Respiratory Medicine Case Reports 22 (2017) 175–178

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Successful treatment of limited-stage small-cell lung cancer in the right mainstem bronchus by a combination of chemotherapy and argon plasma coagulation

Takayuki Takeda [a,*], Hideki Itano [b], Mayumi Takeuchi [a], Yurika Nishimi [a], Masahiko Saitoh [a], Sorou Takeda [a]

[a] *Division of Respiratory Medicine, Department of Internal Medicine, Uji Tokushukai Medical Center, 145, Makishima-cho, Uji City, Kyoto 611-0041, Japan*
[b] *Division of Thoracic Surgery, Department of General Surgery, Uji Tokushukai Medical Center, 145, Makishima-cho, Uji City, Kyoto 611-0041, Japan*

ARTICLE INFO

Article history:
Received 30 March 2017
Received in revised form
12 August 2017
Accepted 14 August 2017

Keywords:
Argon plasma coagulation
Carboplatin
Carcinoma *in situ*
Etoposide
Small-cell lung cancer

ABSTRACT

The current standard-of-care treatment for patients with limited-stage small-cell lung cancer (SCLC) is concurrent chemoradiotherapy for local and systemic control. However, standard-of-care treatment strategies have not been established for those with limited-stage SCLC who have a history of thoracic radiotherapy due to concerns with complications associated with radiation overdose. A 37-year-old male developed an aspergilloma in the postoperative left thoracic space after he was treated with concurrent chemoradiotherapy for mediastinal type lung adenocarcionoma and subsequent left upper lobectomy for heterochronous dual adenocarcinoma. Fiberoptic bronchoscopy was performed to examine the status of the suspected bronchopleural fistula when a polypoid mass was observed in the right mainstem bronchus. A histological examination showed that the mass was SCLC at a clinical stage of cTisN0M0, stageIA, without local invasion. Since thoracic radiotherapy was not an option due to a previous history of thoracic irradiation, a combination treatment of carboplatin and etoposide was administered for 4 cycles and resulted in good partial response. In addition, argon plasma coagulation (APC) was performed as an alternative to curative radiotherapy on day 22 of the 4th cycle. The 5th cycle was administered 7 days after APC at which the anticancer therapy was completed. The patient remains disease-free 60 months after the completion of treatment, which suggests that this combination therapy may resolve very early-stage SCLC.

1. Introduction

Small-cell lung cancer (SCLC) possesses high malignant potential and aggressive clinical course that may spread to regional lymph nodes and distant organs during the early stages [1]. The current standard-of-care treatment for patients with limited-stage SCLC is concurrent chemoradiotherapy for local and systemic control [2,3]. However, there is currently no established strategy for patients with limited-stage SCLC who had previously received thoracic external beam radiation therapy (EBRT).

This report describes a patient with very early-stage SCLC in the right mainstem bronchus (cTisN0M0, stageIA) who had a previous history of thoracic EBRT and was successfully treated with a combination treatment of carboplatin and etoposide followed by argon plasma coagulation (APC). He remains disease-free for 60 months.

2. Case report

A 37-year-old male developed an aspergilloma in the postoperative left thoracic cavity after receiving concurrent chemoradiotherapy for mediastinal type lung adenocarcionoma and subsequent left upper lobectomy for heterochronous dual adenocarcinoma (Fig. 1A). Since the systemic administration of anti-fungal agents was ineffective, thoracic surgery was considered. When fiberoptic bronchoscopy (FOB) was performed, a polypoid lesion was observed in the right mainstem bronchus (Fig. 1B) that exhibited magenta in an autofluorescence image (Fig. 1C). Histological examination demonstrated that the mass was SCLC. Contrast-enhanced CT of the chest did not show the tumor, its invasion into the bronchial cartilage, or apparent metastases into the regional lymph nodes (Fig. 1D). Whole-body evaluation demonstrated no distant

* Corresponding author.
E-mail address: dyckw344@yahoo.co.jp (T. Takeda).

