17 diagnosed as stage IV and 4 were stage I, 26 patients were found triple negative in examination (Estrogen receptor, Progesteron receptor and Her2/neu), ER +ve, PR +ve, Her2/neu +ve and KI67 +ver were found in 14/30, 13/30, 14/30 and 24/30 in synchronous group respectively in synchronous and while 6/16, 6/16, 6/16 and 10/16 in metachronous group respectively.

In our study in synchronous group 16/30 (53.3%) cases treated with bilateral Modified Radical Mastectomy (MRM), 4/30 (13.3%) treated by bilateral Conservative Breast Surgery (CBS) and 10/30 (33.4%) cases treated with combined MRM and CBS. While in metachronous group there were 8/16 (50%) treated by bilateral MRM, 6/16 (37.5%) treated by bilateral CBS and 2/16 (12.5%) treated with MRM and CBS. The clinical, pathological and surgical treatment are present in below Table 1,2 & 3 (Figures 1 & 2).

Table 1: Pathological exam and median age.

Variables	Synchronous		Metachronous	
	1st Tumor	2nd Tumor	1st Tumor	2nd Tumor
Median age at diagnosis in years	50ys (28-71)		50ys (35-65)	
Time interval between the two (in months)	0		60 (12-108)	
Stages				
I	2	1	1	0
II	6	7	4	6
III	18	16	8	6
IV	4	6	3	4

Table 2: Histological type on examination.

Variables	Synchronous		Metachronous	
	1st Tumor	2nd Tumor	1st Tumor	2nd Tumor
Histological type	20	20	14	14
IDC	4	4	2	2
Lobular	2	2	0	0
Mucoid	2	2	0	0
Mixed lobular and ductal	2	2	0	0
Multifocal	2	2	0	0
Associated DCIS	2	0	0	0
Margin	+ve in one case of toilet mastectomy		-	

Table 3: Biological results.

	Synchronous	Metachronous
ER		
+ve	14	6
-ve	16	10
PR		
+ve	13	6
-ve	17	10
Her2/neu		
+ve	14	6
-ve	16	10
KI67		
+ve	24	10
-ve	6	6
Tripple -ve	16	10

Discussion

BBC is a rare clinical entity. Our study is a retrospective study designed between January 2013 to end of December 2014 at Tanta cancer center, Egypt. The incidence of BBC in our study was 3.12% similar to the other published data from different centers [13]. The incidence of SBBC and MBBC varies according to cutoff time to define this entity. The incidence of SBBC and MBBC was 3% and 7% respectively as reported by Chaudary et al [14]. In 1993, Robinson et al. reported the incidence of SBBC as 1.7% and of MBBC as 2.4% [15]. In this study, patients which had contralateral breast cancer

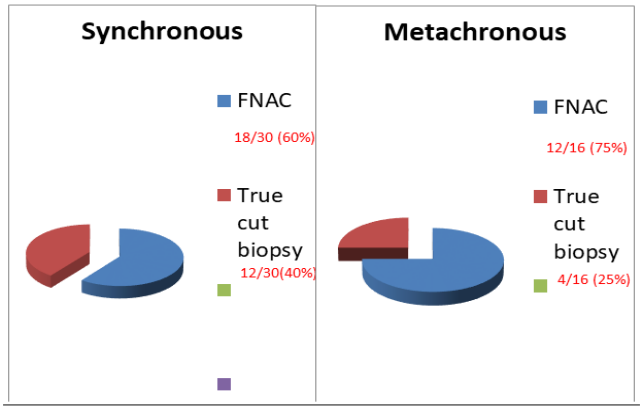

Figure 1:

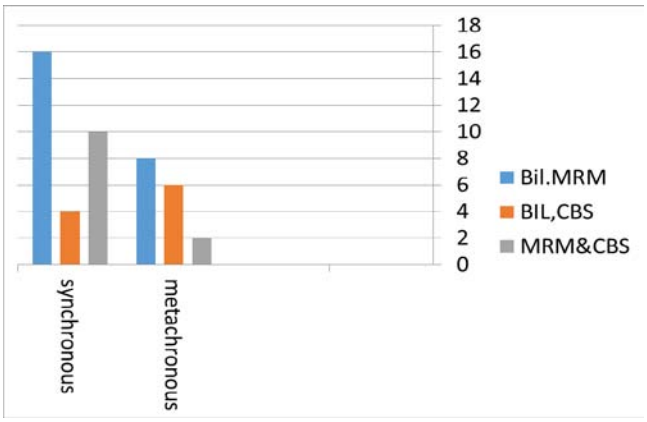

Figure 2:

within 6 months of the primary is considered as Synchronous (SBBC) and those having second primary in the contralateral breast after 6 months of the first primary were defined as Metachronous (MBBC). The incidence of synchronous and metachronous in our study was 2.02% and 1.1%, respectively. There is a three times increased risk of developing a second breast cancer in women who developed first breast cancer before the age of 40 years, compared to those who develop first breast cancer after the age of 40 years [14].

