ANTICANCER RESEARCH *24*: 2097-2100 (2004)

Ten-year Disease-free Survival of a Small Cell Lung Cancer Patient with Brain Metastasis Treated with Chemoradiotherapy

YUZURU NIIBE[1,2], KATSUYUKI KARASAWA[1] and KAZUSHIGE HAYAKAWA[2]

[1]Departments of Radiology and Radiation Oncology, Tokyo Metropolitan Komagome Hospital, 3-18-22, Honkomagome, Bunkyo-ku, Tokyo 113-8677; [2]Department of Radiology, Kitasato University School of Medicine, 1-15-1, Kitasato, Sagamihara, Kanagawa 228-8555, Japan

Abstract. *We report the first case of 10-year disease-free survival in a patient with small cell lung cancer (SCLC) with brain metastasis. A 63-year-old man was found to have SCLC with brain metastasis and underwent chemoradiotherapy. Radiation therapy was delivered to the brain, lungs, mediastinum and supraclavicular fossa. Chemotherapy regimen mainly consisted of etoposide-plus-cisplatin. The patient has remained alive for more than 10 years after the diagnosis of SCLC with brain metastasis with no relapses.*

Chemoradiotherapy has recently improved the treatment results of limited-stage small cell lung cancer (LD-SCLC). Turrisi *et al.* reported that the 5-year overall survival rate of patients with LD-SCLC was 26% (1). On the other hand, patients with extensive-disease small cell lung cancer (ED-SCLC) can not survive for a long time. The most promising treatment, iriontecan-plus-cisplatin (IP), has increased the survival time of patients with ED-SCLC more than treatment with etoposide-plus-cisplatin (EP). However, the median survival time of patients with ED-SCLC treated with IP was 12.8 months and their 2-year survival rate was 19.5%; these results are much inferior to the results of patients with LD-SCLC (2). The prognosis of cases of SCLC with only brain metastasis was considered to be better than that of other ED-SCLC cases. Ruby *et al.* reported that the median survival time of patients with SCLC with only brain metastasis was 14 months (3). However, only a few cases have been reported of patients with SCLC with brain metastasis surviving more than 5 years (3, 4). No cases have been reported of patients with LD-SCLC with brain metastases achieving a 10-year survival.

We report the first case of 10-year disease-free survival of a patient with SCLC with brain metastasis treated by chemoradiotherapy.

Correspondence to: Yuzuru Niibe, MD, PhD, Department of Radiology, Kitasato University School of Medicine, 1-15-1, Kitasato, Sagamihara 228-8555, Japan. Tel: +81-42-778-8111, Fax: +81-42-778-9436, e-mail: joe-n@hkg.odn.ne.jp

Key Words: Small cell lung cancer, brain metastasis, radiation therapy, chemotherapy.

Case Report

A 63-year-old man had experienced cough and bloody sputum since July 1993. In September 1993, a mass was palpable on the left side of his neck. His symptoms gradually worsened. He was admitted to the regional hospital and an abnormal shadow in the left lung was found on the chest radiograph. He was introduced to the Tokyo Metropolitan Komagome Hospital, Japan, for further detailed examinations; small cell lung cancer (SCLC) was diagnosed from a biopsy sample obtained by broncho-fiberscopy. Computed tomography of the chest and abdomen and magnetic resonance imaging of the brain were performed; a large tumor was found in the left lung and a small enhanced lesion, indicative of metastasis, was found in his pons (Figures 1 and 2). Thus, the clinical stages were extensive disease (ED) and stage IV (cT2N3M1) according to the UICC-TNM classification. At the time of SCLC diagnosis, the patient's levels of tumor markers for squamous cell carcinoma related antigen (SCC) and serum carcinoembryonic antigen (CEA) were within the normal ranges. However, the level of neuron-specific enolase (NSE) was elevated to 11.8. The patient underwent external irradiation of the entire brain from December 27, 1993 to January 31, 1994, receiving a total dose of 46 Gy. Chemotherapy using cisplatin and etoposide was administered in two cycles between December 12, 1993 and Feburuary 12, 1994. Chest radiographs demonstrated that

