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THE CLINICAL COURSE AND TREATMENT RESULTS OF LUNG METASTASES FROM BREAST CANCER

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Objective: To analyze the clinical course and treatment result of lung metastases from breast cancer. Method: 122 cases with lung metastases from breast cancer were treated with chemotherapy or chemotherapy plus endocrine therapy, response was assessed according to WHO criteria and survival rate estimated using the life Table. Results: The median time from initial treatment of primary tumor to lung metastases was 22 months. Sites of common consecutive metastases were lung, liver and bone. The overall response rate was 48% with a CR rate of 15%. Compared to non- DDP- encompassing regimen, the CR rate was higher in DDP-based chemotherapy (7% versus 21%, $P<0.05$) with a longer median survival time (MST). The PR rate was higher in regimens containing anthracycline (48%) than in those without anthracycline (20%, $P<0.01$). The response rate was similar between chemotherapy and chemotherapy plus endocrine therapy ($P>0.05$). No difference in MST was observed between patients receiving anthracycline-and non-anthracycline-encompassing regimens. The 1-, 3-, 5-, and 10-year survival rate was 77%, 22%, 11%, and 10%, respectively. Conclusion: Size of primary tumor, the length of disease-free interval, the number of lung metastases may provide additional information for predicting patients survival after treatment of lung metastases. Combination chemotherapy, especially DDP-based chemotherapy may prolong survival time of patients with lung metastases from breast cancer.

Key words: Breast neoplasms, Lung neoplasms/secondary, Lung neoplasms/drug therapy, Lymphatic metastases,

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Survival rate

Approximately 30% of patients with breast cancer have recurrence of disease and metastases within 5 years after operation on primary tumor, with a relatively higher incidence of 12%~18% occurred in lung. From June 1982 to June 1994, 122 patients with lung metastases from breast cancer were treated by chemotherapy with or without endocrine therapy in our hospital. We reported the results as follows.

MATERIALS AND METHODS

General Data

122 patients were all females, with a median age of 46.4 (24~71) years. All primary breast tumors were diagnosed pathologically or cytologically and lung metastases were documented by chest X-ray, CT or MRI. In terms of primary tumors, radical or modified radical mastectomy were performed in 110 cases, simple mastectomy with radiotherapy in 8 cases, lumpectomy and untreated in 2 cases, respectively.

Treatment and Response

86 patients were treated with chemotherapy alone and 36 patients with chemotherapy plus endocrine therapy. Of them, 68 and 54 patients were given DDP (CTX+ADM+DDP or DDP+CTX+5-FU) and non-DDP (CTX+ADM+5-FU) containing regimens, respectively. 56 and 66 patients were given

anthracycline (ADM or MIT) and non-anthracycline containing regimen combination chemotherapy, respectively. Response was assessed according to WHO criteria and survival time estimated using life table. For each patient, menstrual status, initial and adjuvant treatment, lymph node status, length of interval from initial treatment to and number of lung metastases, duration and sites of consecutive metastases, modality and efficacy of first line therapy on recurrence disease were all reviewed in order to determine the relationship between above-mentioned prognostic and survival.

RESULTS

Characteristics of Lung Metastases And Consecutive Metastases

Metastases were documented by routine staging or chest X-ray examination during follow-up in 103 patients (84%), and by chest X-ray due to symptoms of cough, dyspnea and chest pain in 19 patients (16%), 3 patients (2. 4%) had concomitant lung metastases at diagnosis of primary breast cancer. The median time from initial therapy of primary tumor to lung metastases was 22 months (0~196), with single lesion in 39 (32%) patients and multiple lesions in 83 (68%) patients, 55 patients (45%) had initial recurrences in lung. Of them, 30 patients had consecutive metastases. The most common sites of consecutive metastases were lung, liver and bone. The median time of consecutive metastases in lung, liver and bone was 10.5 (2~32), 15.0 (2~25) and 6.0 (1~24) months, respectively. 67 patients (55%) had simultaneous recurrences in other sites.

Treatment Results for Lung Metastases

The overall response rate was 48% with a CR rate of 15%. The response rate of different regimens are listed in Table 1.

