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Clinical results of photodynamic therapy in tracheobronchial malignancy

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ABSTRACT

Photodynamic therapy (PDT) has been adopted as an alternative therapy for lung cancer patients who could not receive surgery due to their poor condition. It also has expanded its roles in lung cancer treatment for palliative treatment for increasing symptoms.

We retrospectively reviewed medical records of patients of tracheobronchial cancers who received photodynamic therapy in our institute. Outcomes of the treatment results were evaluated, and survival analysis was performed via Kaplan–Meier analysis.

We performed 25 cases of photodynamic therapy for tracheobronchial cancer patients between 2003 and 2013. A total of 21 patients were involved. Average ages at the time of treatment were 68.1. In those 25 cases, 8 cases achieved complete remission, and 15 cases remained partial remission. There were 2 cases of no response. Seven patients died during the follow-up periods, but none of these were related with complications. Only two minor complications were observed during the follow-up periods. One was granulation at the site of PDT, and the other was hemoptysis. Average overall survival periods for the therapeutic group were 50.1 months and those of the palliative group were 29.3 months.

Photodynamic therapy was safe and feasible for palliative therapy in tracheobronchial cancer with acceptable complication rates. Also, it could be a treatment option for double primary lung cancer in inoperable patients.

1. Introduction

Of more than one million people newly given a diagnosis of lung cancer annually, many will die of their disease. At present, the most effective treatment modality is surgery even in locally advanced tumors, but unfortunately many lung cancers are inoperable at diagnosis, necessitating alternative treatment modalities [1].

Photodynamic therapy (PDT) is a relatively new local treatment modality that can be administered repeatedly. PDT was first reported as effective treatment of non-small cell lung cancer (NSCLC) by Hayata, et al. in early stage lung cancer [2]. PDT can be applied either as palliative treatment for advanced lung cancer, but also for early stage lung cancer in inoperable cases. The mechanism of PDT is based on the stimulation by light of photosensitizer that is taken up and retained by proliferating cells such as malignant tumors. When the intravenously administered photosensitizer is given, it is excreted by normal tissue but retained in malignant tumor and, on simulation by light of a specific wavelength, singlet oxygen which has cytotoxic effects in tumor cells in which it is taken up. Delivered separately neither sensitizer nor light are harmful, although precautions against skin photosensitivity are necessary.

Among its advantages is that PDT is cancer-specific and can be delivered repeatedly as local treatment. The therapeutic effectiveness is dependent on the delivered light to the tissue. Investigations have been performed to clarify the additive or enhanced effect of simultaneous radiotherapy or chemotherapy.

To gain insight into the applicability of PDT in a specific group of Korean lung cancer patients who were either inoperable or who had multiple malignant lesions and could not easily tolerate pulmonary procedures, we investigated the results of PDT in 25 cases from 2003 to 2013.

2. Patients and Methods

We retrospectively reviewed the medical records of patients who underwent PDT for their lung cancer in our institute between 2003 and 2013. Candidates for PDT were selected as follows: (1) patients with early stage lung cancer but who could not receive surgery because of comorbidities or who refused surgery; (2) patients with double primary lung cancer who had received surgery for the larger one and underwent PDT for the others; (3) patients with recurrent cancer or

Abbreviations: PDT, Photodynamic therapy; CT, Chest Computed Tomography; CR, Complete remission; PR, Partial remission; NR, No response; CCRT, Concurrent Chemoradiotherapy; CTx, Chemotherapy; RTx, Radiotherapy.

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unresectable tumor requiring palliative treatment; (4) patients requiring emergency alleviation of severe pain or obstruction. All enrolled cases came under the heading of tracheobronchial malignancy. Patients who underwent PDT for interstitial lung cancer were excluded. Written informed consent was obtained from all patients, and we obtained IRB approved form our hospital. (IRB Number; B-1501/282-105).

All patients underwent routine laboratory blood tests and careful physical examination. Enhanced Chest Computed Tomography (CT) and positron-emission tomography CT were performed for cancer evaluation and detection of metastasis. Bronchoscopic examination was essential for the assessment of tumor location and dimensions.

PDT consists of two stages: administration of the 2 mg/kg photosensitizer and irradiation with light of a 630 mm wavelength. Then, 24 to 48 h later, the patients underwent endoscopic tumor ablation with a light diffusion catheter (Xcell PDT Balloon with Fiber Optic Diffuser, Cook Endoscopy, Winston-Salem, NC, USA) using a tunable laser (Diomed® 630 PDT Laser System, Diomed, Ltd., Cambridge, UK). The tumor location was identified and laser catheter was delivered using a flexible bronchoscopy.

Among 25 cases, Photofrin (Pinnacle Biologics, Bannockburn, IL, USA) was used for 18 cases. Other options included ladacladin and 5-ALA. They were chosen if Photofrin caused any adverse reactions. Patients were given 120–200 J per session, with treatment duration of 240–500 s.

