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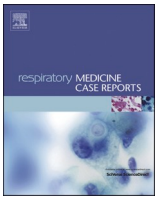

Case Report

Successful stent removal after chemoradiotherapy followed by durvalumab for locally advanced non-small cell lung cancer with airway stenosis: A report of three cases

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ABSTRACT

Airway stents improve respiratory conditions and Eastern Cooperative Oncology Group Performance Status scores in cases of airway stenosis, as observed in patients with stage III non-small cell lung cancer (NSCLC) who experience prolonged survival after undergoing chemoradiotherapy followed by durvalumab treatment. Herein, we report three cases of severe airway stenosis due to stage III NSCLC in patients who underwent airway stenting and subsequent stent removal after chemoradiotherapy and durvalumab administration. The number of stents removed will likely increase in the future due to the high response rates to molecular drugs and immune checkpoint inhibitors.

1. Introduction

Airway stent placement is used as a bridge therapy for the treatment of stenosis caused by malignant airway disease. Even in the presence of severe respiratory failure, if airway stenting improves Eastern Cooperative Oncology Group Performance Status, it can act as a bridge to additional treatment options such as chemotherapy or radiotherapy. In 2018, durvalumab was approved in Japan for the post-chemoradiotherapy (CRT) treatment of non-small cell lung cancer (NSCLC) using the PACIFIC regimen [1]. The positive response of tumors to this additional treatment after airway stenting could allow for the removal of airway stents that are no longer needed. Our institution has encountered three cases of airway stenting removal since 2018, as reported herein, indicating that oncological emergencies due to airway stenosis may be bridged by temporary airway stenting followed by treatment with the PACIFIC regimen.

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2. Case presentation

2.1. Case 1

A 62-year-old man was referred to our hospital for airway stenosis management. Chest computed tomography (CT) revealed severe tracheal stenosis caused by a large mediastinal tumor (Fig. 1A). Oxygen saturation could not be maintained with room air and severe stridor was observed. Therefore, he was started on non-invasive positive pressure ventilation. Because the lesion occupied the length of the trachea, we opted to place an airway stent that could be removed upon completion of treatment. The patient underwent rigid bronchoscopy (EFER bronchoscope; Harada Corporation, Osaka, Japan) under general anesthesia. After balloon dilation of the trachea, an 18 × 80 mm AERO stent (Merit Medical Systems, South Jordan, UT, USA) was placed using a guide wire (Fig. 1B). Based on the diagnostic imaging and pathological findings, the patient was diagnosed with clinical T4N0M0 stage IIIA NSCLC. CRT consisting of carboplatin, paclitaxel, and concurrent thoracic radiation therapy (total doses of 50 Gy) was initiated, which elicited a partial tumor response, at which point durvalumab maintenance therapy was initiated. On day 121 post-stenting, the patient presented to our hospital with complaints of cough, sputum production, and recurrent pneumonia. The stent was removed without complications (Fig. 1C), after which the discomfort improved. Due to the diagnosis of Common Terminology Criteria for Adverse Events grade 1 drug-induced pneumonia, the durvalumab therapy was discontinued after three cycles. The patient continued his chemotherapy regimen but died on day 411 post-stenting due to disease progression and distant metastasis.

2.2. Case 2

A 73-year-old man was referred to our hospital for airway stenosis management. CT revealed enlargement of subcarinal lymph nodes with invasion into the carina and severe stenosis of the airway (Fig. 2A). Hypoxemia was observed and rhonchi were detected during auscultation. The patient underwent rigid bronchoscopy under general anesthesia. Following balloon dilation of the trachea and tumor debulking, a 15 × 12 mm Dumon Y-stent was placed using the pull-back method (Fig. 2B). Based on the diagnostic imaging and pathological findings, the patient was diagnosed with cT4N2M0 stage IIIB NSCLC. CRT consisting of carboplatin, paclitaxel, and concurrent thoracic radiation therapy (total doses of 60 Gy) was initiated 25 days post-stenting, which elicited a partial tumor response, at which point durvalumab maintenance therapy was initiated. The tumor remained in partial remission and the stent was removed without complications on day 266 post-stenting (Fig. 2C). The patient was still alive at 18+ months post-stenting with no signs of disease progression.

