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CASE REPORT

Successful treatment of a tracheal squamous cell carcinoma with a combination of cryoablation and photodynamic therapy

Sung-Jin Nam[1], Chul-Ho Oak[1], Tae-Won Jang[1], Mann-Hong Jung[1] & Bong-Kwon Chun[2]

1 Department of Internal Medicine, Kosin University College of Medicine, Busan, Korea
2 Department of Pathology, Kosin University College of Medicine, Busan, Korea

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Correspondence
Tae-Won Jang
Department of Internal Medicine, Kosin University College of Medicine, Busan 602-702, Korea.
Tel: +82 51 990 6637
Fax: +82 51 248 5686
Email: jangtw@kosinmed.or.kr

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Abstract

Malignant tumors of the trachea are rare, and account for less than 0.1% of all malignancies. Because there are no guidelines based on randomized clinical trials, the choice of treatment modalities and optimal sequences have not yet been established. In most cases of malignant airway obstruction, a single modality is chosen as the treatment of choice for management, but complete ablation becomes increasingly problematic with minimal residual lesions that require additional treatment. There were few case reports of the combined use of cryoablation and photodynamic therapy to treat tracheal cancer. Therefore, we present our experience of successful tracheal cancer treatment using this combination therapy. A bronchoscopic complete regression was obtained using these two modalities, and the procedures proved to be a safe and effective treatment option based on a one-year follow-up.

Introduction

Malignant tumors of the trachea account for less than 0.1% of all malignancies. Because there are no specific respiratory signs and symptoms of the disease, which is potentially resectable and curable, diagnosis is usually delayed until an advanced stage, leading to poor prognoses.[1] As there are no treatment guidelines based on randomized clinical trials due to the rarity of this type of malignancy, the choice of treatment modalities and optimal sequence is at each surgeon's discretion. In about 30% of lung cancer patients, cancer is accompanied by central airway obstruction that causes symptoms including dyspnea and hemoptysis. Local treatment for these symptoms is important to alleviate symptoms and improve quality of life. Several interventional methods have been used to improve airway obstruction in lung cancer patients suffering from central airway obstruction, including electrocautery, brachytherapy, neodymium-doped yttrium aluminum garnet (Nd:YAG) laser therapy, photodynamic therapy (PDT), and cryoablation.[2]

In most cases of malignant airway obstruction, a single modality is chosen as the treatment of choice for management, but complete ablation is problematic when there are minimal residual lesions that require additional treatment. Cryoablation can be used for safe, local control of central airway tumors without causing scarring or cartilage damage and has been noted to allow local control of both lung cancer and cancer bleeding. Its non-thermally disruptive properties make it an attractive alternative therapy for treatment of malignant tumors in the tracheobronchial tree.[3,4] A handful of studies have used the combination of cryoablation and PDT to treat tracheal cancer.[5] In this study, we describe the successful treatment of metastatic tracheal cancer using this combination therapy; complete regression was obtained at a follow-up duration of one year.

Case presentation

A 73-year-old Korean man presented with blood-tinged sputum and mild dyspnea. Five years prior, he had been

treated for supraglottic squamous carcinoma with concurrent chemoradiation therapy. He had undergone three cycles of chemotherapy during radiotherapy, with a cumulative radiation dose estimated at 5040 cGy. He underwent follow-up computed tomography (CT) that showed a suspicious nodule protruding into the lumen of the trachea (Fig 1). Bronchoscopy revealed a tracheal mass in the mid-trachea (4–5 cm from the vocal cords). A biopsy revealed squamous cell carcinoma. We performed −80°C bronchoscopic cryoablation using an Erbokryo cryosurgery unit (ERBE Medizin-technik GmbH, Tubingen, Germany) under local anesthesia with conscious sedation (midazolam 2 mg intravenous injection). There were no immediate complications. The conventional palliative treatment for malignant central airway obstruction is radiation therapy. The patient refused radiation therapy, but was willing to undergo other palliative treatment options such as photodynamic therapy and cryoablation. In view of the extent of the tumor, cryoablation was first used to debulk the tumor mass and then PDT was used seven days later for selective tumor removal without normal adjacent tissue damage. The publication of this case was conducted with the approval of the Kosin University Gospel Hospital Ethics Committee.

