

Bull Yamaguchi Med Sch 40(3-4) : 1993

Computed Tomography Findings of Small Cell Lung Cancer

— Relative to the Therapeutic Response —

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(Received June 15, revised July 30 1993)

Abstract We studied the CT findings in 37 cases of small cell lung cancer, relative to the therapeutic response. After 2 or 3 courses of chemotherapy, subjects were classified into two groups, whose reduction rates were over 70% (Group I), and those under 70% (Group II). The survival period of the cases in Group I was significantly prolonged compared with that in Group II. In Group I, the foci tended to be central and the margin of lesion was relatively regular. Most of the cases had accompanying secondary peripheral change, especially atelectasis was frequently observed. By contrast, in Group II, the margin of lesion was irregular and the degree of irregularity tended to be severe compared with that in Group I. It was suggested that the response to therapy could be predictable based on the CT findings in small cell lung cancer and that we should select the adequate therapy on each case.

Key Words : Small cell lung cancer, Computed tomography, Therapeutic response

Introduction

Small cell lung cancer (SCLC) grows rapidly and disseminates from an early stage, differing from the other histologic types of lung cancer. However, it is highly responsive to not only radiation therapy but also chemotherapy. Recent developments in chemotherapy have helped improve patient survival, but the proportion of long-term disease-free survivors has not increased¹⁾. To increase the number of long-term disease-free survivors, it is necessary to perform adequate therapy, the response to which can be predicted before therapy. In this study, we retrospectively investigated the relationship between thor-

acic computed tomography (CT) findings and the response to chemotherapy, and prognosis of SCLC.

Materials and Methods

Thirty seven patients with histologically or cytologically proved SCLC, which had been treated by chemotherapy (with or without chest irradiation), were evaluated with thoracic CT between January 1986 and March 1993.

The therapeutic effects were evaluated by CT before and after 2 or 3 courses of chemotherapy, according to the General Rule for Clinical and Pathological Record of Lung Cancer²⁾. They were divided into two groups, those whose reduc-

tion rates were over 70% (Group I), and those under 70% (Group II), and we examined the CT findings before therapy in each group.

The CT findings were reviewed for the following findings: (1) central type or peripheral type; (2) irregularity of margin; (3) density of the primary lesions (post contrast enhancement, superiority of low density or soft tissue density); (4) secondary peripheral change; (5) thickening of bronchovascular bundle; (6) density of lymph nodes; (7) pleural effusion, daughter nodules and emphysematous change.

The main type of chemotherapy used was combination chemotherapy, usually COMP-VAN, PVP, CBDCA-VP, CAV (Table 1), and the dose was decided by each doctor for each patient. There was no difference in chemotherapeutic regimen between the two groups. And there was no difference in sex, age, clinical stage, performance status between the two groups (Table 2).

Furthermore, we analyzed the difference in prognosis between them. The survival curves were determined using the Kaplan-Meier method and statistical comparisons were made using the generalized Wilcoxon test.

For the CT scanning TCT-900S (Toshiba) and

Somatom DR3 (Siemens) were used, and in some cases contrast enhancement and high-resolution CT were also performed.

Results

1. Therapeutic effects and survival periods

(Fig. 1)

The survival period of the cases in Group I was significantly prolonged compared with that in Group II ($p < 0.05$). The median survival time was 10 months in Group I (LD: 28 months, ED: 6.75 months) and 6.5 months in Group II (LD: 8.5 months, ED: 6.5 months), and the difference between two groups was

Table 2. Patient characteristics (N=37).