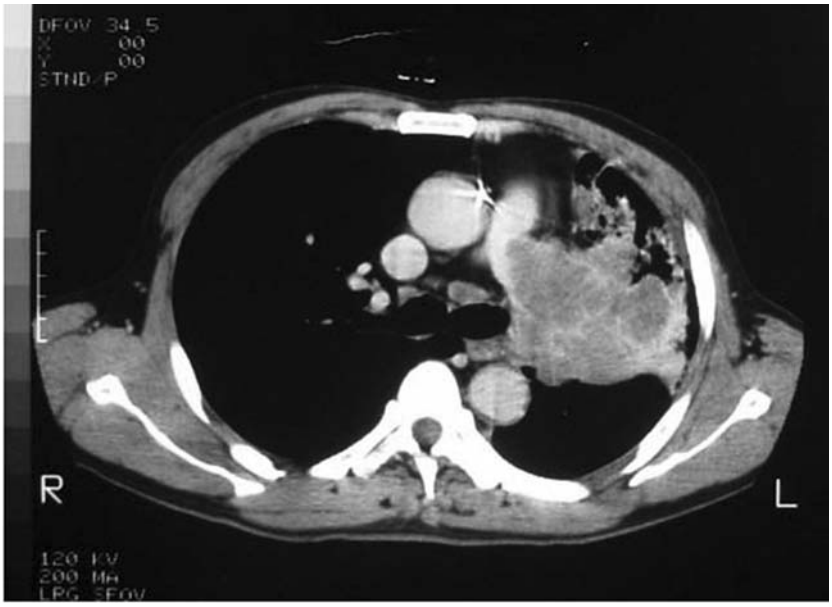

Figure 1. *Computed tomography results of the chest before treatment (mediastinum window). A huge mass was found in the left lung and a small nodule was found in the mediastinum.*

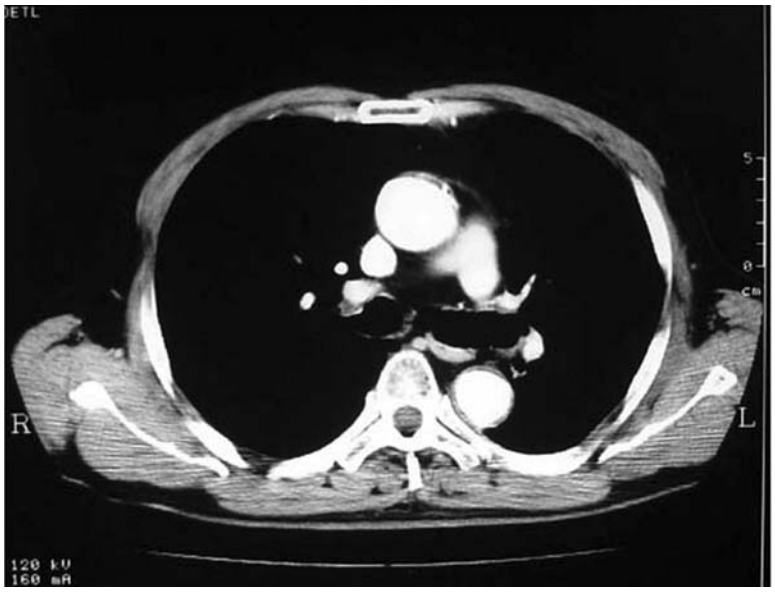

Figure 2. *Computed tomography results of the chest after treatment (mediastinum window). The huge mass had nearly disappeared after chemoradiotherapy.*

the tumor in the left lung had shrunk and decreased in size more than 50%. External irradiation of the lung tumor, mediastinum and supraclavicular fossa was administered from March 15, 1994 to April 22, 1994 (a total dose of 56 Gy, with the cord off after 40 Gy) and 14 Gy of boost irradiation was delivered to the pons lesion (field size, 4 x 5 cm). Concurrent chemotherapy was performed using etoposide and PSK (a protein bound polysaccharide K) as an immunopotentiating biological response modifier. After this treatment, the tumor in the left lung had almost disappeared (Figure 3) and the tumor in the pons completely disappeared (Figure 4). The tumor marker of NSE decreased to 3.8, within the normal range. More than 10 years after the diagnosis of small cell lung cancer with brain metastasis has been made, the patient remained alive without relapse of the disease.

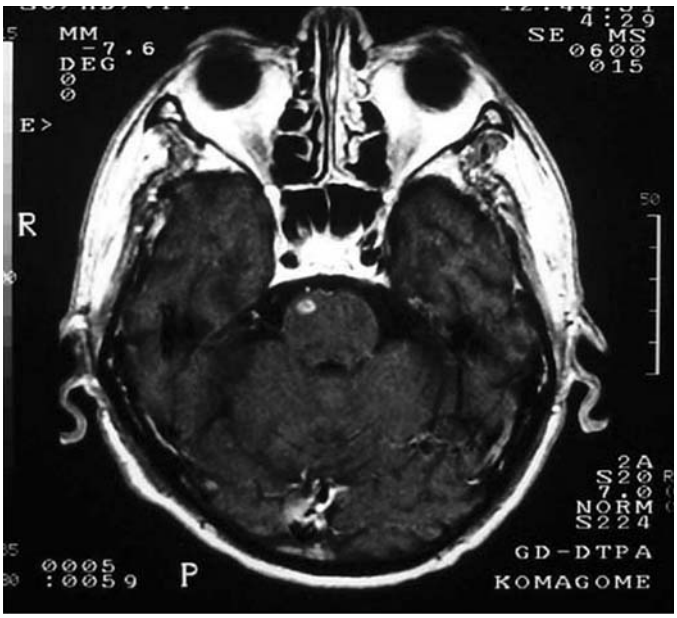

Figure 3. *Computed tomography results of the chest after treatment (mediastinum window). The huge mass had nearly disappeared after chemoradiotherapy.*