Before the PDT procedure, a photosensitizer (Photofrin®: porfimer sodium, AXCAN Pharma Inc. (USA)) was injected intravenously at a dose of 2.0 mg per kg body weight. After Photofrin® injection, the patient was instructed to avoid direct sun exposure for at least two weeks. The laser beam was transmitted via a quartz fiber (400 mm) inserted through the instrumentation channel of a fiber optic bronchoscope. Light at 86 J/cm^2 was delivered to the anterior site using a diode laser (Biolitec Inc., Germany; wavelength: 630 nm) with a 2 cm diffuser for 286 seconds and at 100 J/cm^2 with a 2 cm diffuser for 333 seconds. The next day, booster PDT was performed. The lesion site was irradiated with 100 J/cm^2 of light from a diode laser for 333 seconds using a 2 cm diffuser. Forty-eight hours after the procedure, bronchial toilet was performed and superficial necrotic changes at the tumor site were noted. There were no immediate complications. We performed follow-up bronchoscopic biopsies after one, three, and 12 months. Histological analysis of the tissue samples from the cryoablation and PDT sites revealed focal atypical squamous metaplasia (Fig 2). Complete tumor regression was supported by clinical (bronchoscopic) and pathological examinations. There was no evidence of recurrence during a one-year follow-up period.

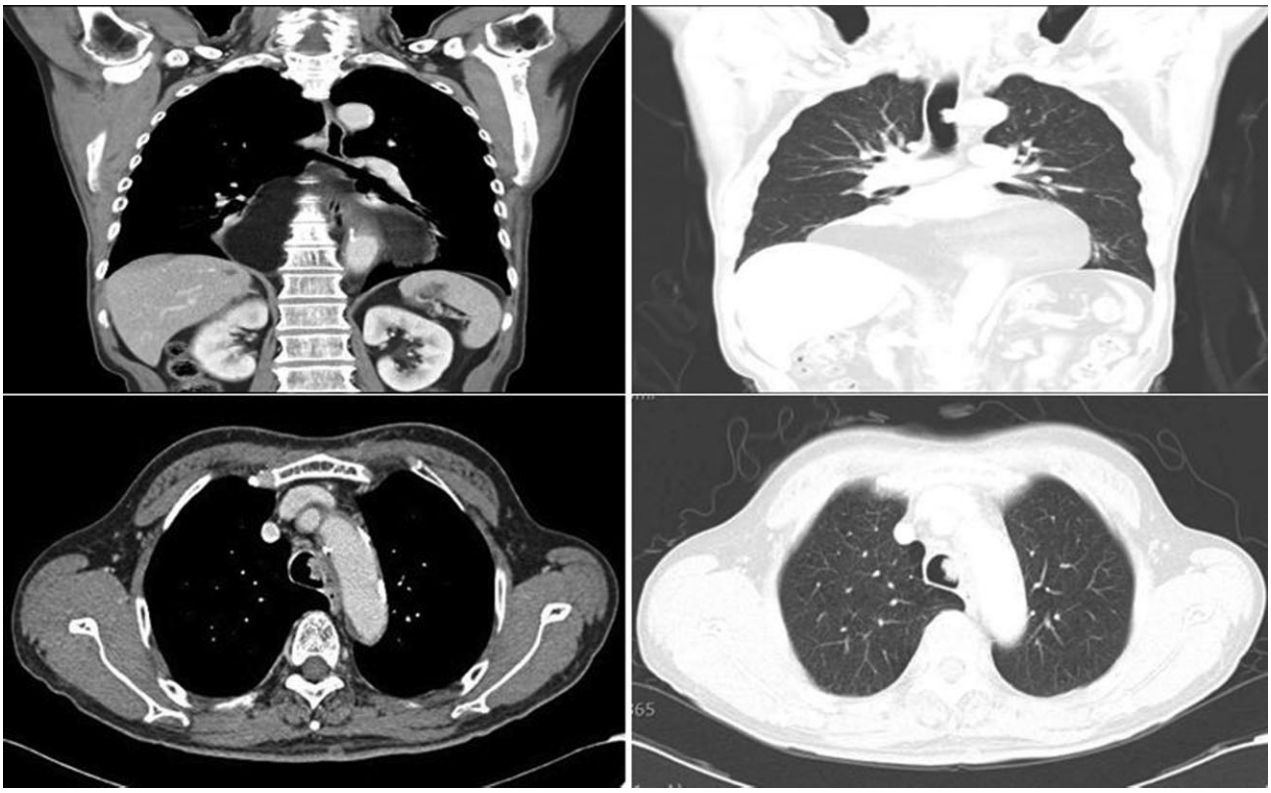

Figure 1 Chest computed tomography (CT) scans showing a tracheal nodule.