	Group I (N=19)	II (N=18)
Sex Male/Female	14/5	15/3
Mean Age	63.8	65.6
in Years (Range)	(45~78)	(51~78)
LD/ED	11/8	10/8
PS		
0	3	2
1	12	12
2	3	3
3	1	0
4	0	1
Chemotherapeutic Regimen		
COMP-VAN	4	4
PVP (or CBDCA-VP)	8	8
CAV-PVP (same above)	6	5
others	1	1

LD: limited disease, ED: extensive disease, PS: performance status

Table 1. Chemotherapeutic regimen

COMP-VAN alternating			
a) COMP			
CPA	270 mg/m ²		dl-5
VCR	1.4mg/m ²		dl
MTX	6.5mg/m ²		dl-5
PCZ	65 mg/m ²		dl-5
b) VAN			
VP-16	140 mg/m ²		d29-32
ADM	40 mg/m ²		d29
ACNU	40 mg/m ²		d29
PVP (CBDCA-VP)			
CDDP	80 mg/m ²		dl
(CBDCA	300 mg/m ²		dl)
VP-16	120 mg/m ²		dl,2,3
CAV			
CPA	800 mg/m ²		dl
ADR	50 mg/m ²		dl
VCR	1.4mg/m ²		dl

CPA: Cyclophosphamide, VCR: Vincristine, MTX: Methotrexate, PCZ: Procarbazine, VP-16: Etoposide, ADR: Adriamycin, ACNU: Nimustine, CDDP: Cisplatin, CBDCA: Carboplatin

Fig. 1. Survival curves of small cell lung cancer patients treated with chemotherapy according to the response.

more significant in the LD cases.

2. Therapeutic effects and CT findings
(Table 3)

1) Primary lesion

In Group I, 16 cases belonged to the central type and 3 belonged to the peripheral type, whereas in Group II, 8 cases belonged to the central type and 10 belonged to the peripheral type.

The margins were irregular in all cases in Group II and the degree of irregularity was

severe. By contrast, in Group I, 5 cases were smooth and the degree of irregularity tended to be mild compared with that in Group II.

The density was heterogenous in most of the cases. Post contrast enhancement, low density area was superior in many cases.

Secondary peripheral changes were recognized in 30 of the 37 cases, especially frequently in Group I. In Group I, 18 of the 19 cases showed changes, and atelectasis was frequently observed, in 7 of them. By con-

Table 3. CT findings of 37 cases.

	Group I			Group II		
	LD 11	ED 8	Total	LD 10	ED 8	Total
1. Primary tumor						
a) Location						
central/peripheral	9/2	7/1	16/3	5/5	3/5	8/10
b) Margin						
irregularity						
-	5	0	5	0	0	0
±	1	2	3	0	3	3
+	4	4	8	6	1	7
++	1	2	3	4	4	8
notch				2		
+						
spicula						
+	1					
c) Density						
homogenous/heterogenous						
plain CT	3/4	1/2	4/6	2/4	0/5	2/9
CE-CT*	2/8	1/7	3/15	2/7	1/6	3/13
low density >	4	4	8	4	5	9
soft tissue density >	4	2	6	3	0	3
mixed	0	1	1	0	1	1
mixed high density area	2	1		1		
calcification		1		1		
cavity		1				
d) Peripheral secondary change						
+/-	10/1	8/0	18/1	7/3	5/3	12/6
increased density	7	4	11	6	4	10
atelectasis	3	4	7	0	1	1
mass lesion	0	0	0	1	0	1
e) Thickening of Broncho-vascular bundle						
+/-	4/7	5/3	9/10	5/5	3/5	8/10
2. Lymph nodes**						
low density	6	4	10	4	5	9
soft tissue density	3	2	5	3	2	5
mixed	1	2	3	3	0	3
(ring enhancement +)	2	3	5	1	1	2)
3. Others						
pleural effusion	3	1	4	3	2	5
emphysematous change	5	1	6	5	3	8
daughter nodules	0	6	6	4	2	6

* Contrast enhancement was not performed in 3 cases.

** Each one case in both groups had no lymph nodes swelling.

trast, only 1 case had accompanying atelectasis in Group II.

The frequency of thickening of broncho-vascular bundle was similar in the two groups.

2) Lymph nodes

Low, soft tissue density and mixed density lymph nodes were observed, and they revealed almost the same distribution in both groups.

3) Others

The frequency of pleural effusion, daughter nodules and emphysematous change showed no significant differences between the two groups. However, daughter nodules were often observed in ED in Group I, and in LD in Group II.