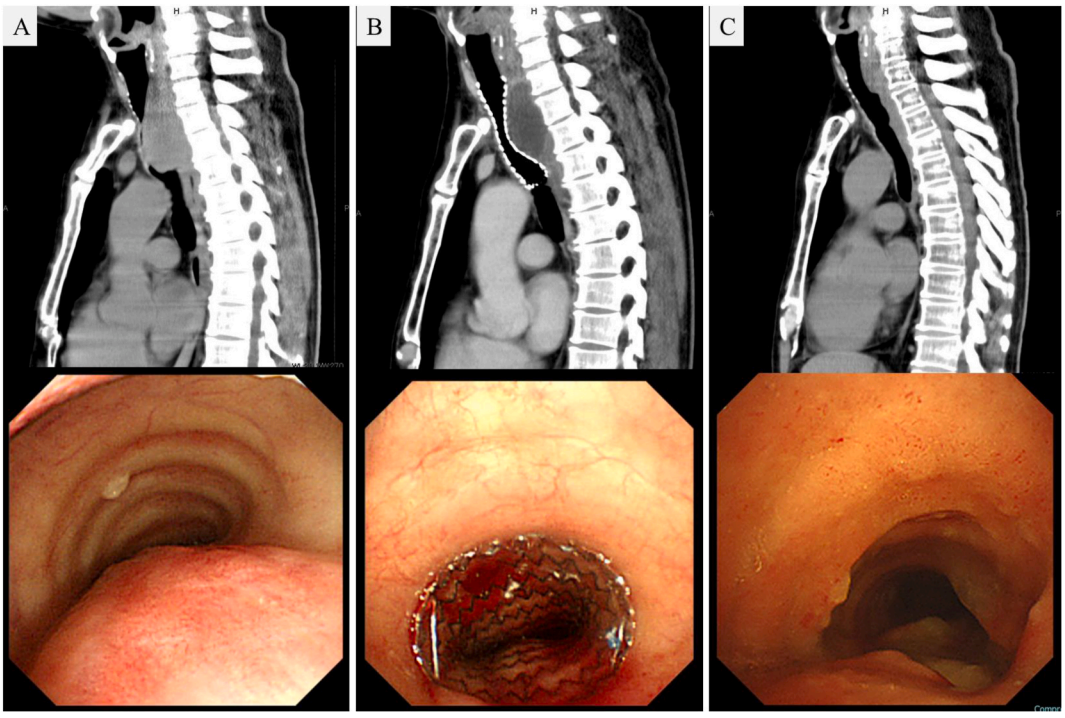

Fig. 1. (A) Computed tomography (CT) image upon admission and bronchoscopy image before stenting in case 1. (B) CT and bronchoscopy images after stenting. (C) CT and bronchoscopy images after stent removal.

