Table 3—*Recurrences in Patients With GGO-Dominant Tumors*

Patient	Age, y	Sex	Whole Tumor Size, cm	Solid Tumor Size, cm	SUVmax	Procedure	ly	v	pl	n	Recurrence Site	Outcome
1	82	M	2.6	1.0	1.5	Segmentectomy	0	0	0	0	Peritoneum	25 mo, alive
2	61	F	3.0	1.2	1.8	Lobectomy	0	0	0	0	Brain	67 mo, alive

F = female; ly = lymphatic invasion; M = male; n = lymph node metastasis; pl = pleural invasion; v = vascular invasion. See Table 1 legend for expansion of other abbreviations.

Sublobar resection generally is indicated for a small lung cancer, such as those ≤ 2 cm.[3,18,19] However, in the current study, GGO-dominant T1b tumors rarely showed pathologic invasiveness or lymph node metastasis. Moreover, there were no differences in 3-year RFS and OS between patients with GGO-dominant

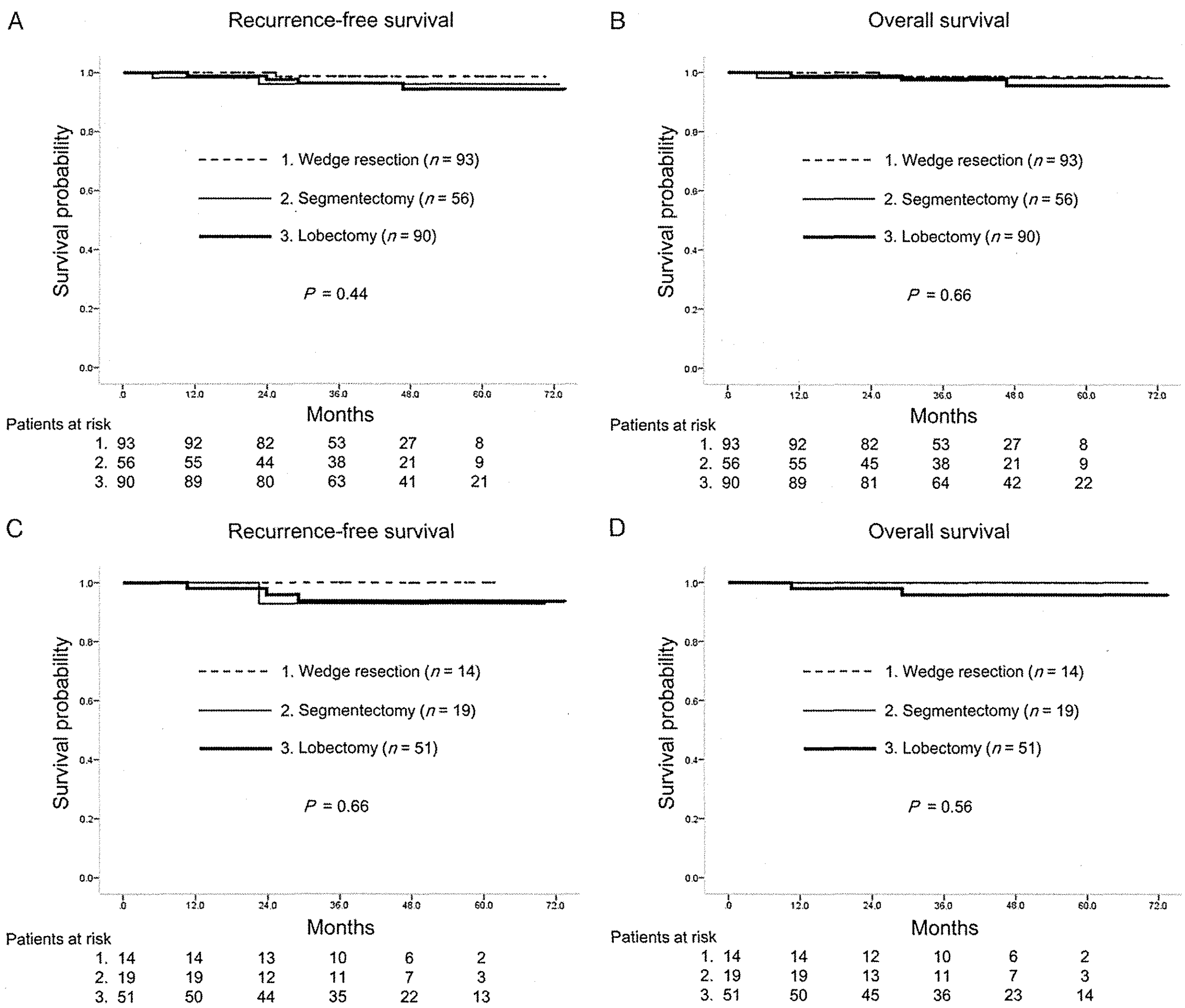

FIGURE 1. Recurrence-free survival (RFS) and overall survival (OS) curves for patients with ground-glass opacity (GGO) tumors who underwent lobectomy and sublobar resection. A, Three-year RFS rate for patients with GGO-dominant tumors who underwent wedge resection (98.7%; mean RFS, 69.8 mo; 95% CI, 68.6-70.9 mo), segmentectomy (96.1%; mean RFS, 70.3 mo; 95% CI, 67.3-73.4 mo), and lobectomy (96.4%; mean RFS, 71.4 mo; 95% CI, 61.9-73.7 mo; $P = .44$). B, Three-year OS rate for patients with GGO-dominant tumors who underwent wedge resection (98.7%; mean OS, 69.8 mo; 95% CI, 68.6-70.6 mo), segmentectomy (98.2%; mean OS, 71.4 mo; 95% CI, 69.0-73.7 mo), and lobectomy (97.6%; mean OS, 72.0 mo; 95% CI, 70.0-74.0 mo; $P = .66$). C, Three-year RFS rate for patients with GGO-dominant T1b tumors who underwent wedge resection (100%; mean RFS, not determined), segmentectomy (92.9%; mean RFS, 66.7 mo; 95% CI, 60.3-73.1 mo), and lobectomy (93.7%; mean RFS, 70.3 mo; 95% CI, 66.7-73.9 mo; $P = .66$). D, Three-year OS rate for patients with GGO-dominant T1b tumors who underwent wedge resection (100%; mean OS, not determined), segmentectomy (100%; mean OS, not determined), and lobectomy (95.9%; mean OS, 71.3 mo; 95% CI, 68.3-74.3 mo; $P = .56$).

