A Case of Long-term Survival with Stage IV Small Cell Lung Cancer and Early-stage Central-type Squamous Cell Lung Cancer Treated by Photodynamic Therapy

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The present report is on a 67-year-old man with stage IV small cell lung cancer and early-stage centrally located squamous cell cancer of the lung. He was diagnosed as small cell lung cancer with multiple metastasis to the ipsilateral lung and was found to have a central-type early-stage squamous cell cancer by bronchoscope. After obtaining a complete response to the small cell lung cancer with chemotherapy and radiotherapy, photodynamic therapy was applied to the squamous cell carcinoma, resulting in complete disappearance of the tumor. Recurrence of small cell cancer occurred at the ipsilateral lung and this patient died of small cell cancer 8 years after initiation of treatment. Post mortem examination confirmed complete disappearance of squamous cell cancer treated by photodynamic therapy. This is a rare case of long-term survival with stage IV small cell lung cancer and early-stage central-type squamous cell lung cancer successfully treated by photodynamic therapy.

Key words: small cell lung cancer – long-term survival – photodynamic therapy

INTRODUCTION

Long-term survivors with small cell lung cancer (SCLC) and roentgenographically occult lung cancer are known to have a high risk of development of second primary cancer (1,2). It has been reported that the risk of non-small cell lung cancer (NSCLC) and aerodigestive cancer in patients who survived SCLC increased more than sixfold from 2% per patient per year during 2–4 years to 12.6 and 14.4%, respectively, after more than 10 years (3). In roentgenographically occult lung cancer, mainly early-stage central-type squamous cell lung cancer, the risk of secondary primary lung cancer is at a rate of ~5% per year (1). Synchronous multiple primary cancer has also been reported (4). Because no standard option for the management of synchronous cancers exists, it is important to evaluate a case with multiple primary cancer who received treatment. Here, we report a patient with stage IV small cell lung cancer and early-stage centrally located squamous cell cancer of the lung who survived 8 years.

CASE REPORT

A 67-year-old man presented with an abnormal chest roentgenogram from a routine examination in August 1987. He had a smoking history of 50 pack-years and a history of hypertension. Radiography of the chest showed a huge mass on right middle lobe and multiple pulmonary nodule on the right lung (Fig. 1a and 1b). Transcutaneous needle biopsy was performed and pathologic examination confirmed the presence of a small cell carcinoma (Fig. 2). Bronchoscopy revealed thickening of the spur between the lingular and upper division bronchus of the left lung (Fig. 3). Transbronchial biopsy showed squamous cell cancer (Fig. 4). A CT of the head and abdomen and bone scintigraphy and bone marrow aspiration cytology were normal. He was diagnosed as having stage IV small cell lung cancer with ipsilateral pulmonary metastasis and stage I squamous cell lung cancer. Serum NSE of the patient was 9 ng/ml (normal range <10 ng/ml). Because the small cell cancer was confined to one hemithorax, the patient was thought to have limited disease. Chemotherapy with cisplatin, etoposide and Adriamycin was initiated in September 1987. Marked reductions of the primary tumor and pulmonary meta-
Figure 1. Chest roentgenogram (a) and chest CT (b) in August 1987, showing middle lobe mass and multiple right intrapulmonary metastasis.

Figure 2. Specimen obtained by percutaneous fine needle biopsy from right middle lobe mass, interpreted as small cell carcinoma. (Hematoxylin-eosin; original magnification, ×100.)