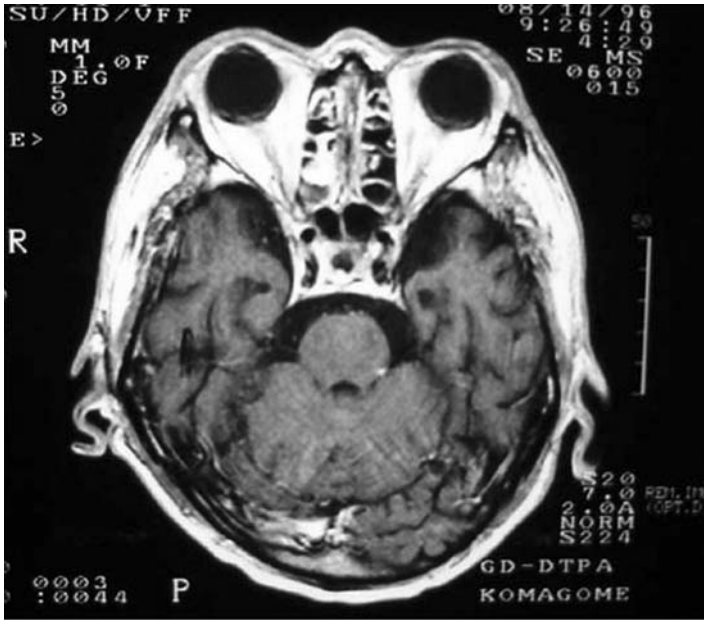

Figure 4. *Enhanced MRI results of the brain before treatment. A small enhanced lesion was found in the pons.*

Discussion

Small cell lung cancer (SCLC) was reported to comprise about 20% of all lung cancers (5). Of these, about 10% had brain metastases at the time of SCLC diagnosis (6). The prognosis for cases of SCLC with only brain metastases was considered to be superior to those of other ED-SCLC cases. Noda *et al.* reported that the best treatment outcome of ED-SCLC resulted in a median survival time of 12.8 months. The treatment regimen of this study was irinotecan-plus-cisplatin (IP), which meant using a new drug (irinotecan) produced in Japan (2). On the other hand, the median survival time in cases of SCLC with only brain metastasis was reported to be 14.0 months, although these patients were treated with a regimen consisting mainly of cisplatin, etoposide and

cyclophosphamide, which meant it did not include any new drugs (3). Noda *et al.* reported that treatment with etoposide-plus-cisplatin (EP) achieved 9.4 months of median survival in patients with ED-SCLC (2). These findings suggest that treatment of cases of SCLC with only brain metastasis has a relatively better prognosis than treatment of other ED-SCLC cases.

The patient in the current case underwent chemo-radiotherapy to treat SCLC with brain metastasis. The chemoradiotherapy regimen was EP because IP was not recognized as the standard regimen for the treatment of ED-SCLC at the time of his diagnosis. The reason for his long survival is obscure. However, Furuta *et al.* pointed out that some types of SCLC progress slowly and suggested that these should be distinguished from the common type of SCLC (7). SCLC with only brain metastasis might have different biological features from other kinds of ED-SCLC. Moreover, in most SCLC with only brain metastasis, the radiation fields are able to cover all detected tumors. Thus, these patients may be good candidates for appropriate brain and thoracic irradiation combined with chemotherapy if their medical condition and performance status permit aggressive treatment.

In any event, this still appears to be the first demonstration of 10-year disease-free survival of SCLC with brain metastasis after successful treatment.

References

1 Turrisi AT 3rd, Kim K, Blum R, Sauce WT, Livingston RB, Komaki A, Wagner H, Aisner S and Johnson DH: Twice-daily compared with once-daily thoracic radiotherapy in limited small-cell lung cancer treated concurrently with cisplatin and etoposide. N Engl J Med *340*: 265-271, 1999.

2 Noda K, Nishiwaki Y, Kawahara M, Negoro S, Sugiura T, Yokoyama A, Fukuoka M, Mori K, Watanabe K, Tamura T, Yamamoto S, SaijoN and Japan Clinical Oncology Group: Irinotecan plus cisplatin compared with etoposide plus cisplatin for extensive small-cell lung cancer. N Engl J Med *346*: 85-91, 2002.

3 Kochhar R, Frytak S and Shaw EG: Survival of patients with extensive small-cell lung cancer who have only brain metastases at initial diagnosis. Am J Clin Oncol *20*: 125-127, 1997.

4 Imai R, Hayakawa K, Sakurai H, Nakayama Y, Mitsuhashi N and Niibe H: Small cell lung cancer with a brain metastasis controlled for 5 years: a case report. Jpn J Clin Oncol *31*: 116-118, 2001.

5 Hoffman PC, Mauer AM and Vokes EE: Lung cancer. Lancet *355*: 479-485, 2000.

6 Newman SJ and Hassen HH: Frequency, diagnosis, and treatment of brain metastases in 247 consecutive patients with bronchogenic carcinoma. Cancer *33*: 492-496, 2000.

7 Furuta M, Hayakawa K, Kato S, Mitsuhashi N, Nakajima T and Niibe H: Malignant neuroendocrine tumor presenting a huge mediastinal mass controlled with radiation therapy. Lung Cancer *22*: 55-58, 1998.

Received February 24, 2004
Accepted April 21, 2004