http://dx.doi.org/10.1016/j.rmcr.2017.08.014

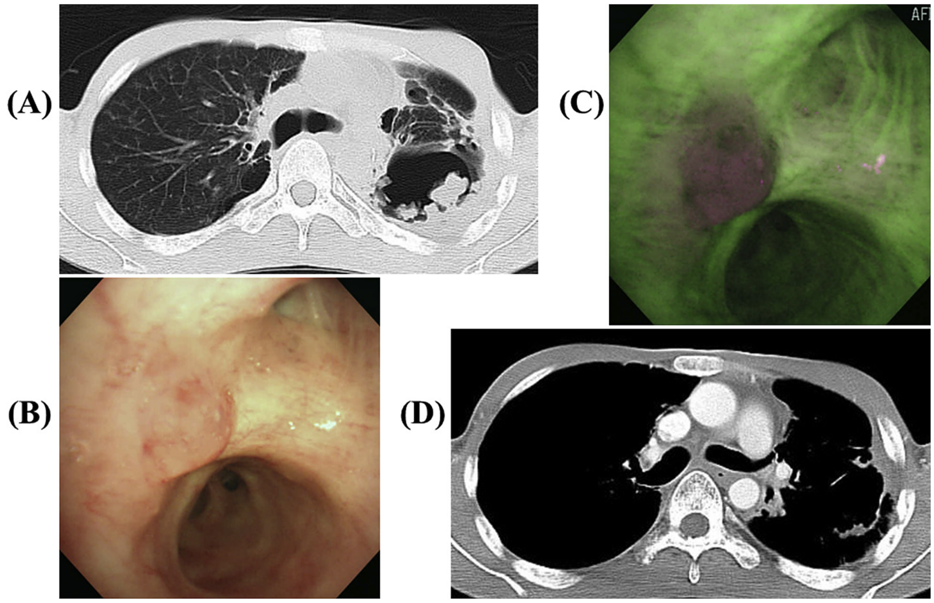

Fig. 1. Images of the chest CT (A, D) before the treatment showed an aspergilloma located in the left thoracic cavity (A). However, it was difficult to detect a mass in the right mainstem bronchus and marked lymph nodes swelling (A, D). Images from white-light (B) and autofluorescence (C) bronchoscopy demonstrated a polypoid lesion in the right mainstem bronchus that is shown in magenta in the autofluorescence image.

organ metastases. Although endobronchial ultrasound was not available, the macroscopic findings from FOB and contrast-enhanced CT of the chest suggested that the lesion was confined in the bronchial mucosa without local invasion. Therefore, the clinical stage was considered to be cTisN0M0, stageIA.

Since additional EBRT could not be administered due to a previous history of thoracic EBRT, a combination treatment of carboplatin and etoposide was administered. The tumor response was assessed by FOB after 2 cycles and showed good partial response. With the intention for complete cure, APC [4] was employed for local treatment on day 22 of the 4th cycle in order to have local control. An image from a FOB session on day 22 prior to APC is shown in Fig. 2A.

Under topical anesthesia, a fiberoptic bronchoscope was inserted and an axial probe tip was selected for APC. APC was performed using the following parameters: pulsed mode, effect 1, argon gas

