Factors Affecting Survival in Patients With Lung Cancer and Brain Metastasis

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Abstract

To determine the factors affecting prognosis in lung cancer patients with synchronous or metachronous brain metastasis, 103 lung cancer patients (6 female, 97 male; mean age 52.75±8.87 years) with brain metastases were examined prospectively with regard to differences in survival.

Histopathology of the tumor, performance status (PS), sex, localization of tumor, localization of metastases, time period between diagnosis and brain metastases, presence of distant metastases, presence of lung symptoms during brain metastases, and treatment modality of the brain metastases were evaluated with regard to survival period. Kaplan-Meier, Cox-regression tests were used in the statistical analyses.

Sixty two patients (60.2%) were diagnosed as small-cell lung cancer and 41 (39.8%) as non-small-cell lung cancer (NSCLC). Median survival after brain metastases was 3 months (95% confidence interval [CI], 2 to 4). The brain metastasis was diagnosed at the same time as the lung cancer in 29 patients (28.2%) and at a later date in 74 (71.8%). Brain metastases synchronous with lung cancer and a better PS score were found to be parameters significantly correlated with a better survival (wald x2= 8.707, p= 0.003; wald x2=20.809, p= 0.000; respectively). Survival was also significantly longer in patients with SCLC (wald x2=4.255, p= 0.039). The findings indicate that PS of the patient, histopathology of the tumor, and the time period between the diagnosis of the lung cancer and that of the brain metastases are all factors affecting survival.

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Keywords: *lung cancer, brain metastasis, survival, synchronous tumor, metachronous tumor*

Introduction

Development of brain metastases is a devastating event in lung cancer patients and appears in approximately 30% of patients with non-small-cell lung cancer (NSCLC) before death (1). Nearly one half of the patients with brain metastases have solitary lesions on computed tomography (CT) scan. When these lesions are symptomatic the median survival without therapy is limited to 1 month (2). Even in patients treated with radiotherapy (RT) and/or chemotherapy (ChT), the median survival has been reported to be approximately 6 months (3). For patients with a single brain metastasis, surgical resection followed by whole brain radiation therapy was associated with increase in survival from 6 months to 10 months (4). In this study we aimed to investigate the survival rate of lung cancer patients with either synchronous or metachronous brain metastases.

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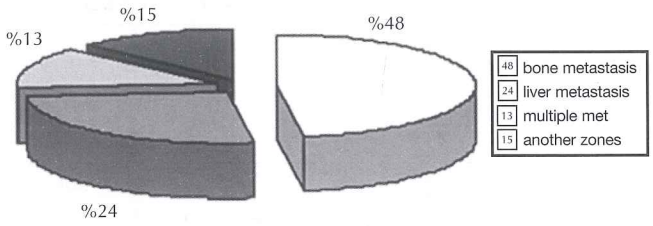
Materials and Methods

We examined lung cancer patients with brain metastases who were diagnosed and treated at SSK Sureyyapasa Chest and Cardiovascular Diseases Hospital from December 1997 through December 1999. Follow-up from the time of lung cancer diagnosis until the time of death was obtained in 103 cases (6 female, 97 male; mean age 52.75±8.87, range 42-71). Patients who were unavailable for follow-up were excluded from the study. Fiberoptic bronchoscopy (FOB) and transthoracic needle aspiration were generally used to diagnose endobronchial tumors and peripheral mass lesions respectively. In patients with palpable supraclavicular and axillary lymph nodes, surgical extirpation was performed. Computerized tomography was used for distant metastases detection. For the treatment of limited SCLC and stage IIIB NSCLC patients ChT and RT combination was chosen. In disseminated disease ChT alone was given. Radical RT was used for patients who had inoperable tumors. The diagnosis of brain metastases was confirmed by CT in symptomatic patients. Performance status (PS) was evaluated according to the Eastern Cooperative Oncology Group (ECOG) criteria. Treatment modalities for brain metastases were RT, ChT+RT, and symptomatic treatment according to the patients' PS. Brain metastases diagnosed within 3 months of lung cancer diagnosis were accepted as synchronous, and those diagnosed ≥3 months after lung cancer were accepted as metachronous brain metastases. Histopathology of the tumor, PS, sex, localization of the tumor, localization of the metastases, the time period between diagnosis and detection of brain metastases, presence of distant metastases, presence of lung symptoms during brain metastases, treatment modality of the brain metastases were recorded for each patient. These factors were evaluated with regard to survival. Survival was estimated from the date of diagnosis to death of patient. SPSS software was used for the statistical analyses. All parameters listed above were evaluated with the Cox-regression test. A P value of < 0.05 was considered as statistically significant. Survival from the date of diagnosis of lung cancer was estimated using the Kaplan-Meier method.