Case 1

A 67-year-old female complained of facial edema. The patient was diagnosed by trans-bronchial biopsy (PS 1, LD, Stage III B). The reduction rate after 2 courses of chemotherapy was 94.3%.

Chest CT revealed a slightly heterogenous mass with a relatively smooth margin, which was accompanied by atelectasis in the right upper lobe (Fig. 2a). There were multiple swollen mediastinal lymph nodes (Fig. 2b).

After 2 courses of chemotherapy, the mass, atelectasis and swollen mediastinal lymph nodes almost disappeared (Fig. 3ab).

After 3 courses of chemotherapy and chest irradiation were performed, this patient

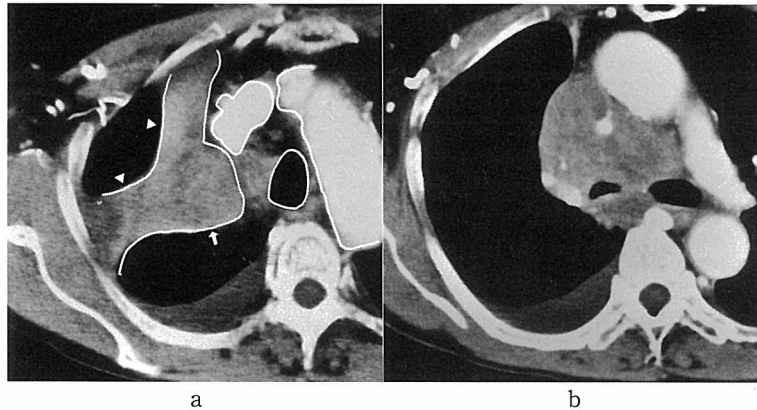


Fig. 2a. Chest CT shows a slightly heterogenous mass with a relatively smooth margin (†), which is accompanied by atelectasis (▽).

Fig. 2b. There are multiple swollen mediastinal lymph nodes.



Fig. 3ab. After 2 courses of chemotherapy, the mass, atelectasis and swollen mediastinal lymph nodes almost disappear.

attained a complete response, and she is alive now after 15 months.

This case is included in Group I.

Case 2

A 63-year-old male with a dry cough diagnosed by transbronchial biopsy (PS 1, LD, Stage IV). The reduction rate after 3 courses of chemotherapy was 56.5%.

Chest CT revealed a heterogenous mass with an irregular margin (Fig. 4a), and it had multiple daughter nodules (Fig. 4b). Although the mass had accompanying increased density of peripheral lung field, no

atelectasis was observed (Fig. 4b).

After 3 courses of chemotherapy, although the mass and daughter nodules decreased, there were residual masses (Fig. 5ab).

Seven courses of chemotherapy and chest irradiation were performed, but this patient died 10 months after diagnosis.

This case is included in Group II.

Discussion

Many prognostic factors for SCLC have already been reported³⁾⁻⁵⁾. Although there is controversy, performance status, clinical

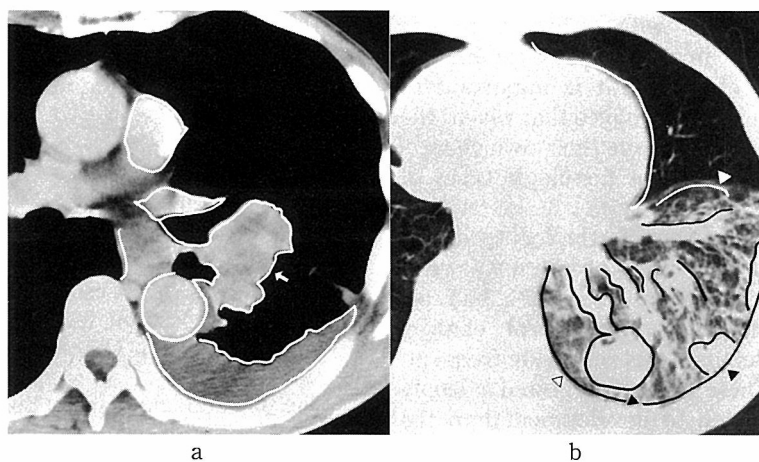


Fig. 4a. Chest CT shows a heterogenous mass with an irregular margin (†).
Fig. 4b. The mass has multiple daughter nodules (▼). Although the mass is accompanied by an increased density of peripheral lung field (▽), no atelectasis is observed.