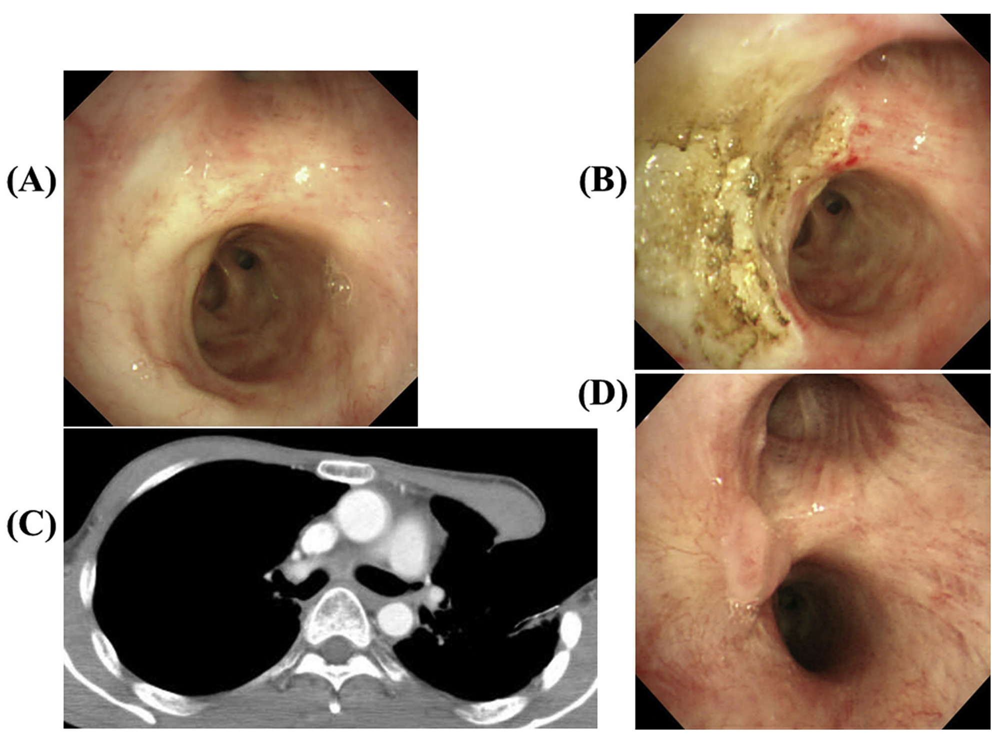

Fig. 2. Images of fiberoptic bronchoscopy (FOB) obtained on day 22 of the 4th cycle before (A) and after (B) treatment by argon plasma coagulation (APC) are shown. A scar-like lesion was observed (A), and APC was conducted by using appropriate settings (B). Images of chest CT (C) and FOB (D) obtained 24 months after the APC are shown. Chest CT showed the postoperative status of the left cavernostomy and no abnormalities in the right mainstem bronchus were found (C). A scar-like epithelial thickening was observed by white-light bronchoscopy (D).

flow 0.8 L/min, a maximum of 35 W, and setting a margin of 5 mm around the pre-treatment image. After each session, the loss of magenta emission was confirmed by autofluorescent imaging to ensure APC was properly added. The color of the bronchial mucosa became brown inside of the preset margin area after the end of the entire procedure (Fig. 2B). The procedure was performed under oxygen administration of 1 L per minute. The time required for the entire procedure was 20 minutes.

A 5th cycle of chemotherapy was performed 7 days after APC when the anticancer therapy was completed. The patient subsequently underwent staged thoracostomy and cavernostomy in order to stabilize the aspergillosis.

He currently remains disease-free for 60 months, and contrast-enhanced CT of the chest and FOB showed only a scar-like lesion (Fig. 2C and D, respectively). Considering the aggressive nature and high malignant potential of SCLC, the disease was completely resolved by the combination of chemotherapy and APC.

3. Discussion

Although various cancer treatments are being developed to improve prognosis, the number of heterochronous dual lung cancer is still increasing [5–7]. Since SCLC possesses high malignant potential [1], surgery is applied in limited cases. Therefore, chemoradiotherapy is the standard-of-care treatment for patients with limited-stage SCLC [2,3]. However, a standard treatment strategy for patients with a previous history of thoracic EBRT is not yet established. In these cases, curative doses of additional EBRT is intolerable and, as a result, other strategies need to be considered for a complete cure. Although cures are considered impossible without chemoradiotherapy for cases with regional lymph node metastases, a combination treatment of endobronchial therapy and chemotherapy could lead to the complete cure in cases with limited-stage SCLC that is confined in the mucosa without extracartilaginous invasion.

The detection of SCLC *in situ* is quite rare, and the primary strategy is concurrent chemoradiotherapy, which is similar to limited-stage SCLC. In our case, the lesion was incidentally detected during a preoperative survey by white-light and autofluorescence bronchoscopy. A combined chemotherapy preceded a local treatment due to previous EBRT. After confirming the response of chemotherapy by FOB, additional treatment for local control was considered that would take into consideration the previous history of EBRT.

Although the previous EBRT was considered to be an absolute contraindication for future EBRT, the development of intensity modulated radiation therapy (IMRT) has changed the therapeutic options. IMRT has come to be employed in some cases as an alternative method for reirradiation. However, IMRT has relatively short history, and the long-term adverse events after reirradiation with IMRT are unclear. Therefore, endobronchial therapies are usually performed in these cases.

Several types of endobronchial therapies are performed in the management of lung cancer [8–12] such as photodynamic therapy [13–15], high-dose-rate brachytherapy [15–21], electrocautery [22], APC [4,23], neodymium yttrium-aluminium-garnet (Nd-YAG) laser therapy [24,25], and cryotherapy [26]. These methods have been used for both the palliation of obstructing inoperable lung cancers in combination with [18,21] or after EBRT [16], and primary treatment of early-stage radiographically occult non-small cell lung cancer [17]. Most have been performed for early-stage non-small cell lung cancer, and their application to SCLC is quite rare. In particular, the application of APC is quite rare; one case reported the application of APC to central type squamous cell carcinoma [4] and another used a combination of APC and electrocautery in a patient with SCLC to palliate bronchial obstruction [23].

APC is a monopolar electrosurgical procedure that transfers electrical energy to the target tissue using a jet of ionized argon gas and leads to coagulation necrosis of the superficial tumor without damaging the surrounding tissue. Once the argon gas is sparked, it turns into plasma, and the energy transfer between the electrode and the tissue occurs by electrophysical laws in contrast to laser technology that is under optical laws. Therefore, the plasma is sprayed toward the target tissue without causing the tumor and surrounding tissues to bleed. The application of energy with pulsed APC effect 1 enables higher energy output per pulse with longer intervals between pulses (approximately 1 pulse per second), which provides a safer and stronger antitumor action. Since tissue injury is caused by endogenous heating of the target tissue through an electrical current, pulsed APC, effect 1, and maximum 35 W were selected as the most appropriate settings to limit the depth of thermal injury to the surrounding tissue (estimated maximum coagulation depth ranging between 1.5 and 2.0 mm).