Results

The characteristics of the 103 patients included in the study and comparison of the findings between them are shown in Table 1. Lung cancer diagnosis was achieved by fiberoptic bronchoscopy in 72 patients (69.9%), by transthoracic needle aspiration in 20 (19.4%), by lymphadenomegaly extirpation in 10 (9.7%), and by sputum cytology in one patient. The brain metastasis was diagnosed at the same time as the lung cancer in 29 (28.2%) patients while in 74 (71.8%), it was diagnosed later (after a median period of 3 months). Distant metastases other than brain detected at the time of the initial diagnosis are shown in Figure 1. There was no statistically significant difference in survival of patients with or without



Another zones: supraglandular metastasis, vertebral metastasis, and esophageal metastasis

Figure 1. *Distant metastases other than brain.*

metastases other than brain. In 34 (33%) patients, the distant metastases developed after the diagnosis and there were no significant survival differences between this group and the remaining patients. The median duration of time from presentation of brain metastases to death was 3 months (95% CI, 2 to 4). Maximum survival was 16 months (in 1 patient). Possibility for 1 month survival was found as 88.35%, 2 months as 65.05%, 3 months as 47.57%, 4 months 39.81%, 5 months 35.92%, 6 months 26.21%. There were no statistically significant differences between survival rates of patient groups who had received RT alone, ChT+RT, and symptomatic treatment alone. Sex, localization of tumor, localization of metastases, and presence of lung symptoms during brain metastases were not correlated with significant differences in survival. Patients with solitary brain metastases tended to have longer survival than patients with multiple metastases but the difference was not statistically significant. The most effective factor for survival was PS. Presence of brain metastases during initial diagnosis was another factor affecting survival (Figure 2). Survival was significantly longer in patients with good PS and brain metastases synchronous with lung

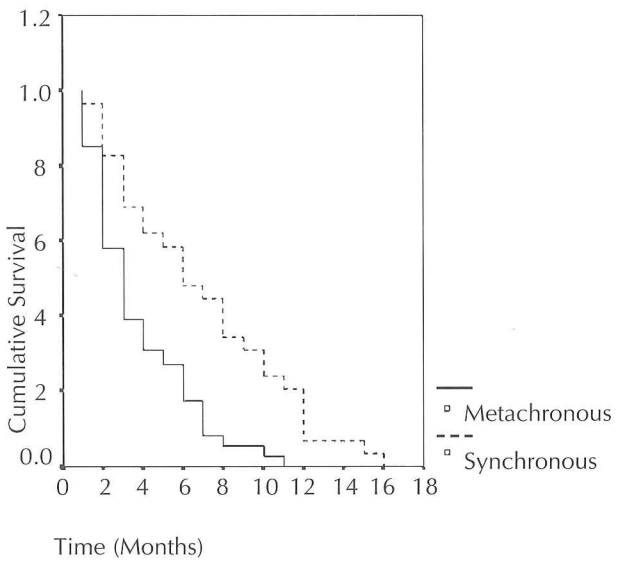


Figure 2. *Survival curves of patients with synchronous and metachronous brain metastases.*