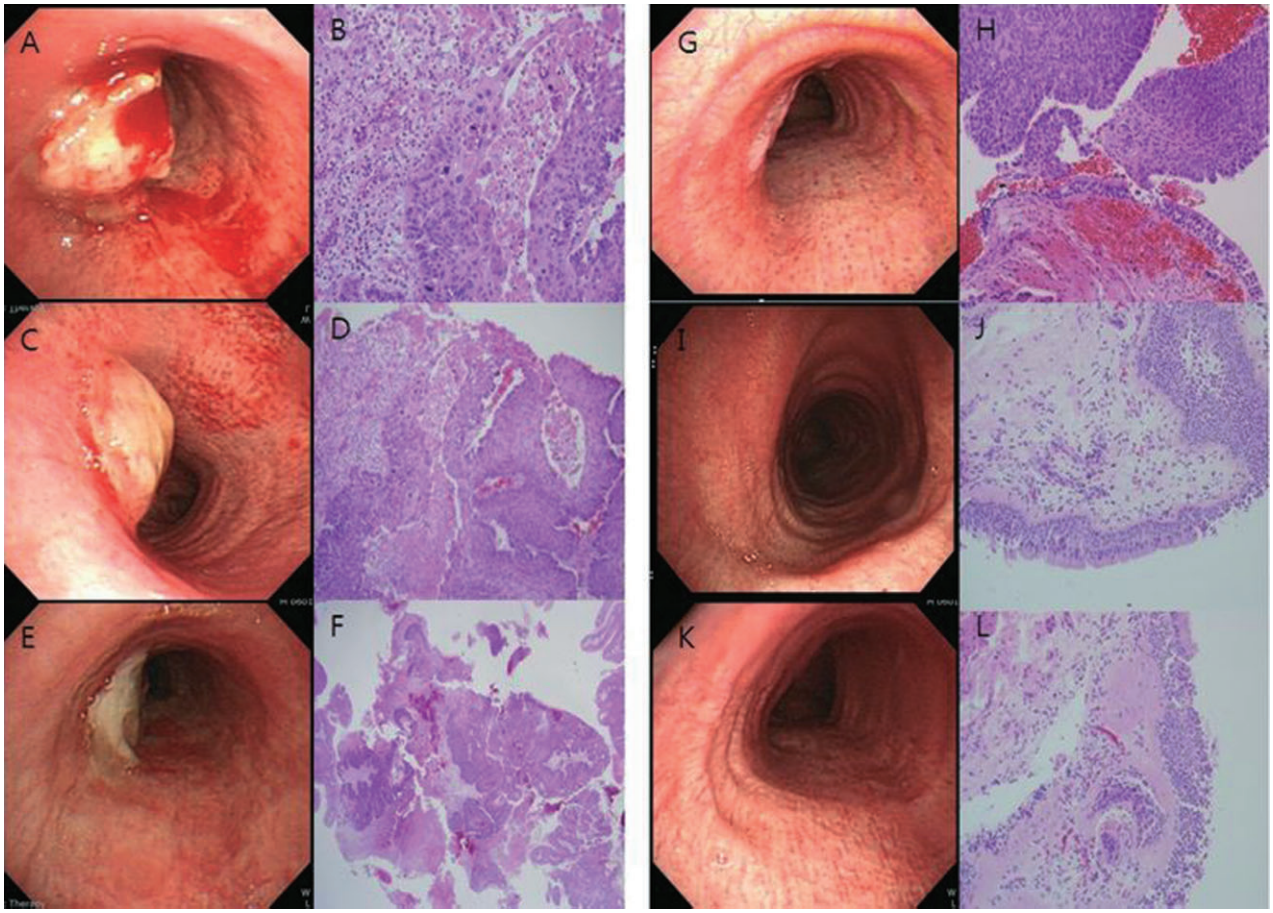

Figure 2 Bronchoscopic and pathologic changes before and after treatment. (a) Initial bronchoscopic findings in the trachea before treatment. (b) Squamous cell carcinoma, moderately differentiated (H&E x200). (c) Bronchoscopic findings after cryoablation. (d) Same as above (H&E x40). (e) Bronchoscopic findings after photodynamic therapy (PDT). (f) Same as above (H&E x20). (g) Bronchoscopic findings at one month after treatment: partial response state. (h) Same as above (H&E x40) and (i) Three months after treatment: complete regression. (j) Atypical squamous metaplasia (H&E x100) and (k) one year after treatment: no evidence of recurrence. (l) No evidence of malignancy (H&E x100).