Table 4—*Pathologic Findings for GGO-Dominant T1a and T1b Tumors*

Variable	T1a Tumors (n = 155)	T1b Tumors (n = 84)	*P* Value
Lymphatic invasion	1 (0.6)	2 (2.4)	.28
Vascular invasion	1 (0.6)	1 (1.2)	1.0
Pleural invasion	0 (0)	1 (1.2)	.35
Lymph node metastasis	0 (0)	2 (2.4)	.12

Data are presented as No. (%). See Table 1 legend for expansion of abbreviation.

T1b tumors who underwent lobectomy and those who underwent sublobar resection. Therefore, GGO-dominant T1b tumors could also be candidates for sublobar resection. We recommend segmentectomy and not wedge resection for sublobar resection of a GGO-dominant T1b tumor because these tumors could involve lymph node metastasis, and taking a sufficient surgical margin by wedge resection often is difficult in a T1b tumor.

In the current study, we found that two of 84 patients (2.4%) with GGO-dominant T1b tumors had lymph node metastases. No lymph node metastases were found for those with GGO-dominant T1a tumors. However, segmentectomy can approach hilar lymph nodes, whereas wedge resection cannot; thus, we should choose an optimal surgical procedure to avoid local recurrence in hilar lymph nodes, surgical stump, or residual lung. Segmentectomy would be superior to wedge resection for taking a sufficient surgical margin and for assessing hilar lymph nodes. Because sublobar resection includes both wedge resection and segmentectomy, it is necessary to distinguish between wedge resection and segmentectomy to clarify which procedure was used.

We encountered two distant recurrences with GGO-dominant T1b tumors: a brain metastasis after lobectomy and a peritoneal metastasis after segmentectomy, which could not be avoided even by standard lobectomy. One of the most important issues with sublobar resection is local control. Sublobar resection would be suitable for a GGO-dominant tumor because in this study, no intrathoracic local recurrence was observed, although a longer follow-up will be necessary before arriving at a definitive conclusion because of the indolent nature of GGO-dominant tumors.