Table 1. Response rate for lung metastases from breast cancer

Regimens	Number of patients	CR (%)	PR(%)	S (%)	P (%)	CR+PR(%)
DDP-containing	68	14 (21)	20 (29)	26 (38)	8 (12)	34 (50)
Non-DDP Containing	54	4 (7)	20 (37)	16 (30)	14 (26)	24 (44)
P value		<0.05	>0.05	>0.05	>0.05	>0.05
Anthracycline -containing	56	5 (9)	27 (48)	19 (34)	5 (9)	32 (57)
Non-anthracycline-containing	66	13 (20)	13 (20)	23 (35)	17 (25)	26 (39)
P value		>0.05	<0.001	>0.05	<0.05	<0.05
Chemotherapy alone	86	14 (16)	31 (36)	29 (34)	12 (14)	44 (52)
Chemotherapy plus endocrine	36	4 (11)	9 (25)	13 (36)	10 (28)	13 (36)
P value		>0.05	>0.05	>0.05	<0.05	>0.05

Prognostic Factors Related to Survival

As listed in Table 2, patients who acquired CR had better survival than those achieved PR, so did patients with PR or SD when compared to those with PD ($P<0.05$, for all). Median survival time (MST) was similar between patients with PR and SD. Compared to non-DDP -encompassing regimens, a longer MST

Table 2. Median survival time from first lung metastases and prognostic factors related to survival

Factors	Number of patients	Median survival (month)
Response		
CR	18	39
PR	40	20
SD	42	21
PD	22	11
Regimens		
(1)DDP-containing (including 6 Carboplatin-containing)	68	22
Non-DDP-containing	54	18
(2)High-dose DDP (50mg/m^2 x 2 or 60mg/m^2)	27	22
standard dose DDP (20~50mg/day)	35	20
(3)Anthracycline-containing	56	19
non-anthracycline-containing	66	20
(4)chemotherapy alone	86	22
Chemotherapy plus endocrine	36	16
Lymph node metastases		
	45	21
yes	77	18
Size of primary tumor		
<2cm	38	24
2~5cm	72	17
>5cm	12	13
Adjuvant chemotherapy (>6 cycles)		
no	50	21
yes	72	19
Adjuvant endocrine therapy		
no	107	19
yes	15	21
Adjuvant radiotherapy		
no	50	21
yes	72	19
Disease-free interval (month)		
>60	21	26
24~60	36	23
12~24	32	20
<12	33	12
Menopausal status at lung metastases		
Premenopause	69	18
Postmenopause	53	21
Age at lung metastases		
<50	73	18
>50	49	20
Number of lung metastases		
Single	39	22
Multiple	83	18
Lung metastases alone	55	22
Lung metastases concomitant with other sites	67	17

was observed in DDP-based combination chemotherapy. No difference in MST was observed between patients receiving anthracycline-and non-anthracycline-encompassing regimens. However, MST was longer in patients receiving chemotherapy than chemotherapy plus endocrine therapy. The size of primary tumor (<2 cm or >5 cm), the length of disease-free interval (<12 months or >12 months), number of lung metastases, and lung metastases with or without involvement of outside of lung may provide information for predicting patient's survival. 1- year, 2- year, 3- year, 5- year and 10- year survival rate in this study was 77%, 40%, 22%, 11% and 10% respectively.

DISCUSSION

Although articles on bone metastases from breast cancer are frequently reported, less attention has been paid to studying lung metastases. In a study by Schlappack of 44 patients with breast cancer, the median time from initial treatment of primary tumor to lung was 18 months, and 56% of those patients had consecutive metastases at a mean time of 4 months which more likely involved bone (25%), liver (17%) and chest wall (17%). In our study, the median time from initial therapy to lung metastases was 22 months and the consecutive metastases mainly occurred in lung. The delayed recurrence of disease in this study may be due to the result of efficacious treatment. The results suggest that consecutive metastases in lung was the main cause of treatment failure.

Our study showed a higher overall response rate of 48% than that (34%) reported by Schalppack. The fact that DDP-containing and anthracycline-containing regimens resulted in higher response rate than non-DDP- containing and non-anthracyline-containing regimens is consistent with the results of our previous study that DDP and CBP exerted better efficacy in the treatment of lung metastases from breast cancer. It has been well known that tamoxifen is not the preferred treatment for women who have rapidly growing diseases, like lung metastases and massive liver involvement. Our study offered an additional information that combination treatment of chemotherapy with endocrine therapy did not increase response rate.

The significant correlation of response rate with median survival in our study suggest that the improvement of CR rate by using actively effective therapy is the key to prolong survival time of the patients. Compared to non-DDP-containing regimen, the longer MST in DDP-containing regimens probably attributed to its higher CR rate.

There are different views on the potential prognostic factors for correlation with recurrent breast cancer. Howell pointed out that axillary lymph node status and tumor size were predictors of recurrence, but neither influenced the length of survival after relapse. Clark considered that ER status, size of primary tumor at diagnosis, axillary lymph node status, adjuvant chemotherapy and radiotherapy, length of disease-free interval correlated with tumor recurrence and patient's survival, whereas adjuvant endocrine therapy, menstrual status have no relation to survival. Schlappack concluded that, instead of axillary nodal and menstrual status, ER status and the length of disease-free interval influenced greatly on survival. Our results revealed that except for size of primary tumor, the length of disease-free interval, number of lung metastases, and lung metastases with concomitant involvement of outside of lung other factors investigated in this study have no correlation with patient's survival.

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