Discussion

A review of the literature revealed no theoretical reasons why cryoablation and photodynamic therapy should not be combined. We tailored this combined treatment for our patient. Because the distal portion of the tracheal tumor had less vasculature with a necrotic area, and was therefore considered unlikely to cause massive bleeding, we chose to perform cryoablation first. In the previous study, the tumor base and adjacent dysplastic area had feeding vessels that were friable. PDT is more tumor-selective than cryoablation and slows tumor regression by vessel occlusion. We therefore chose to use PDT as the second treatment modality.

It is obvious that PDT is not essential to all cancer therapies. Although PDT had its advantages and disadvantages, we tried PDT because of its great strength: PDT is effective in removing the remaining cancer tissues in unresectable regions after photochemical reaction. Logically, there is no established consensus on radiation treatment or PDT as a palliative treatment for a malignant tumor in central airway. But, in this case study, the patient had received radiation treatment before and refused radiation treatment because of grade 4 radiation esophagitis previously. The patient was not at risk of imminent respiratory failure and the tumor was localized in the trachea. Furthermore, we carried out PDT with the patient's consent because the stability and low-toxicity offered by this treatment were the main priorities in choosing a therapy method for central airway obstruction.

We removed a distal part of the tumor by cryoablation to leave the vasculature and proximal tumor tissue intact in order to allow the photosensitizer, Photofrin, to accumulate in the residual tumor tissue. Laser irradiation (*e.g.*, Nd-YAG) and electrocautery, together with mechanical tumor removal, allowed us to achieve complete tumor regression. Firstly, the

distal tumor protruding toward the intra-airway was removed by cryoablation. After observing with bronchoscopy that the blood vessel was not exposed, and confirming with biopsy that tumor tissue and vessel were intact, we performed photodynamic therapy. As we can see from bronchoscopic biopsy findings (Fig 2c,d) of proximal tumor left, through histologic examination we confirmed that the blood vessel was intact in three days after cryoablation and injected photofrin for PDT. While the prominent mass was removed, the vessel under the mucous membrane was not damaged by cryoablation. Therefore, we conclude, there is no problem with conducting PDT within a few days after cryoablation. The local control was done by cryoablation only but curative therapy is not expected.

Cryoablation is suitable for reducing bulky, protruding mass lesions, while PDT is good for lesions with a depth of 0.7 mm–1 cm. We therefore first performed cryoablation and then PDT. Cryoablation-PDT offers several advantages for the treatment of malignant airway obstructions. PDT, through flexible bronchoscopy after cryoablation, enables precise tumor removal with minimal or no damage to surrounding tissue. The technique is easy to learn and extremely efficient.[6] Cryoablation is a technique that involves tissue destruction by freezing. It is the least expensive treatment method available. Deygas *et al.*[7] reported cryoablation results for 35 patients (41 cancers) with early stage lung cancer. Complete remission was obtained in 91% of the patients with a recurrence rate of 28% within four years. A long-term response rate of 63% was achieved, similar to that of PDT. As the cryoprobe is able to both ablate and coagulate, no instrument changes are required during the procedure, which minimizes bleeding and enables the obstructing lesions to be removed during a single procedure. Additionally, cryoablation can be performed within 10 minutes, which is comparable with the time required for other ablation modalities such as laser ablation, electrocautery, and argon plasma coagulation.

Dougherty *et al.* first reported PDT,[8] and the procedure has since attracted interest worldwide. PDT is approved for palliative treatment of malignant endobronchial obstructions. Furthermore, response to PDT is not dependent on the tumor cell type. PDT can be performed in patients who have already undergone surgery, radiation, or chemotherapy. Light penetration is limited to 5-10 mm from the tissue surface. Invading tumors more than 1 cm deep may therefore be difficult to manage with PDT alone. The effectiveness of PDT for symptom palliation and survival has been evaluated in patients with advanced inoperable bronchogenic cancer and endobronchial obstruction. Moghissi *et al.*[9] reported on 100 patients of whom 82% had received prior chemotherapy and/or radiotherapy treatment. Diminished endoluminal obstruction (18%) was achieved in 86 patients after PDT.

We, therefore, combined cryoablation and PDT to treat our patient and achieved complete tumor ablation. At the one-year follow-up, bronchoscopy showed complete regression and no complications, such as bleeding or stricture of the tracheal cartilage.

Conclusions

We present a case of teacheal cancer that was successfully treated with a combination of cryoablation and PDT. The procedures proved to be a safe and effective treatment option, resulting in the complete regression of a protruding squamous cell carcinoma of the trachea.

Disclosure

No authors report any conflict of interest.

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