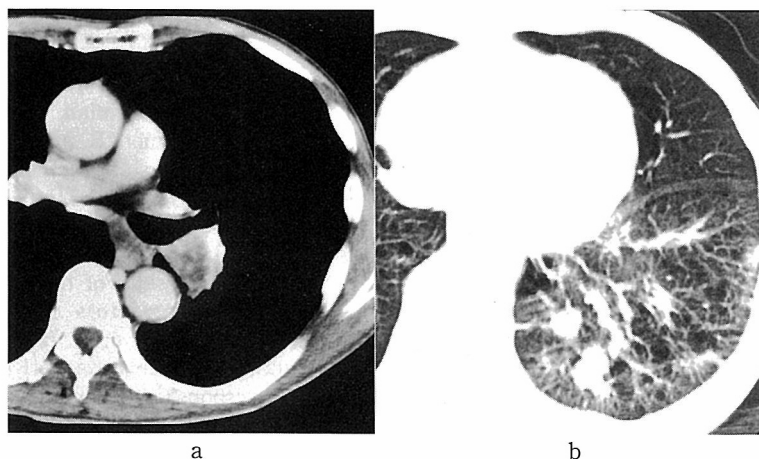


Fig. 5ab. After 3 courses of chemotherapy. Although the mass and daughter nodules decrease, there are residual masses.

stage, and therapeutic response are factors to be considered to have influenced survival in general. Our study on the relationship between therapeutic response and prognosis revealed that the survival rate in Group I was significantly prolonged compared with that in Group II. Then we suggest that if the therapeutic response could be predicted based on the images, the prognosis also could be predicted; moreover it would become possible to select adequate therapy to increase the number of long-time survivors.

Since SCLC shows intratumoral heterogeneity, the whole tumor should be examined. However, as SCLC is rarely resected compared with other histologic types, it is often impossible to examine the whole tumor. Therefore, it is important to evaluate the tumor by images that reveal the whole tumor and that have their own characteristics according to the histologic types of lung cancer.

In our study, in Group I, the foci tended to be central and the margin of lesion was relatively regular. Most of the cases had accompanying secondary peripheral change, especially atelectasis was relatively frequently observed. These images suggested a deeply infiltrating fashion of development into the tissue out of the bronchial wall through the submucosal layer forming a solitary tumor mass⁶⁾, resembling that of squamous cell carcinoma. Therefore, these cases may contain the components of squamous cell carcinoma which shows a better prognosis⁷⁾.

By contrast, in Group II, there were some cases of peripheral type and the margin of lesion was irregular and the degree of irregularity tended to be severe. A few cases had a notch sign. Although many cases had an accompanying increased density of lung field, atelectasis was rarely observed. These findings are not in contradiction to the images of large cell carcinoma⁸⁾, and these cases may include large cell components that bring about a poorer response to chemotherapy⁹⁾.

In other findings, the cases which had daughter nodules showed a relatively poor response even in the LD cases.

Some findings were obtained in the study of CT findings relative to the therapeutic response. Because the median survival time is

significantly prolonged in the LD cases in Group I, the number of long-term disease-free survivors may be increased by performing intensive therapy in the LD cases which have CT findings resembling those of the cases in Group I. On the contrary, since the cases which showed CT findings resembling those of the cases in Group II might have a poorer response, the use of different drugs or combined irradiation therapy earlier, may be necessary to improve patient survival.

In this study, since the number of cases is small, these findings may not be applied to all cases. However, it is important to predict the therapeutic response from the images before therapy, to choose the most appropriate method of therapy. This study is being continued to increase the number of cases.

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