4. Conclusions

In this patient, we employed APC as endobronchial therapy because the tumor was confined in the mucosa without apparent invasion, and also to avoid in-depth tissue injury to prevent complications, such as bleeding and bronchial perforation, due to a previous history of EBRT.

This study is the first to apply APC for the treatment of limited-stage SCLC for a complete cure with a documented long-term disease-free survival.

Disclosure statements

The authors declare no conflicts of interest. Informed consent for publication was obtained from the patient.

References

[1] E. Vallières, F.A. Shepherd, J. Crowley, P. Van Houtte, P.E. Postmus, D. Carney, K. Chansky, Z. Shaikh, P. Goldstraw, International Association for the Study of Lung Cancer International Staging Committee and Participating Institutions, the IASLC Lung Cancer Staging Project: proposals regarding the relevance of TNM in the pathologic staging of small cell lung cancer in the forthcoming (seventh) edition of the TNM classification for lung cancer, J. Thorac. Oncol. 4 (2009) 1049–1059.

[2] J.P. Pignon, R. Arriagada, D.C. Ihde, D.H. Johnson, M.C. Perry, R.L. Souhami, O. Brodin, R.A. Joss, M.S. Kies, B. Lebeau, T. Onoshi, K. Østerlind, M.H.N. Tattersall, H. Wagner, A meta-analysis of thoracic radiotherapy for small-cell lung cancer, N. Engl. J. Med. 327 (1992) 1618–1624.

[3] P. Warde, D. Payne, Does thoracic irradiation improve survival and local control in limited-stage small-cell carcinoma of the lung? A meta-analysis, J. Clin. Oncol. 10 (1992) 890–895.

[4] T. Kono, S. Lee, J. Nohara, Y. Sakaguchi, T. Noguchi, Y. Terada, A case of bronchogenic carcinoma which obtained long-term relapse free survival by argon plasma coagulation, Nihon Kokyuki Gakkai Zasshi 47 (2009) 1093–1097.

[5] T.W. Shields, E.W. Humphrey, G.A. Higgins, R.J. Keehn, Long-term survivors after resection of lung carcinoma, J. Thorac. Cardiovasc. Surg. 76 (1978) 439–445.

[6] D.A. Cortese, P.C. Pairolero, E.J. Bergstralh, L.B. Woolner, M.A. Uhlenhopp, J.M. Piehler, D.R. Sanderson, P.E. Bernatz, D.E. Williams, W.F. Taylor, W.S. Payne, R.S. Fontana, Roentgenographically occult lung cancer. A ten-year experience, J. Thorac. Cardiovasc. Surg. 86 (1983) 373–380.

[7] F.B. Zimmermann, M. Molls, B. Jeremic, Treatment of recurrent disease in lung cancer, Semin. Surg. Oncol. 21 (2003) 122–127.

[8] T.G. Sutedja, A.J. van Boxem, P.E. Postmus, The curative potential of intraluminal bronchoscopic treatment for early-stage non-small-cell lung cancer, Clin. Lung Cancer 2 (2001) 264–270.

[9] P.N. Mathur, E. Edell, T. Sutedja, J.M. Vergnon, American College of Chest Physicians, Treatment of early stage non-small cell lung cancer, Chest 123 (2003) 176S–180S.

[10] C.T. Bolliger, T.G. Sutedja, J. Strausz, L. Freitag, Therapeutic bronchoscopy with immediate effect: laser, electrocautery, argon plasma coagulation and stents, Eur. Respir. J. 27 (2006) 1258–1271.