Table 5—*Multivariate Analysis for Recurrence-Free Survival for Patients With GGO-Dominant Tumors*

Variable	HR (95% CI)	*P* Value
Age	1.08 (0.97-1.20)	.15
Male vs female sex	0.85 (0.18-3.91)	.83
T1b vs T1a descriptor	1.17 (0.20-6.70)	.86
Solid tumor size	6.37 (0.45-89.9)	.17
SUVmax	0.99 (0.52-1.90)	.99
Lobectomy vs sublobar resection	1.27 (0.20-7.93)	.82

HR = hazard ratio. See Table 1 legend for expansion of other abbreviations.

In the current study, the surgical procedure used and T descriptors were not independent prognostic factors of RFS in patients with GGO-dominant tumors, which also supports that a sublobar resection, such as a wedge resection or a segmentectomy, is suitable for GGO-dominant clinical stage IA lung adenocarcinomas, even for T1b tumors. In addition, solid tumor size and SUVmax were not independent prognostic factors of RFS. We previously reported that solid tumor size on HRCT scan and SUVmax on FDG-PET/CT scan were independent prognostic factors for lung adenocarcinoma.[14,20-22] However, patients with GGO-dominant lung adenocarcinomas have an excellent prognosis regardless of solid tumor size or SUVmax.

We speculate that GGO-dominant tumors indicate a uniform group exhibiting less tumor invasiveness and a favorable prognosis. In the current study, GGO-dominant tumors had small solid tumor sizes (median, 0.2 cm) and low SUVmax (median, 0.9). Prognosis based on solid tumor size and SUVmax may be useful, particularly for solid-dominant lung adenocarcinomas. In a previous study, we proposed N0 criteria that use a solid tumor size of < 0.8 cm or SUVmax of < 1.5 for predicting true N0 in clinical stage IA lung adenocarcinoma; patients who met these N0 criteria could be candidates for sublobar resection, such as wedge resection and segmentectomy.[11] Furthermore, patients with GGO-dominant tumors as well as those who meet the N0 criteria can be good candidates for wedge resection or segmentectomy.

Because this was a retrospective study, it is possible that patients who underwent sublobar resection were highly selective. Clinical trials comparing surgical results between lobectomy and sublobar resection (segmentectomy or wedge resection) for clinical T1aN0M0 NSCLC are currently being conducted by the Cancer and Leukemia Group B (CALGB 140503) and the Japan Clinical Oncology Group/West Japan Oncology Group (JCOG0802/WJOG4607L). These study results should indicate the significance of sublobar resection for small NSCLCs.[23] Regarding T1b tumors, a prospective study of segmentectomy for GGO-dominant tumors is warranted.

In conclusion, GGO-dominant clinical stage IA lung adenocarcinomas are a uniform group of tumors that exhibit low-grade malignancy and have a favorable prognosis. Patients with GGO-dominant tumors can be treated with wedge resection for T1a tumors and segmentectomy for T1b tumors.

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Author contributions: Drs Tsutani and Okada had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Dr Tsutani: contributed to study design, data acquisition, manuscript preparation, and approval of the final manuscript.
Dr Miyata: contributed to manuscript preparation and approval of the final manuscript.
Dr Nakayama: contributed to data acquisition, manuscript preparation, and approval of the final manuscript.
Dr Okumura: contributed to manuscript preparation and approval of the final manuscript.
Dr Adachi: contributed to manuscript preparation and approval of the final manuscript.
Dr Yoshimura: contributed to data acquisition, manuscript preparation, and approval of the final manuscript.
Dr Okada: contributed to study design, manuscript preparation, and approval of the final manuscript.
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Original Article

Sequential Stenting for Extensive Malignant Airway Stenosis

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Purpose: Malignant airway stenosis extending from the bronchial bifurcation to the lower lobar orifice was treated with airway stenting. We herein examine the effectiveness of airway stenting for extensive malignant airway stenosis.

Methods: Twelve patients with extensive malignant airway stenosis underwent placement of a silicone Dumon Y stent (Novatech, La Ciotat, France) at the tracheal bifurcation and a metallic Spiral Z-stent (Medico's Hirata, Osaka, Japan) at either distal side of the Y stent. We retrospectively analyzed the therapeutic efficacy of the sequential placement of these silicone and metallic stents in these 12 patients.

Results: The primary disease was lung cancer in eight patients, breast cancer in two patients, tracheal cancer in one patient, and thyroid cancer in one patient. The median survival period after airway stent placement was 46 days. The Hugh–Jones classification and performance status improved in nine patients after airway stenting. One patient had prolonged hemoptysis and died of respiratory tract hemorrhage 15 days after the treatment.

