A case of small cell lung cancer treated with chemoradiotherapy followed by photodynamic therapy

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ABSTRACT

Here, we present the case of a 51-year-old man with limited-stage small cell lung cancer (LS-SCLC) who received concurrent chemoradiotherapy and photodynamic therapy (PDT). The patient was diagnosed as having LS-SCLC with an endobronchial mass in the left main bronchus. Following concurrent chemoradiotherapy, a mass remaining in the left lingular division was treated with PDT. Clinical and histological data indicate that the patient has remained in complete response for 2 years without further treatment. This patient represents a rare case of complete response in LS-SCLC treated with PDT.

Currently, patients with small cell lung cancer (SCLC) are treated with chemotherapy with or without thoracic radiotherapy. Radiation therapy is generally accepted as an essential component of limited-stage SCLC (LS-SCLC). However, the local failure rate after chemotherapy and radiotherapy remains high, ranging from 30% to 70%.[1] More effective means are needed to decrease the local recurrence rate.

Endobronchial photodynamic therapy (PDT) is used to treat patients who have central-type lung cancer, with the objective of palliation in advanced cases and curative intent in patients with early-stage disease.[2 3] Furukawa *et al* reported that PDT resulted in a complete response (CR) rate of 92.8% in patients with lesions of <1.0 cm; recurrences after a CR were seen in 9 of 77 lesions (11.7%) <1.0 cm.[4] When the extent of the tumour and the depth of the bronchogenic carcinoma have been evaluated, PDT can be an effective local treatment modality.[4]

A few studies have described the treatment of SCLC using PDT. Moghissi *et al*[5] reported that 10 of 100 patients with advanced SCLC underwent PDT for palliation. Kato *et al*[6] and Okunaka *et al*[7] evaluated the effectiveness of PDT in the treatment of early-stage SCLC. However, none of these studies detailed a single case of SCLC treated with PDT.

Here, we present a case in which PDT was used with curative intent in a patient having endobronchial cancer, following standard treatment for SCLC and in addition to concurrent chemotherapy and radiotherapy.

CASE REPORT

A 51-year-old man presented to our clinic with a 6-month history of worsening dyspnoea on exertion. His symptoms included a nearly constant dry cough, diminished appetite without weight loss, and fatigue. He had previously been diagnosed as having diabetes mellitus with an uncontrolled glucose level and hypertension. The patient was a smoker with a ⩾40 pack-per-year history. The Eastern Cooperative Oncology Group performance status was grade 1.

The patient had undergone testing at an outside facility because of his symptoms; a plain chest *x* ray revealed opacity in the left lung field (fig 1A). As a result, the patient was diagnosed with pneumonia and treated with antibiotics. Despite antibiotic treatment, the resolution of pneumonic consolidation was delayed. Thus, the patient was referred to our hospital. Chest CT revealed an endobronchial protruding mass in the distal left main bronchus (LMB) with a near total collapse of the left lung and a small granuloma in the posterior segment of the right upper lobe (fig 1B). No evidence of mediastinal nodal disease or a metastatic focus was detected. Bronchoscopic examination showed functional vocal cords and a pedunculated mass in the LMB (fig 1C). Bronchoscopic washing and biopsies failed to demonstrate a specific cell type. A rigid bronchoscopic biopsy was performed, and the pathological examination confirmed the presence of small cell carcinoma based on immunostaining for CD56, synaptophysin, chromogranin and leucocyte common antigen (LCA) using the initial paraffin-embedded biopsy specimen. The results were consistent with SCLC. CT of the brain was normal. Therefore, the patient was diagnosed with LS-SCLC.

Chemotherapy with cisplatin and irinotecan was initiated, but the chemotherapeutic regimen was changed to cisplatin and etoposide (EP) after one cycle due to grade 4 diarrhoea. Concurrent with the second and third cycles of EP, the total dose of thoracic radiation therapy was 45.6 Gy in 38 fractions (120 cGy per fraction). Treatment was given twice daily, at least 6 h apart, on weekdays. Thoracic radiation therapy was delivered with 6–10 MV photons using custom-made blocks. With re-expansion of the lung on plain chest *x* ray (fig 1D), the patient's dyspnoea was found to be greatly improved. Post-treatment chest CT showed that the endobronchial protruding mass in the distal LMB was noticeably smaller, with a residual small soft tissue nodule in the left upper lobe (fig 1E). Bronchoscopy revealed a pedunculated mass in the orifice of the lingular division (fig 1F). To evaluate the size of the tumour and identify any unknown synchronous cancer, autofluorescence bronchoscopy was performed. We applied PDT to remove the remaining tumour completely, because high dose rate brachytherapy and stereotactic radiation

