

Nine Cases of Bilateral Breast Cancer

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Abstract 154 patients with breast cancer were treated at our department from January 1981 to December 1990, 9 of which had bilateral involvement. Two patients had synchronous primary cancer, 5 had metachronous primary cancer and 2 had metachronous metastatic cancer.

The second cancer was usually detected through self examination by patients and presented at an earlier stage than the primary cancer in our series. Since bilateral breast cancer is not uncommon, patients will require close follow up after their initial cancer had been treated. Any suspicious masses should be biopsied. Diagnosis of a second primary versus metastatic cancer is made based on histological and clinical criteria.

Key words: Bilateral breast cancer. Synchronous primary breast cancer. Metachronous primary breast cancer. Metastatic breast cancer. Intraductal component.

Introduction

The incidence of breast cancer is occurring with alarming frequency. It is, however, associated with a good prognosis if detected and treated early. We report 9 recently treated cases of bilateral breast cancer at our department; reviewing their histological and clinical characteristics.

Materials and methods

All female patients with breast cancer treated at our department from January 1981 to December 1990 were reviewed. Of the 154 patients, 9 (5.8%) had bilateral breast cancer. Two patients had been initially treated elsewhere and pathological specimens were unavailable. Patients with mastectomy scars

were regarded as having been previously treated for breast cancer.

Breast cancer was classified according to the guide "General rule for clinical and pathological record of mammary cancer¹⁾".

Definition

When cancer is detected in the second breast, there is always the question of whether this cancer is a primary or a metastatic tumor. We based our diagnosis of a second primary breast cancer if any of the following conditions existed:

- 1 Either or both tumors were carcinoma in-situ.
- 2 The tumor in the second breast was of a distinctly different histology or embryological origin from the cancer

in the first breast.

3 The second tumor had intraductal cancer components contiguous with the invasive cancer.

4 There was no evidence of distant metastases shortly after detection of tumor in the second breast.

Tumors were considered synchronous if they were detected within one year of each other. If both tumors were detected at the same time, smaller one was considered the second breast tumor.

Results

① Incidence

Of the 154 female patients, 9 (5.8%) had bilateral breast cancer. Two (1.3%) patients had synchronous primary breast cancer, 5 (3.2%) patients had metachronous primary breast cancer and 2 (1.3%) patients had metachronous metastatic breast cancer to the opposite breast.

② Age

The average age of patients with synchronous primary breast cancer was 56.9 years. Those with metachronous primary breast cancer and metastatic breast cancer at the time of the first diagnoses were 46.3 years and 61.4 years respectively.

③ Interval

The average interval between initial diagnosis and the discovery of metachronous primary breast cancer and metastatic breast cancer were 5.2 years

and 2.7 years, respectively.

④ Family history

All patients in this series had a negative family history of breast cancer.

⑤ Location

So-called "mirror image location²⁾" was observed in 2 of 7 patients, both whose pathological specimens were available. One had metachronous breast cancer, located in the lower, inner quadrant bilaterally, and the other had metachronous metastatic cancer, located in the upper, inner quadrant bilaterally.

⑥ Histology

All patients with synchronous primary breast cancer and metachronous metastatic breast cancer had invasive ductal carcinoma bilaterally. Of three patients with metachronous primary breast cancer, whose pathological specimens from both breast were available, 2 had invasive ductal carcinoma bilaterally and the other had Paget's disease in the first breast and invasive ductal carcinoma in the second.

⑦ Tumor size

Both patients with synchronous primary breast cancer had tumors of greater than 5.1 cm bilaterally. There were 3 patients with metachronous primary breast cancer and 2 with metastatic breast cancer, whose pathological specimens from both breast were available. The second tumor was smaller in 4 of 5 patients.

⑧ Lymph nodes involvement

Both patients with synchronous pri-

Table 1. Cases of synchronous bilateral primary breast cancer

	Age	Detection	Region	Size(cm)	tnm	stage	Histological type	Intraductal component	Hormone receptor	Treatment
No.1	45	Self palpation	lt. ACBDE	9×9	t ₄ n ₂ m ₀	IV	scirrhous	+	ER(-)PgR(*)	B _r +A _x +M _j +M _n
		Self palpation	rt. ABCDE	7×7	t ₂ n ₂ m ₀	III	scirrhous	+	ER(+)PgR(*)	B _r +A _x +M _j +M _n
No.2	68	Self palpation	lt. ACBDE	24×23	t ₃ n ₄ m ₀	IV	scirrhous	+	ER(*)PgR(*)	B _r +A _x +M _j +M _n +P _s +S _c
		Self palpation	rt. DBACE	14×19	t ₃ n ₃ m ₀	IV	scirrhous	+	ER(*)PgR(*)	B _r +A _x +M _j +M _n