Figure 3. Bronchoscopic appearance of the spur between lingular and upper division bronchus of the left lung, showing thickening of the spur.

sis were obtained. During the second cycle of chemotherapy, 40 Gy of thoracic radiotherapy was administered concurrently with cisplatin and etoposide. Two cycles of chemotherapy with cisplatin, etoposide and doxorubicin were added after completion of the concurrent chemoradiotherapy. Complete response was obtained to small cell lung cancer with four cycles of chemotherapy combined with thoracic radiotherapy. Bronchoscopy after the treatment showed the presence of squamous cell cancer of the left bronchus. Photodynamic therapy (PDT) was performed on the lesion in January 1988. A 2 mg/kg dose of photofrin II was administered intravenously 48 h before light irradiation using an argon dye laser. Complete disappearance of the tumor was confirmed cytologically by subsequent bronchoscopic examinations. In September 1990, recurrence of small cell carcinoma at the ipsilateral lung occurred. He responded to the second line chemotherapy with weekly administration of cisplatin, etoposide,
vindesine, cyclophosphamide and doxorubicin. He died of SCLC on November 11, 1995, 8 years after initiation of treatment.

At autopsy, SCLC involved right lung and pleura, with metastasis to liver, abdominal and cervical lymph nodes. However, no tumor of squamous cell cancer treated by PDT was found. Immunohistochemical stain of SCLC was positive to p53 (Dako A/S, Denmark) and bcl-2 (Dako A/S). The labeling index of proliferating cell nuclear antigen (PCNA) was 22%. The mean labeling index of PCNA in 19 patients with SCLC treated in our institution was 48.5% (T. Kawaguchi, unpublished data).

**DISCUSSION**

In staging of SCLC, a simple two-stage system developed by the Veteran’s Administration Lung Cancer Study Group has been employed (5). This system classifies patients as having limited disease (LD) when the tumor is confined to one hemithorax and its regional lymph nodes, including the ipsilateral mediastinal, ipsilateral supraclavicular and contralateral hilar nodes. Tumors that present with ipsilateral pleural effusion, left laryngeal nerve involvement or superior vena cava obstruction are considered LD. According to the revised TNM staging (6), a patient with ipsilateral pulmonary metastasis is classified as stage IV. However, the same patient is considered as LD because the tumor is confined to one hemithorax. Hence the present case would be considered LD or stage IV.

For treatment of SCLC, combination chemotherapy has been the cornerstone of management (7). Meta-analyses of studies which evaluated the role of thoracic irradiation for LD-SCLC showed a modest improvement in survival with addition of thoracic irradiation (8). An analysis of treatment factors contributing to long-term survival revealed that concurrent chemotherapy and radiotherapy achieved better local control than sequential therapy (9). In the 1980s, pilot studies of concurrent irradiation and chemotherapy using cisplatin and etoposide (PE) showed excellent survival and acceptable toxicities (10–12). These results were confirmed by multi-institutional phase III studies (13,14). At present, early administration of concurrent irradiation and PE is one of the standard treatments for LD-SCLC. The present case was not a candidate for a clinical trial for SCLC because of the synchronous multiple cancers. After the first course of chemotherapy, a marked reduction of the primary tumor and pulmonary metastasis was achieved. In the second cycle of chemotherapy, we treated the patient with concurrent PE and irradiation. After the first recurrence of SCLC in the ipsilateral lung, he survived more than 6 years. The present case showed a low labeling index of PCNA of 22%. It has been reported that positive staining of PCNA was significantly associated with overall survival in patients with lung cancer (15). Hence the relatively long survival time of the patient may be explained in part by the low labeling index of PCNA.

Photodynamic therapy (PDT) is a newly developed local therapeutic modality that has been shown to result in complete response and cure in centrally located early-stage lung cancer (4,16,17). An excellent result of 97.8% complete response has been reported for the treatment of tumors with limited longitudinal extent (≤ 1 cm) in a prospective phase II trial of PDT (18). The present case achieved a complete response to the centrally located squamous cell lung cancer with PDT. Complete disappearance of the tumor was confirmed by the post mortem examination 7 years and 10 months after PDT. Hence it is reasonable to consider that the present case appears to have been cured by PDT.
No standard principles or recommendations were available for the management of synchronous multiple cancers. It will be important to make a decision based on a profound understanding of the natural history of each cancer, effects and sequela of treatment modalities.

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References