

Chemotherapy for Breast Cancer –Current Topics-

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Chemotherapy for breast cancer has been showing remarked progress, and preoperative chemotherapy for locally advanced breast cancer has also been widely performed. The advantages of preoperative chemotherapy are 1) being able to evaluate the effect of chemotherapy objectively by measuring how to reduce the size of tumor and 2) expanding the possibility of breast-conserving surgery.

Recently, there have been many reports of the relevance of breast cancer clinicopathological features to the outcome of chemotherapy. In this reports, topics regarding chemotherapy for breast cancer will be addressed, introducing recent reports and providing data on preoperative chemotherapy for breast cancer in Juntendo University Nerima Hospital.

1. How the histological features are related to sensitivity to chemotherapy in breast cancer?

This topic has been the focus of many studies. Some reports have shown that the histological features of breast cancer, such as high-grade, basal-like or HER2 subtypes, negativity for hormone receptors and localized tumor (so-called solid-tubular carcinoma categorized in the General Rules for Clinical and Pathological Recording of Breast Cancer of the Japanese Breast Cancer Society), were significantly associated with sensitivity to chemotherapy.

In Juntendo University Nerima Hospital, 175 cases of breast cancer underwent preoperative chemotherapy. These cases were categorized into three groups: sensitive, partial response and non-sensitive by their sensitivity to chemotherapy. In sensitive cases, those with pCR (disappearance of all invasive cancer of the primary breast tumor) and almost pCR (few remnants of markedly degenerated tumor cells) were included. On the other hand, if the tumor showed little degeneration, with the disappearance of less than one third of tumor cells, the case was assessed as non-sensitive. In 175 cases, sensitive, partial response and non-sensitive cases were 45 (25.7%), 67 (38.3%), and 63 (36%), respectively. The distribution of cases is summarized in Table 1. In sensitive cases, the rates of HER2 or basal-like subtype, high-grade tumor and hormone receptor negativity tended to be higher than in partial response or

non-sensitive cases, as in other literature.

Table 1. Relation between histopathological features and sensitivity to chemotherapy in breast cancer

		sensitive	partial sensitive	non sensitive	total
subtypes					
	luminal A	13	45	45	103(58.9%)
	luminal B	8	5	1	14(8.0%)
	HER2	12	10	8	30(17.1%)
	basal-like	12	7	9	28(16.0%)
	total	45	67	63	175
histological grade					
	I	0	8	13	21(12%)
	II	21	38	25	84(48%)
	III	23	14	22	59(33.7%)
	ILC	1	5	0	6(3.4%)
	other type	0	2	3	5(2.9%)
	total	45	67	63	175

2. Which histological features are different between sensitive and non-sensitive cases in high-grade breast cancers?

From the point of view of histological grade, low-grade carcinoma (grade I) tended to be non-sensitive to chemotherapy. On the other hand, it seemed that high-grade carcinoma (grade III) was one of the histological features of chemo-sensitive carcinoma; however, some cases of high-grade carcinoma were less sensitive to chemotherapy. Some reports have documented that high-grade carcinoma has a poor prognosis if pathologically complete remission is not achieved after chemotherapy.

So which histological features influence chemo-sensitivity in high-grade breast cancers? In this hospital, there were 59 cases of high-grade carcinoma. Twenty-three cases were chemo-sensitive carcinoma and 22 cases were non-sensitive among them. Which histological features are different between sensitive and non-sensitive cases of high-grade breast cancers? In non-sensitive carcinoma, these seemed to be more cases of hormone receptor-positive carcinoma and carcinoma with necrosis. In particular, necrosis seemed to be a very important histological feature for predicting sensitivity to chemotherapy. In this hospital, there were 19 cases of carcinoma with necrosis, of which 13 cases were non-sensitive carcinoma and had a

poor prognosis. To assess the correlation between necrosis and sensitivity to chemotherapy, further studies will be needed.

3. How should the surgical margins be decided in post-chemotherapy cases of breast cancer? Should total mastectomy or breast-conserving surgery be chosen in each post-chemotherapy case?

It is difficult for surgeons to decide the operative procedure for post-chemotherapy cases of breast cancer because how the tumor cells respond to chemotherapy differs greatly in each case. If the breast cancer shows a good response to chemotherapy, the tumor should be shrinking; however, there are some cases in which residual tumor cells show spottily and the size remains unchanged, and other case include an intraductal lesion in the tumor and only ductal carcinoma in situ remains after chemotherapy.

So, should total mastectomy or breast-conserving surgery be chosen in each post-chemotherapy case?

Among the 175 cases in this hospital, breast-conserving surgery and mastectomy were performed in 73 and 102 cases, respectively. The rate of breast conservation was 41.7%; however, 14 of 73 cases (19.2%) were margin positive. The histological features of margin-positive cases are summarized in Table 2.

Table 2. Histological features of margin-positive cases after chemotherapy

case	age	Histology					
		type	¹⁾ subtype	²⁾ ductal component	response	sensitivity to chemotherapy	positive component
1	53	IDC	scirrhou	++	multiple	non-sensitive	DCIS
2	49	IDC	solid	+	stable	non-sensitive	DCIS
3	39	ILC		-	spotty	non-sensitive	ILC
4	43	mucinous		++	stable	non-sensitive	DCIS
5	41	IDC	papillotubular	-	shrink	non-sensitive	³⁾ ly
6	53	IDC	papillotubular	+	multiple	non-sensitive	DCIS
7	37	IDC	papillotubular	++	stable	non-sensitive	DCIS
8	39	IDC	papillotubular	+	stable	non-sensitive	DCIS
9	60	IDC	papillotubular	-	multiple	non-sensitive	IDC
10	52	IDC	solid	-	shrink	non-sensitive	ly
11	47	mucinous		++	stable	partial response	DCIS
12	61	IDC	papillotubular	+	spotty	partial response	DCIS
13	60	IDC	scirrhou	+	spotty	partial response	DCIS/IDC
14	51	IDC	solid	++	shrink	partial response	DCIS

1) Categorized in the General Rules for Clinical and Pathological Recording of Breast Cancer of the Japanese Breast Cancer Society. 2) -: no, +: including ductal component, ++: predominantly ductal component. 3) Cancer cells were positive in lympho-vessels of margins.

The age of the 175 cases ranged from 28 to 80 years (median 55 years). In margin-positive cases, the patients tended to be younger (37 to 61 years, median 50 years). In 10 cases, the lesions of ductal carcinoma in situ were positive in the surgical margins. In such cases, the ductal component predominantly included mixed and invasive carcinoma. As described in other reports, the benefit of breast-conserving surgery after chemotherapy is questionable in invasive lobular carcinoma.