Table 1. Survival data with respect to patient characteristics

Characteristics	Groups	n(%)	Median survival (months)	Range of survival (months)	p
Age (years) and survival (months)	≥53	48 (46)	3	1-16	0.681
	<53	55 (53.4)	4	1-15	
Sex	female	6 (5.8)	3.5	2-5	0.608
	male	97 (94.2)	3	1-16	
Tumor localization	RUL	23 (22.3)	3	1-11	0.187
	RLL	15 (14.6)	3	1-12	
	RML	15 (14.6)	4	1-15	
	LUL	29 (58.2)	4	1-16	
	LLL	12 (11.5)	3.5	1-10	
	LS	9 (8.7)	3	1-8	
PS	0	6 (5.8)	8.5	4-12	0.00
	1	29 (28.2)	6	1-16	
	2	38 (36.9)	3	1-12	
	3	28 (37.2)	2	1-7	
	4	2 (1.9)	1.5	1-2	
Neurologic complications*	headachee	40 (38.8)	3	1-16	0.084
	epilepsy	17 (18.3)	6	1-12	
	Hemiparesis	14 (13.6)	2	1-6	
	hemiplegia	10 (9.7)	3	2-15	
Cranial CT findings**	sing. ST	24 (23.3)	5.5	1-16	0.283
	multip. ST	21 (20.4)	3	1-12	
	multiple	47 (45.6)	3	1-15	
	multip. IT	6 (5.8)	3	1-4	
	sing. IT	5 (4.9)	6	2-10	

RUL: Right upper lobe; RLL: Right lower lobe; RML: Right middle lobe; LUL: Left upper lobe; LLL: Left lower lobe; LS: Lingular segment.

* Ten complaints were analyzed statistically; data pertaining to common complaints are given in the table.

** ST: Supratentorial, IT: Infratentorial

cancer (p=0.000 and p=0.003, respectively). Sixty two patients (60.2%) were diagnosed as small-cell lung cancer (SCLC), 41 (39.8%) were non-small-cell lung cancer (NSCLC). Histopathology was found to be related significantly with survival in these patient groups (p=0.039).

Discussion

Dissemination of lung cancer to the brain carries a poor prognosis. It has been shown in many clinical trials that the primary factor affecting survival in patients with brain metastases was the performance status of the patients (5-9). Our results were in agreement with these reports. In our study, patients whose PS scores were 0 and 1 survived significantly longer than patients with PS scored greater than 1. We also found that brain metastases synchronous with lung cancer were significantly associated with a better survival than brain metastases which developed subsequent to the lung cancer. This finding does not agree with the report by Abrahams et al who found that patients with metachronous brain metastases had longer survival compared with patients with synchronous brain metastases (5).

However, it must be noted that the cases in this previous study consisted of NSCLC patients only, where as our study included both SCLC and NSCLC patients. In some studies no significant difference was found in survival between patients with synchronous and metachronous onset of the metastases (10-12). Burt et al, in their review of 185 patients who had undergone craniotomy for resection of brain metastases from NSCLC also found no survival differences between patients with metachronous vs synchronous presentation (13). As shown in Table 1, in our study, patients with single brain metastases appeared to have longer survival than patients with multiple metastases, this difference was not statistically significant. Vecht et al reported similar results (5). However, there are some reports indicating that patients with solitary brain metastases live significantly longer than patients with multiple brain metastases (14,15). It has also been shown that bilateral metastases are indicative of a poor prognosis (6). In this paper survival was determined significantly longer in SCLC patients than NSCLC patients. It is probably due to delayed diagnosis in NSCLC patients who already have disseminated disease and radiosensitivity of SCLC as opposed to NSCLC.

As a conclusion; PS of the patient, histopathology of tumor, and time period between lung cancer diagnosis and brain metastases were found as the factors affecting survival in our patient groups.

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