Family history and younger age are the main risk factors for development of bilateral breast cancer from literatures [16-18], the median age of presentation in our study is 50 years in both synchronous and metachronous groups but tend to be more younger in synchronous group (28-71) than in metachronous (35-65), 10 patients were diagnosed in premenopausal and 20 patients diagnosed at postmenopausal age in the synchronous group while 8 patients diagnosed in both pre and postmenopausal age in metachronous group, with family history was found positive in 3/46 patients (6.5%). 10 cases had neo adjuvant treatment in SBBC group while 4 in MBBC group subjected to neoadjuvant treatment, while all cases had adjuvant treatment according to stage and nodal status with either uni or bilateral axillary irradiation.

In our study, in synchronous group 18/30 (60%) of primary tumor of cases diagnosed as stage III while 16/30 (53.3%) diagnosed at the contralateral tumor, in metachronous group there were 8/16 (50%) diagnosed as stage III in first tumor while 6/16 (37.5%) diagnosed in contralateral tumor with the same stage, some of literatures indicated the association of grade of primary tumor and development of secondary tumor [19].

In postoperative pathological examinations, Robbins and Berg first reported lobular carcinoma as the most common histology for BBC [20]. The most common histology reported by Bernstein et al [20] was medullary carcinoma and according to Li et al [17]. But in our study, most of cases diagnosed as Infiltrating Duct Carcinoma (IDC) in both groups 20/30 (66.6%) in synchronous and 14/16 (87.5%) in metachronous group with other types of pathology diagnosed as lobular carcinoma in 4/30 (13.3%) in synchronous and 2/16 (12.5%) in metachronous, mixed lobular and ductal type found in 2/30 (6.66%) in synchronous group, mucoid carcinoma in 2/30 (6.66%) and multifocal pathology found in 2/30 (6.66%) of cases in synchronous group only while Duct Carcinoma in Situ (DCIS) detected in 2/30 cases also.

Few studies reported the relation between ER, PR and HER2 status and risk of developing second breast cancer; Women with ER positive breast cancer are associated with lower risk of recurrence and good prognosis [21]. The reduced risk of Bilateral Breast Cancer (BBC) in premenopausal women with ER positive first tumor was also reported by Mariani et al [22]. No association of BBC with hormonal status has been reported by Li et al [17]. Saad et al., and Beckmann et al., reported 76% and 87% ER positivity in BBC [23,24].

In our study, most of cases found as triple -ve (ER, PR and HER2) in 16/30 (53.3%) in synchronous and 10/16 (62.5%) in metachronous group, ER +ve, PR +ve, Her2/neu +ve and KI67 +ve were found in 14/30, 13/30, 14/30 and 24/30 in synchronous group respectively in synchronous and while 6/16, 6/16, 6/16 and 10/16 in metachronous group respectively. Most of the surveillance guidelines suggest yearly examination and mammography for patients with breast cancer after 5 years [25,26].

Follow up of patients for 56 months after collection of data of patients till end of august 2019 with mammographic examination every 6months for 2 years then annually with the regular clinical exam found that in synchronous group only one patient had multiple bone metastasis within one year with one patient developed supraclavicular LN 4ys later after finishing treatment and in metachronous group there were 4 cases with local recurrence in one side within 3-4ys. After 56 months of follow up, there were 26/30 still live (86.6%) at synchronous group while 10/16 from the metachronous group (62.5%). Heavy nodal infiltration found with synchronous group more than metachronous group.

Conclusion

BBC represents a small subset of breast cancer. The incidence of BBC is higher in postmenopausal patients more than premenopausal in SBBC with poor prognosis and local recurrence in MBBC than the SBBC. There is a role for mammographic examination and the regular clinical examination in detecting of BBC in early stage, treatment should be planned according to the stage and characters of each case.

References

1. Nelson HD, Zakher B, Cantor A, Fu R, Griffin J, O'Meara ES, et al. Risk

factors for breast cancer for women aged 40 to 49 years: a systematic review and meta-analysis. Ann Intern Med. 2012; 156: 635-648.