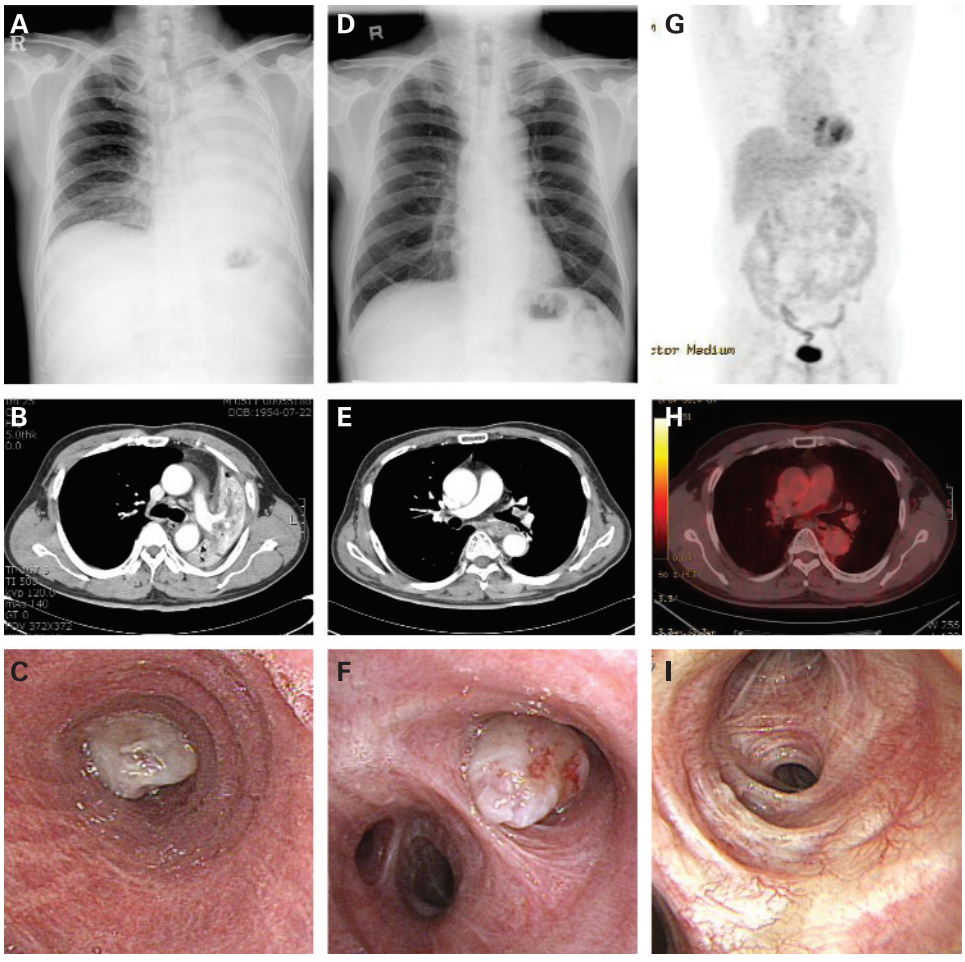

Figure 1 Summary from the initial diagnostic investigation to last follow-up (A–C) Initial diagnostic investigation on June 2006. (D–F) Response evaluation after chemoradiotherapy in October 2006. (G and H) Positron emission tomography (PET)–CT without increased glucose uptake in October 2007. (I) There is no evidence of recurrence in December 2008.

techniques were not available in our hospital. The remaining tumour was treated with PDT after wire basket removal of the pedunculated mass via flexible bronchoscopy. A 2.5 mg/kg dose of haematoporphyrin derivate (Photogem, Moscow Institute of High Chemical Technologies, Russia) was administered intravenously 48 h before irradiation. Using a diode laser (wavelength = 630 nm; Biolitec, Jena, Germany), a light with a 3 cm cylindrical diffuser was introduced through the working channel of an autofluorescence fibreoptic bronchoscope. Illumination was carried out in the left second carina and orifice of the lingular division. The light dose was 100 J/cm. Bronchoscopy followed PDT for debridement and detection of PDT-related complications. No immediate complications occurred.

The complete disappearance of the tumour was confirmed pathologically by subsequent bronchoscopic biopsy and radiologically by chest CT after 4 weeks. No evidence of recurrence was observed from October 2006 to December 2008. One year after PDT, combined positron emission tomography (PET) and CT revealed no metabolic evidence of recurrence. Two years after PDT, chest CT and bronchoscopy demonstrated a complete response in this patient (fig 1G,H). The patient refused prophylactic cranial irradiation.

DISCUSSION

PDT as a local therapeutic modality often results in a CR of centrally located early-stage lung cancer. Kato *et al*[3] reported that PDT resulted in a CR in about 94% of patients with centrally located early lung cancer (squamous cell type) with a limited longitudinal extent (<1 cm). Moghissi *et al*[5] suggested that the benefits of PDT did not differ between patients with SCLC and non-small cell lung cancer (NSCLC); however, patients with SCLC may be deprived of PDT because SCLC grows rapidly and spreads to other organs earlier than NSCLC.