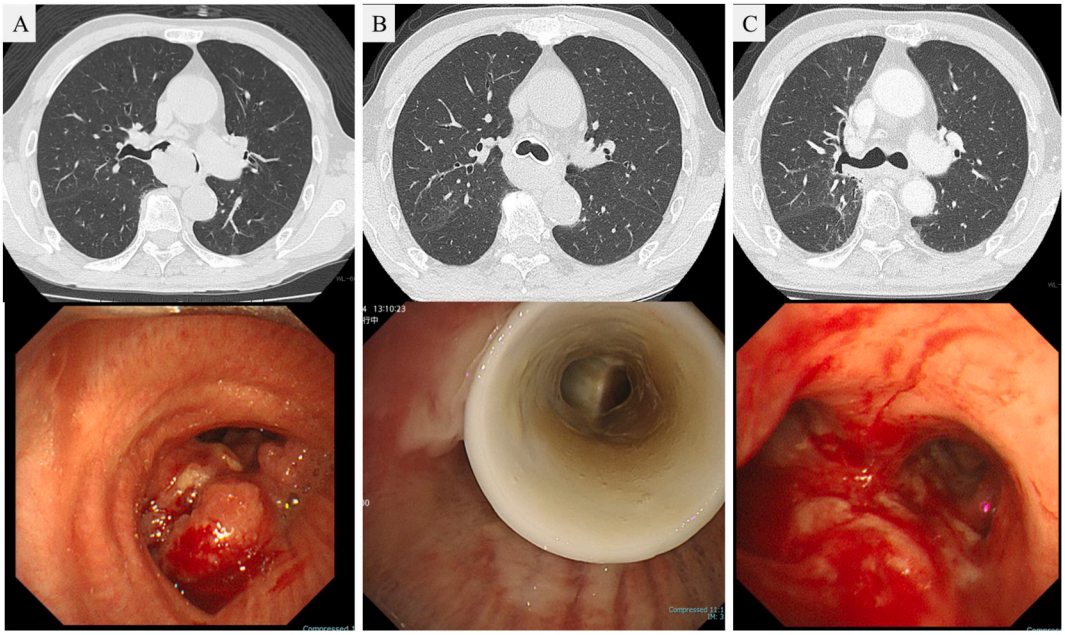

Fig. 2. (A)Computed tomography (CT) image upon admission and bronchoscopy image before stenting in case 2. (B) CT and bronchoscopy images after stenting. (C) CT and bronchoscopy images after stent removal.

2.3. Case 3

A 68-year-old man was referred to our hospital with tumor progression and tracheal edema caused by radiotherapy. Based on the diagnostic imaging and pathological findings in a nearby hospital, the patient was diagnosed with clinical T4N2M0 stage IIIB NSCLC. CRT consisting of cisboplatin, vinorelbine, and concurrent thoracic radiation therapy (planned doses of 60 Gy) had been initiated at the nearby hospital, and dyspnea appeared on day 2 of radiation therapy (total dose, 4 Gy). Upon referral to our hospital, CT indicated a risk of complete airway obstruction due to an enlarged primary lesion and tracheal edema (Fig. 3A). Oxygen saturation could not be

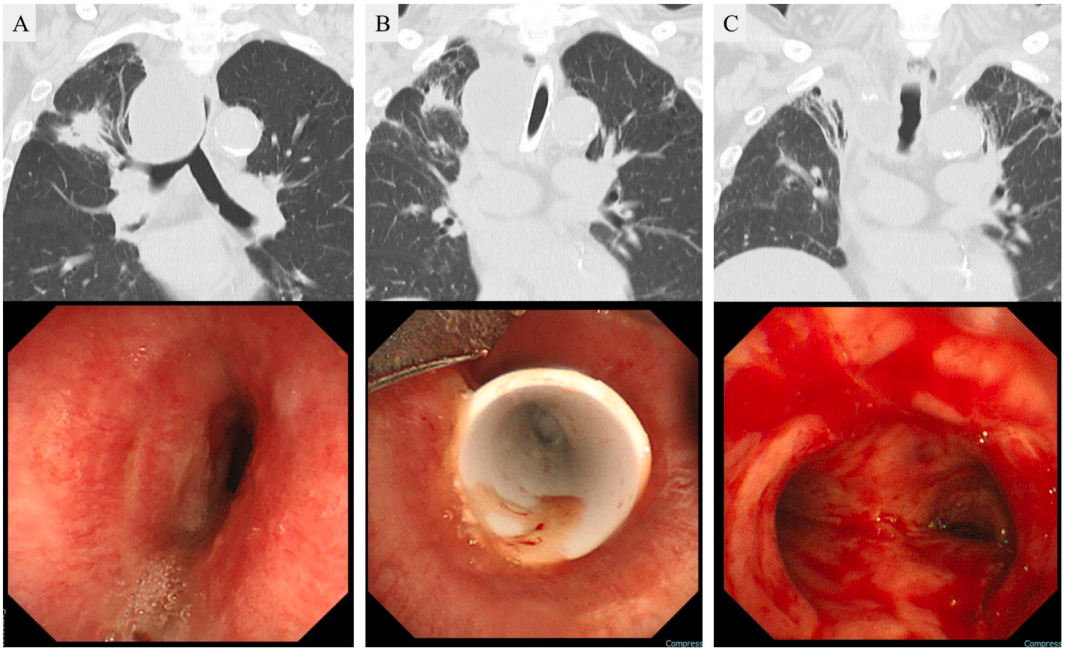

Fig. 3. (A) Computed tomography (CT) image upon admission and bronchoscopy image before stenting in case 3. (B) CT and bronchoscopy images after stenting. (C) CT and bronchoscopy images after stent removal.