[11] T.C. Kennedy, A. McWilliams, E. Edell, T. Sutedja, G. Downie, R. Yung, A. Gazdar, P.N. Mathur, American College of Chest Physicians, Bronchial intraepithelial neoplasia/early central airways lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition), Chest 132 (2007) 221S–233S.
[12] K.P. Suraj, Endobronchial electrocautery and argon plasma coagulation, Pulmon 10 (2008) 75–83.
[13] J.S. McCaughan Jr., T.E. Williams, Photodynamic therapy for endobronchial malignant disease: a prospective fourteen-year study, J. Thorac. Cardiovasc. Surg. 114 (1997) 940–946.
[14] L. Corti, L. Toniolo, C. Boso, F. Colaut, D. Fiore, P.C. Muzzio, M.I. Koukourakis, R. Mazzarotto, M. Pignataro, L. Loreggian, G. Sotti, Long-term survival of patients treated with photodynamic therapy for carcinoma in situ and early non-small-cell lung carcinoma, Lasers Surg. Med. 39 (2007) 394–402.
[15] B.D. Weinberg, R.R. Allison, C. Sibata, T. Parent, G. Downie, Results of combined photodynamic therapy (PDT) and high dose rate brachytherapy (HDR) in treatment of obstructive endobronchial non-small cell lung cancer (NSCLC), Photodiagn. Photodyn. Ther. 7 (2010) 50–58.
[16] G. Sutedja, G. Baris, C. Schaake-Koning, N. van Zandwijk, High dose rate brachytherapy in patients with local recurrences after radiotherapy of non-small cell lung cancer, Int. J. Radiat. Oncol. Biol. Phys. 24 (1992) 551–553.
[17] H. Marsiglia, P. Baldeyrou, E. Lartigau, E. Briot, C. Haie-Meder, T. Le Chevalier, G. Sasso, A. Gerbaulet, High-dose-rate brachytherapy as sole modality for early-stage endobronchial carcinoma, Int. J. Radiat. Oncol. Biol. Phys. 47 (2000) 665–672.
[18] H. Langendijk, J. de Jong, M. Tjwa, M. Muller, G. ten Velde, N. Aaronson, R. Lamers, B. Slotman, M. Wouters, External irradiation versus external irradiation plus endobronchial brachytherapy in inoperable non-small cell lung cancer: a prospective randomized study, Radiother. Oncol. 58 (2001) 257–268.
[19] C.A. Mantz, D.E. Dosoretz, J.H. Rubenstein, P.H. Blitzer, M.J. Katin, G.R. Garton, B.M. Nakfoor, A.D. Siegel, K.A. Tolep, S.E. Hannan, R. Dosani, A. Feroz, C. Maas, S. Bhat, G. Panjikaran, S. Lalla, K. Belani, R.H. Ross, Endobronchial brachytherapy and optimization of local disease control in medically inoperable non-small cell lung carcinoma: a matched-pair analysis, Brachytherapy 3 (2004) 183–190.
[20] M. Aumont-le Guilcher, B. Prevost, M.P. Sunyach, D. Peiffert, P. Maingon, L. Thomas, D. Williaume, M. Begue, D. Lerouge, L. Campion, M.A. Mahe, High-dose-rate brachytherapy for non-small-cell lung carcinoma: a retrospective study of 226 patients, Int. J. Radiat. Oncol. Biol. Phys. 79 (2011) 1112–1116.
[21] N. Rochet, H. Hauswald, E.M. Stoiber, F.W. Hensley, H.D. Becker, J. Debus, K. Lindel, Primary radiotherapy with endobronchial high-dose-rate brachytherapy boost for inoperable lung cancer: long-term results, Tumori 99 (2013) 183–190.
[22] T.J. Van Boxem, B.J. Venmans, F.M. Schramel, J.C. van Mourik, R.P. Golding, P.E. Postmus, T.G. Sutedja, Radiographically occult lung cancer treated with fiberoptic bronchoscopic electrocautery: a pilot study of a simple and inexpensive technique, Eur. Resp. J. 11 (1998) 169–172.
[23] A. Kiani, A. Khosravi, A.S. Moghaddam, H. Jabbari, M. Fakhri, Long-term survival of a small cell lung cancer patient with proper endobronchial management, Pneumologia 61 (2012) 245–248.
[24] B. Zaric, T. Kovacevic, V. Stojsic, T. Sarcev, M. Kocic, M. Urosevic, D. Kalem, B. Perin, Neodymium yttrium-aluminium-garnet laser resection significantly improves quality of life in patients with malignant central airway obstruction due to lung cancer, Eur. J. Cancer. Care 24 (2015) 560–566.
[25] K. Furukawa, T. Okunaka, H. Yamamoto, T. Tsuchida, J. Usuda, H. Kumasaka, J. Ishida, C. Konaka, H. Kato, Effectiveness of photodynamic therapy and Nd-YAG laser treatment for obstructed tracheobronchial malignancies, Diagn. Ther. Endosc. 5 (1999) 161–166.
[26] G.C. Jones, J.D. Kehrer, J. Kahn, B.N. Koneru, R. Narayan, T.O. Thomas, K. Camphausen, M.P. Mehta, A. Kaushal, Primary treatment options for high-risk/medically inoperable early stage NSCLC patients, Clin. Lung Cancer 16 (2015) 413–430.