2. Confortini CC, Krong B. Breast cancer in the global south and the limitations of a biomedical framing: a critical review of the literature. Health Policy Plan. 2015; 30: 1350-1361.
3. Molina-Montes E, Pollan M, Payer T, Molina E, Dávila-Arias C, Sánchez MJ. Risk of second primary cancer among women with breast cancer: a population-based study in Granada (Spain). Gynecol Oncol. 2013; 130: 340-345.
4. Hartman M, Czene K, Reilly M, Adolfsson J, Bergh J, Adami HO, et al. Incidence and prognosis of synchronous and metachronous bilateral breast cancer. J Clin Oncol. 2007; 25: 4210-4216.
5. Heron DE, Komarnicky LT, Hyslop T, Schwartz GF, Mansfield CM. Bilateral breast carcinoma: Risk factors and outcomes for patients with synchronous and metachronous disease. Cancer. 2000; 88: 2739-2750.
6. Newman LA, Sahin AA, Cunningham JE, Bondy ML, Mirza NQ, Vlastos GS, et al. A case-control study of unilateral and bilateral breast carcinoma patients. Cancer. 2001; 91: 1845-1853.
7. Chen Y, Thompson W, Semenciw R, Mao Y. Epidemiology of contralateral breast cancer. Cancer Epidemiol Biomarkers Prev. 1999; 8: 855-861.
8. Hislop TG, Elwood JM, Coldman AJ, Spinelli JJ, Worth AJ, Ellison LG. Second primary cancers of the breast: Incidence and risk factors. Br J Cancer. 1984; 49: 79-85.
9. Takahashi H, Watanabe K, Takahashi M, Taguchi K, Sasaki F, Todo S, et al. The impact of bilateral breast cancer on the prognosis of breast cancer: A comparative study with unilateral breast cancer. Breast Cancer. 2005; 12: 196-202.
10. Levi F, Randimbison L, Te VC, La Vecchia C. Prognosis of bilateral synchronous breast cancer in Vaud, Switzerland. Breast. 2003; 12: 89-91.
11. 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: 388-391.
12. Kollias J, Ellis IO, Elston CW, Blamey RW. Prognostic significance of synchronous and metachronous bilateral breast cancer. World J Surg. 2001; 25: 1117-1124.
13. El Hanchi Z, Berrada R, Fadli A, Ferhati D, Brahmi R, Baydada A, et al. Bilateral breast cancer. Incidence and risk factors. Gynecol Obstet Fertil. 2004; 32: 128-134.
14. Chaudary MA, Millis RR, Hoskins EO, Halder M, Bulbrook RD, Cuzick J, et al. Bilateral primary breast cancer: A prospective study of disease incidence. Br J Surg. 1984; 71: 711-714.
15. Robinson E, Rennert G, Rennert HS, Neugut AI. Survival of first and second primary breast cancer. Cancer. 1993; 71: 172-176.
16. Bernstein JL, Lapinski RH, Thakore SS, Doucette JT, Thompson WD. The descriptive epidemiology of second primary breast cancer. Epidemiology. 2003; 14: 552-558.
17. Li CI, Malone KE, Porter PL, Daling JR. Epidemiologic and molecular risk factors for contralateral breast cancer among young women. Br J Cancer. 2003; 89: 513-518.
18. Malone KE, Daling JR, Weiss NS, McKnight B, White E, Voigt LF, et al. Family history and survival of young women with invasive breast carcinoma. Cancer. 1996; 78: 1417-1425.
19. Storm HH, Jensen OM. Risk of contralateral breast cancer in Denmark 1943-80. Br J Cancer. 1986; 54: 483-492.
20. Robbins GF, Berg JW. Bilateral primary breast cancer; a prospective clinicopathological study. Cancer. 1964; 17: 1501-1527.
21. Henderson IC, Patek AJ. The relationship between prognostic and predictive factors in the management of breast cancer. Breast Cancer Res Treat. 1998; 52: 261-288.
22. Mariani L, Coradini D, Biganzoli E, Boracchi P, Marubini E, Pilotti S, et al. Prognostic factors for metachronous contralateral breast cancer: A comparison of linear Cox regression model and its artificial neural network expression. Breast Cancer Res Treat. 1997; 44: 167-178.
23. Saad RS, Denning KL, Finkelstein SD, Liu Y, Pereira TC, Lin X, et al. Diagnostic and prognostic utility of molecular markers in synchronous bilateral breast carcinoma. Mod Pathol. 2008; 21: 1200-1207.
24. Beckmann KR, Buckingham J, Craft P, Dahlstrom JE, Zhang Y, Roder D, et al. Clinical characteristics and outcomes of bilateral breast cancer in an Australian cohort. Breast. 2011; 20: 158-164.
25. Smith TJ. Breast cancer surveillance guidelines. J Oncol Pract. 2013; 9: 65-67.
26. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Breast Cancer Version 1. 2017.

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