maintained with room air, and severe stridor was observed. Two hours after admission, the patient underwent rigid bronchoscopy under general anesthesia. Following balloon dilation of the trachea, a 15 × 12 mm Dumon Y-stent was placed (Fig. 3B). The day after stenting, the patient was referred to a nearby hospital where his CRT treatment was restarted and completed. The tumor partially responded, at which point durvalumab maintenance therapy was initiated. The tumor remained in partial remission, and the Dumon Y-stent was removed without complications on day 360 post-stenting (Fig. 3C), after which the patient's cough and sputum production reduced. The patient was still alive at 12+ months post-stenting with no evidence of disease progression.

3. Discussion

The three cases presented herein are summarized in Table 1. Airway stenting in patients with malignant central airway obstructions has been reported to prolong survival time [2,3]. However, considering that the overall survival of patients with airway stents is reported to be approximately 3–6 months [4], all three patients presented herein exceeded the expected survival time, surviving for >1 year. Moreover, two of these patients (cases 2 and 3) were still alive with no evidence of disease progression at the time this manuscript was submitted. Thus, CRT followed by maintenance durvalumab and subsequent stent removal may prolong survival and overcome oncological emergencies in patients with NSCLC. Additionally, the median progression-free survival in CRT followed by durvalumab was 16.8 months (95 % confidence interval [CI], 13.0–18.1) vs. 5.6 months (95 % CI, 4.6–7.8) when followed by a placebo [1]. The use of durvalumab may maintain tumor shrinkage and decrease the probability of airway re-stenosis.

Treatment of oncologic emergencies with airway stenting will become increasingly important as the use of molecularly targeted drugs and immune checkpoint inhibitors (and combination with chemotherapy) increases. Silicone and AERO stents, which can be removed after airway stenosis improves in response to anticancer treatment, have good indications for use with high response rates. We previously reported that airway stenosis in anaplastic lymphoma kinase- and epidermal growth factor receptor-positive [5,6] stage IV lung adenocarcinoma with severe airway stenosis improves after the administration of tyrosine kinase inhibitor and the placement of an airway stent as bridge therapy, which is removed after improvement of the stenosis.

All patients presented herein had stage III locally advanced NSCLC and did not receive anticancer treatment or had just initiated CRT treatment; therefore, we selected the AERO (case 1) or silicone (cases 2 and 3) stents for placement, which could be removed following a response to the anticancer therapy. Comparatively, metallic airway stents are often difficult to remove from the airway, even if the stent is not necessary [7]. Additional treatment after stent placement improves patient prognosis, even in severe cases [8,9]; therefore, if a patient has a poor PS due to airway stenosis and is treatment-naive, a removable stent is preferable.

As shown in case 3, airway stenosis sometimes occurs immediately after initiation of treatment for lung cancer. Himeji et al. [10] reported that patients with stage IV NSCLC developed severe airway stenosis after the first administration of pembrolizumab, which was treated by Dumon Y-stent placement as bridge therapy. Severe stenosis, especially if it occurs between the trachea and carina, can be fatal if it results in severe respiratory failure; therefore, temporary airway stent placement should be considered as a bridge until radiotherapy, immunotherapy, and/or chemotherapy can be completed.