* : not tested

B_r : resection of breast

A_x : dissection of axillary lymph node

M_j : resection of major pectoral muscle

M_n : resection of minor pectoral muscle

P_s : dissection of parasternal lymph node

S_c : dissection of supraclavicular lymph node

Table 2. Cases of metachronous bilateral primary breast cancer

	Age	Interval of 1st and 2nd ca.	Detection	Region	Size(cm)	tnm	stage	Histological type	Intraductal component	Hormone receptor	Treatment	Remarks
No.1	38	2Y6M	self palpation	rt.A	3.5×4.0	t ₂ n ₀ m ₀	I	papillotubular	+	ER(*)PgR(*)	B _r +A _x +M _j +M _n +P _s	no signs of recurrence
	40		self palpation	lt.C	2.0×2.0	t ₁ n ₀ m ₀	I	papillotubular	+	ER(-)PgR(-)	B _r +A _x +M _j +M _n	
No.2	51	4Y6M	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	no signs of recurrence
	55		self palpation	rt.C	1.5×1.0	t ₁ n ₀ m ₀	I	solid-tubular	+	ER(*)PgR(*)	B _r +A _x +M _j +M _n +P _s +S _c	
No.3	29	29Y	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	unknown	no signs of recurrence
	58		self palpation	rt.BADEC	12×14	t ₄ n ₀ m ₀	IV	solid-tubular	+	ER(*)PgR(*)	B _r +A _x +M _j +M _s +P _s +S _c + resection of chest wall	
No.4	44	1Y2M	self palpation	rt.B	2.9×2.1	t ₁ n ₁ m ₀	IV	scirrhous	+	ER(*)PgR(*)	B _r +A _x +M _j +M _n +P _s +S _c + resection of chest wall	recurrence of rt. axillary lymph node 10 M later after 1st operation
	45		self palpation	lt.B	1.5×1.0	t ₁ n ₀ m ₀	I	papillotubular	+	ER(*)PgR(*)	B _r +A _x +M _n	
No.5	67	12Y	erosion of nipple	lt.ECA	2.7×1.5	t ₂ n ₀ m ₀	I	Paget's disease	+	ER(*)PgR(*)	B _r +A _x +M _j +M _n	no signs of recurrence
	79		self palpation	rt.C	3.0×2.6	t ₂ n ₁ m ₀	III	papillotubular	+	ER(*)PgR(*)	B _r +A _x	

* : not tested B_r : resection of breast
A_x : dissection of axillary lymph node
M_j : resection of major pectoral muscle
M_n : resection of minor pectoral muscle
P_s : dissection of parasternal lymph node
S_c : dissection of supraclavicular lymph node

Table 3. Cases of metastatic breast cancer

	Age	Interval of 1st and 2nd ca.	Detection	Region	Size(cm)	tnm	stage	Histological type	Intraductal component	Hormone receptor	Treatment	Remarks
No.1	63	4Y7M	self palpation	rt.A	7.0×4.0	t ₃ n ₁ m ₀	III	scirrhous	+	ER(+)PgR(-)	B _r +A _x +M _j +M _n +P _s	recurrence of local and rt. cervical lymph node 4Y7M later after first operation
	68		self palpation	lt.A	3.0×2.0	t ₂	-	papillotubular	-	ER(*)PgR(-)	biopsy	
No.2	58	10M	self palpation	rt.CD	5.0×7.0	t ₃ n ₂ m ₀	III	scirrhous	+	ER(-)PgR(-)	B _r +A _x +M _j +M _n +P _s	recurrence of local, rt. supraclavicular lymph node and lt. axillary lymph node 7M later after first operation
	59		self palpation	lt.C	4.0×4.0	t ₂	-	scirrhous	-	ER(*)PgR(*)	biopsy	

* : not tested B_r : resection of breast
A_x : dissection of axillary lymph node
M_j : resection of major pectoral muscle
M_n : resection of minor pectoral muscle
P_s : dissection of parasternal lymph node

mary breast cancer were beyond n₂ stage¹⁾ bilaterally. Of 5 patients with metachronous primary breast cancer, 2 had uninvolved lymph nodes at the second cancer.

⑨ *tnm staging*¹⁾

Of 2 patients with synchronous primary breast cancer, 3 of the 4 tumors were stage IV. Of 5 patients with meta-

chronous primary breast cancer, 3 were stage I at the second cancer. Of 3 patients with metachronous primary breast cancer, whose pathological specimens from both breast were available, 2 were of the same or lower stage at the second cancer compared to the first. 2 patients with metastatic breast cancer were stage III.

⑩ Treatment (Operation)

All cases of synchronous and metachronous primary breast cancer underwent either one of the following operations, 1) standard radical mastectomy 2) modified radical mastectomy 3) extended radical mastectomy for the second cancer. All cases of metastatic breast cancer underwent only tumor-ectomy without lymph node dissection for the second cancer.

⑪ Hormone receptors

Only one case of synchronous primary breast cancer was evaluated for estrogen receptors on both tumors. Estrogen receptor was positive in the right and negative in the left breast tumor.