Follow-up bronchoscopy was performed 2 days after the first treatment. Mechanical debridement of necrotic tissue was performed if necessary. All patients were recommended to avoid sunlight for 4 to 6 weeks after the final PDT. Follow-up endoscopy was performed at 1, 3, and 6 months after the first PDT. Chest CT was also performed 6 months after PDT.

Treatment results were categorized into 3 groups: complete remission (CR), defined as no evidence of disease on follow-up chest CT or endoscopy 6 months after PDT; partial remission (PR), in which tumor regressed or was still observed in the tumor bed or there was regrowth after remission; or no response (NR), defined as up to 50% of the tumor remaining or an increase in tumor size after PDT.

We evaluated treatment response in each case. Local recurrence was defined as emergence of tumor regrowth after complete or partial remission on follow-up endoscopy or chest CT. Survival and complication rates were calculated using Kaplan–Meier survival analysis. SPSS 20.0 (IBM, New York, NY, USA) was used for statistical analysis. Disease-free survival in the PR group was defined as no tumor progression during the follow-up periods.

3. Results

3.1. Patient Characteristics

Of the total of 25 cases all except one were men. The median follow-up period was 20.5 months. Average age at the time of treatment was 68.4 (±6.00 years. PDT was performed for therapeutic purposes on 12 cases, (48.0%) and for palliative purposes on 13 cases (52.0%). Information on patients is summarized in Table 1, and the concurrent treatment modalities with PDT are categorized in Table 1.

Table 1
Patient characteristics.

Variables	Tumor characteristics (Number)					
	Primary	Double	Multiple	Recurred	Metastasis	Total
Age (years)	68.4 ± 6.00					
Median follow-up periods (months)	20.5 ± 28.20 (1.33–105.30)					
Gender						
Male	6	3	7	8	0	24
Female	0	0	0	0	1	1
Stage						
Tis	0	0	1	0	0	1
T1	2	3	4	0	0	9
T2	3	0	2	0	0	5
T3	1	0	0	0	0	1
T4	0	0	0	0	0	0
Others	0	0	0	8	1	9
Concurrent treatment						
None	3	1	5	5	1	15
CCRT	1	0	0	0	0	1
CTx	2	2	1	1	0	6
CTx with operation	0	0	1	0	0	1
RTx	0	0	0	2	0	2
Indication						
Therapeutic	5	3	3	1	0	12
Palliative	1	0	4	7	1	13
Total	6	3	7	8	1	25

3.2. Treatment Results

CR was achieved in 8 (32.0%) of the 25 cases. One patient who had multiple primary lung cancer had received PDT 4 times and attained CR. Two cases in the CR group showed local recurrence and PDT was performed repeatedly on the recurrent sites. No patient in the CR group died during the follow-up periods.

PR was observed in 15 (60.0%) cases. One patient in the PR group underwent surgery after PDT. Another patient had been recommended repeated PDT for remnant cancer, but he refused. 5 patients with PR died during the follow-up periods (33.3%). Three of them died from cancer progression, and one patient from liver failure. The death of the last patient was related to tongue cancer.

There were 2 cases of NR (8.0%). All patients who refused any kind of anticancer treatment including surgery, died during the follow-up periods. One patient died from cancer progression, but the other died from a cardiac problem.

Most common tumor locations were RUL superior segmental bronchus (6 cases, 24.0%). Four cases were in the trachea, and another four cases were in the left main bronchus (16.0% respectively). There were two cases of left lingular segmental bronchus, two cases of left anterior segmental bronchus, and two cases of left upper lobar bronchus. Other sites of tumor locations included left lower lobar bronchus, basal segmental bronchus of the left lower lobe and right lower lobe, left second carina, and right upper lobar bronchus (each site had one case). The mean tumor sizes were 8.2 mm (±4.33 ranged from 1.8 to 15.8), when we measured based on chest CT images.

There were only two cases of complications. One was granulation tissue on the PDT site, and the other was mild hemoptysis. No complication-related death was observed.

Local recurrence was observed in 9 patients (36.0%). Among the PR cases, there were 7 cases of recurrence, defined as regrowth of tumor in follow-up examination. Of those 7 patients, 1 died of cancer progression. After detection of recurrence, 3 patients received chemotherapy, 3 received PDT repeatedly, and one patient received chemotherapy. Results of treatments are summarized in Table 2.

Table 2
Results of treatments. CR was achieved in 8 (32.0%), and PR was observed in 15 (60.0%) cases. 2 cases of NR died during the follow-up periods because of the disease progression.

Results of treatment	Tumor characteristics (Number)					
	Primary	Double	Multiple	Recurred	Metastasis	Total
CR	2	2	3	1	0	8
PR	2	1	4	7	1	15
NR	2	0	0	0	0	2
Total	6	3	7	8	1	25