Improvement in PS after stent placement allows for additional treatments, even in patients with severe respiratory dysfunction. If the tumor responds to anticancer treatment, the stent becomes unnecessary, and the patient may be eligible for stent removal. Oki et al. [11] reported that the removal of airway stents improves pulmonary function and respiratory symptoms; therefore, an airway stent that is no longer necessary should be removed once additional treatment elicits a response. Table 2 shows the improvement in the peak flow (L/s) and forced expiratory volume in 1 s before and after stent removal, which resulted in the improvement of subjective symptoms or peak expiratory flow. There is a risk of pneumonia due to mucus plug obstruction if unnecessary stents are left in the airway; therefore, it may be preferable to remove stents as early as possible. Although the criteria and timing for removal are controversial, early stent removal once tumor reduction has been achieved by anticancer therapy and airway stenosis improvement is seen on imaging, may prevent stent-related complications. Some case of airway stent removal after CRT have been reported [12] and based on the success of the cases presented herein, stent removal for stage III airway stenosis may increase with the increased administration of the PACIFIC regimen. The ADRIATIC study recently reported the efficacy of CRT followed by durvalumab maintenance therapy for patients with limited-stage small-cell lung cancer (SCLC). Airway stenting therapy could be an important strategy for not only NSCLC but also SCLC in the near future [13].

4. Conclusion

Temporary oncological emergencies due to airway stenosis in patients with stage III NSCLC may be bridged by airway stenting. Furthermore, additional therapy with durvalumab after CRT may improve patient prognosis and ensure safe stent removal.

CRediT authorship contribution statement

Yuki Takigawa: Conceptualization, Data curation, Writing – review & editing. **Ken Sato:** Conceptualization. **Daisuke Minami:** Data curation. **Kenichiro Kudo:** Data curation. **Shoichiro Matsumoto:** Data curation. **Miho Fujiwara:** Data curation. **Takeru Ichikawa:** Conceptualization. **Tomoyoshi Inoue:** Data curation. **Suzuka Matsuoka:** Data curation. **Hiromi Watanabe:** Data curation. **Akiko Sato:** Data curation. **Hiroyasu Shoda:** Data curation. **Nobuhisa Ishikawa:** Data curation. **Keiichi Fujiwara:** Data curation. **Takuo Shibayama:** Data curation.

Table 1
Summary of cases who had successful stent removal after chemoradiotherapy followed by durvalumab for locally advanced non-small cell lung cancer with airway stenosis.

No.	Age (yrs)	Sex	Primary	Degree of stenosis[a]	Stent	Supplemental Oxygen (L/minutes)		ECOG PS		Chemotherapy	Radiation doze (Gy)	Cycles of DUR	OS (days)
						Before stenting	After stenting	Before stenting	After stenting				
1	62	M	Sq	5	AERO	NPPV	0	4	1	CBDCA + PTX	50	3	411
2	73	M	Sq	4	Dumon Y	5L/min	0	2	1	CBDCA + PTX	60	21	600>
3	68	M	Sq	5	Dumon Y	IPPV	0	4	1	CDDP + VNR	60	3	365>

Abbreviations: Yrs, years; Sq, squamous cell carcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; IPPV, Invasive positive pressure ventilation; NPPV, Non-invasive positive pressure ventilation; irAE, immune-related adverse events; CBDCA, carboplatin; PTX, paclitaxel; CDDP, cisplatin; VNR, vinorelbine DUR, Durvalumab.

[a] According to the classification described by Freitag L (Freitag L., Ernst A., Unger M., Kovitz K., Marquette C.H.: A proposed classification system of central airway stenosis. Eur Respir J 2007; 30: pp. 7–12. [Epub 2007 March 28]. PMID: 17392320) Class 4 indicates more than 75 % stenosed and 5 shows more than 90 % stenosed.

Table 2
Comparison of Respiratory function and symptoms before and after stentremoval

No.	Peak Flow (L/s)		FEV 1.0 (L)		Symptoms
	Before removal	After removal	Before removal	After removal	Relief of cough and sputum production
1	4.45	5.70	1.82	2.59	Yes
2	5.94	7.34	2.04	2.10	No
3	4.66	4.88	2.38	2.16	Yes

Abbreviations: forced expiratory volume in 1 s, FEV1.0.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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