Discussion

When a second cancer is detected in the other breast, either synchronously or metachronously, there is always the question of whether this cancer is a primary or a metastatic tumor. There is no general agreement on how this distinction is made. Haagensen³⁾, stating only from a clinical viewpoint that it was a new primary cancer, when there was no evidence of local spread of the cancer in the first breast across the midline of the chest to the second breast. But this definition is too vague. Hojyo et al⁴⁾ added pathological criteria: the cancer in the second breast was a new primary if it was non-invasive and/or had a distinctly different histology or em-

bryological origin from the first and/or if there were no recurrence after curative resection for first cancer and no distant metastasis was detected shortly after operation for the second cancer. Some early breast cancer may give rise to distant metastasis shortly after resection. So if this should happen at the discovery of the second primary cancer, the later would be mistakenly regarded as a metastatic cancer. Similarly, if a second primary cancer should be discovered with distant metastasis, which had arisen from the second primary, it would be mistakenly regarded as a metastatic cancer. Robinson and Berg⁵⁾ noted that metastases was not associated with contiguous in situ cancer, as was often the case with primary tumors. Kasumi⁶⁾ also felt that if the second cancer had intraductal components, it was a new primary. This definition is simple at first, but when intraductal components are not seen on histological slides, it does not mean that the tumor is a metastatic cancer. There is the possibility that an intraductal component may exist in a small section of the tumor, so many samples must be examined. It is sometimes uncertain if the cancer had invaded the basement membrane on Hematoxyline-Eosin stains. Additional special stains, such as type IV collagen stain, which stains the basement membrane⁷⁾ are needed. Based on the above, we established a set of criteria, mainly from histology, placing importance on the pres-

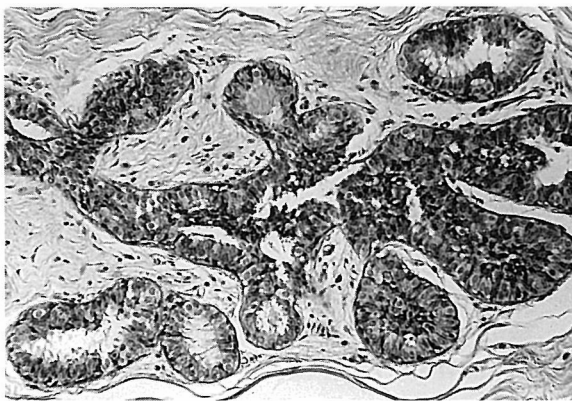


Fig.1 Intraductal component of primary breast cancer (H&E, original magnification X100).

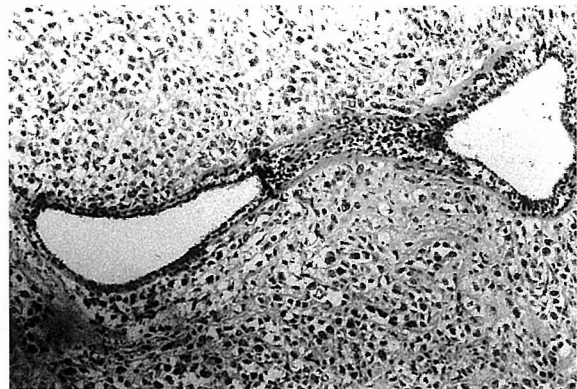


Fig.2 Histological appearance of metastatic breast cancer. The basement membrane of normal cells of mammary gland is not invaded by cancer cells (H&E, original magnification X100)

ence of intraductal component, and clinically. Although two cases did not have intraductal component in maximum cut surface, they were diagnosed as metastatic cancer without examining samples from another part of the tumors because of recurrence after the first operation.

A collective review by Nabeya et al⁸⁾ revealed an overall incidence of bilateral breast cancer of 3.33% among 83478 cases with 0.85% being synchronous primary cancer, 1.99% metachronous primary cancer and 0.49% metastatic cancer from the opposite breast. Since the criteria for classifying the second cancer varies with each department, the incidental rates are not comparable, but the total incidence is comparable. Total incidence in our series is 5.8%, which is higher than in Nabeya's review⁸⁾. The metachronous second cancer were discovered by patient's self palpation and in four cases, they were detected at a smaller size than the first tumor. This shows that patients take an interest in their breast cancer. They presented to our department at the second cancer as there were good relationships between the patients and our department. Kasumi⁹⁾ reported that the annual incidence of contralateral breast cancer after mastectomy as 4‰ and the incidence of breast cancer among Japanese women was as low as one-sixth that of Americans. However the rate of bilateral breast cancer is high and is almost similar to that in the USA. Regular follow up, including examination of the opposite breast by self examination, examination by trained physicians and mammographic surveillance must be established in all breast cancer patients. If there are suspicious physical or radiographic findings, biopsy should be performed. If it is a primary breast cancer, it should be treated by radical operation. If it is metastatic cancer, it might be better treated with chemo-endocrine therapy; regarding it as a systemic disease. All of our patients with a second primary breast cancer underwent either one of the following operations 1) standard radical mastectomy 2) modified radical mastectomy 3) extended radical mastectomy. Presently, in our department the mode of surgery had swung away from stan-

dard or extended radical mastectomy to modified radical mastectomy. On the other hand, all patients with metastatic cancer underwent only tumorectomy without lymph node dissection and received chemo-endocrine therapy. In metachronous cases, estrogen receptor status of the second cancer may be considerably influenced by adjuvant tamoxifen therapy for the first cancer⁹⁾. In our series estrogen receptor status of metachronous breast cancers was not examined.

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