A combined modality consisting of thoracic radiotherapy and systemic chemotherapy is widely accepted as the standard treatment for LS-SCLC. For cases in which a tumour remains after standard treatment, clinicians should consider additional treatment modalities, including pneumonectomy, sleeve lobectomy or intraluminal brachytherapy. In this study, we had to consider the specific features of the tumour, which was located in the bronchial mucosa without invasion into the cartilaginous layer. Although the adverse effects of PDT include photosensitivity skin reaction (sunburn) in 5–28% of cases, respiratory complications in 0–18% and non-foetal haemoptysis in 0–7.8%, PDT is a safe method.[8]

To reduce the local recurrence rate after PDT, both the extent and the depth of an endobronchial tumour must be known. Autofluorescence bronchoscopy and endobronchial ultrasonography (EBUS) may be useful as additional examination methods.[9] Miyazu *et al*[10] demonstrated that the depth of tumour invasion estimated by EBUS was accurate based on histological findings after surgical resection.

According to the guidelines released in 2003 concerning early-stage NSCLC, PDT should be considered as a treatment option in early superficial squamous cell carcinoma, especially for inoperable cases.[11] Regarding the extent and depth of an endobronchial lesion, PDT may be an effective treatment for

superficial airway lesions ⩽1 cm in length, despite a diagnosis of SCLC. In this case, we applied PDT without confirming the depth of the lesion and without confirming that viable tumour remained after chemotherapy and radiotherapy, although radiological findings were highly suggestive of viable tumour. This case is the first report of the non-recurrence of SCLC.

This case suggests that PDT can be effectively used with curative intent.

Competing interests: None.

Patient consent: Obtained.

REFERENCES

1. **Passlick B.** Can surgery improve local control in small cell lung cancer? *Lung Cancer* 2001;**33**:147S–51S.
2. **Jones BU,** Helmy M, Brenner M, *et al*. Photodynamic therapy for patients with advanced non-small-cell carcinoma of the lung. *Clin Lung Cancer* 2001;**3**:37–41.
3. **Kato H,** Okunaka T, Shimatani H, *et al*. Photodynamic therapy for early stage bronchogenic carcinoma. *J Clin Laser Med Surg* 1996;**14**:235–8.
4. **Furukawa K,** Kato H, Konaka C. Locally recurrent central-type early stage lung cancer <1.0 cm in diameter after complete remission by photodynamic therapy. *Chest* 2005;**128**:3269–75.
5. **Moghissi K,** Dixon K, Stringer M, *et al*. The place of bronchoscopic photodynamic therapy in advanced unresectable lung cancer: experience of 100 cases. *Eur J Cardiothorac Surg* 1999;**15**:1–6.
6. **Kato H,** Usuda J, Okunaka T, *et al*. Basic and clinical research on photodynamic therapy at Tokyo Medical University Hospital. *Lasers Surg Med* 2006;**38**:371–5.
7. **Okunaka T,** Kato H, Konaka C, *et al*. Photodynamic therapy for multiple primary bronchogenic carcinoma. *Cancer* 1991;**68**:253–8.
8. **Moghissi K,** Dixon K. Update on the current indications, practice and results of photodynamic therapy (PDT) in early central lung cancer (ECLC). *Photodiagnosis Photodynam Ther* 2008;**5**:10–8.
9. **Furukawa K,** Ikeda N, Miura T, *et al*. Is autofluorescence bronchoscopy needed to diagnose early bronchogenic carcinoma? *J Bronchol* 2003;**10**:64–9.
10. **Miyazu Y,** Miyazawa T, Kurimoto N, *et al*. Endobronchial ultrasonography in the assessment of centrally located early stage lung cancer before photodynamic therapy. *Am J Respir Crit Care Med* 2002;**165**:832–7.
11. **Mathur PN,** Edell E, Sutedja T, *et al*. Treatment of early stage non-small cell lung cancer. *Chest* 2003;**123**:176S–80S.

Lung alert

Financial incentives for smoking cessation

Successful smoking cessation is fundamental to reducing the worldwide healthcare burden of chronic disease. This randomised controlled trial investigated the impact of financial incentives on smoking cessation among employees of a multinational company in the USA.

The study randomised 878 employees to receive information on available smoking cessation programmes (n = 442) or the same information with financial incentives (n = 436). These included $100 for completing a cessation programme, $250 for smoking cessation within 6 months of study enrolment and $400 for abstinence for a further 6 months from initial cessation. Smoking cessation was confirmed biochemically using a cotinine test.

The financial incentive group had higher rates of enrolment and completion of a smoking cessation programme. The smoking cessation rate was significantly higher in the financial incentive group at the primary end point, which was 9 or 12 months after enrolment depending on whether initial cessation was reported at 3 or 6 months. A significantly higher cessation rate was also found at 15 or 18 months after enrolment in the financial incentive group. However, relapse rates in both groups were higher at the 9- or 12- and 15- or 18-month visits than in other studies and were higher in the incentive group than the control group.

This large trial highlights the potential benefits of financial incentives in increasing smoking cessation rates. It remains unclear if the effectiveness of this company-based strategy would translate into a wider population, and it appears the success may be limited to the duration of the financial incentive. Targeting behaviour change through financial incentives, although controversial, may deliver public health objectives more effectively than current incentives in place for healthcare providers.

► Volpp KG, Troxel AB, Pauly MV, *et al*. A randomized controlled trial of financial incentives for smoking cessation. *N Engl J Med* 2009;**360**:699–709.

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