Conclusion: Because the initial disease was advanced and aggressive, the prognosis after sequential airway stent placement was significantly poor. However, because respiratory distress decreased after the treatment in most patients, this treatment may be acceptable for selected patients with extensive malignant airway stenosis.

Keywords: airway stent, malignant airway stenosis, metallic stent, silicone stent

Introduction

Airway stent placement for malignant airway stenosis relieves symptoms immediately and improves quality of life. The clinical indications for airway stenting are (1) extrinstic stenosis of the central airway with or without intraluminal components; (2) complex, inoperable tracheobronchial strictures; and (3) recurrent intraluminal tumor growth.[1] The anatomical criteria for airway stenting are a stenosis that is distal to the cricoid and proximal to the lobar orifice, as well as the presence of patent lobar or segmental orifices.[2] Extensive airway stenosis, such as stenosis extending from the bronchial bifurcation to the lower lobar orifice, may also be treated by airway stent placement when the stenosis site meets both the clinical and anatomical criteria. For these patients, we sequentially place a silicone Y-shaped stent at the bronchial bifurcation and an expandable metallic stent at the distal airway. In the present study, we investigated the clinical courses of patients treated by sequential airway

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stenting and examine the effectiveness of airway stenting for extensive malignant airway stenosis.

Materials and Methods

Informed consent was obtained from all patients included in this study. Additionally, the institutional ethics committee approved this study. From January 2003 to December 2012, a total of 270 patients with malignant airway stenosis were treated in our institute. All stenosis sites met both the clinical and anatomical criteria. Twelve of these 270 patients with airway stenosis extending from the central to the peripheral airways were treated with two airway stent placement techniques. The silicone Dumon Y stent (Novatech, France) is recommended for treatment of airway stenosis at the bronchial bifurcation.[3,4] When the length of the airway stenosis is extensive, an uncovered metallic stent should be chosen to maintain mucociliary clearance.[5,6] Because peripheral airway stenosis was present in our patients, tapered airway stents were required. Therefore, we used the silicone Dumon Y stent at the bronchial bifurcation and the tapered Spiral Z-stent (Medico's Hirata, Japan) peripheral to the main bronchus. The reticulation of the Spiral Z-stent is loose enough to maintain ventilation of the right upper lobe when it is placed from the right main bronchus to the trunks intermedius. These two airway stents were placed simultaneously using rigid bronchoscopy under general anesthesia. The endoluminal tumor at tracheal bifurcation was debulked. In first, the tumor tissue on either side which did not lead peripheral stenosis was debulked to maintain intraoperative ventilation. After sufficient airway preparation, the silicone Dumon Y stent was placed at the tracheal bifurcation. The Spiral Z-stent was sequentially placed internally from the end of the Dumon Y stent using a guide wire under fluoroscopic guidance. We retrospectively analyzed the therapeutic efficacy of the sequential placement of these silicone and metallic stents. Patients treated with silicone stents for fistulae between an airway and an adjacent organ were excluded from this study. The overall survival rate after airway stent placement was calculated by the Kaplan–Meier method.

Results

Two etiologies of airway stenosis were identified in these patients. A noticeably enlarged lymph node of the tracheal bifurcation caused airway stenosis through the tracheal bifurcation to either side of the peripheral airway

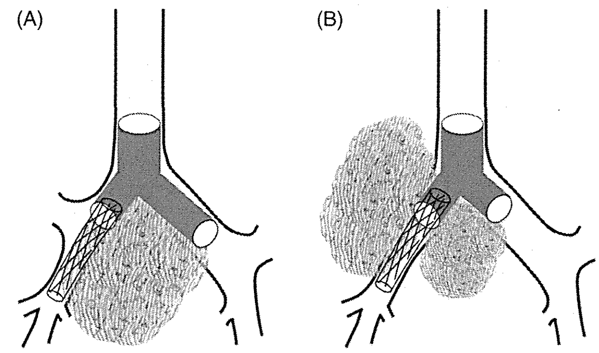

Fig. 1 (**A**) Noticeably enlarged lymph node of the tracheal bifurcation caused airway stenosis through the tracheal bifurcation to the peripheral airway on either side. (**B**) Combination of a mass lesion in the right upper lobe and an enlarged lymph node of the tracheal bifurcation caused extensive airway stenosis.

(**Fig. 1A**). Right-sided airway stenosis was observed in seven patients, and left-sided airway stenosis was observed in only one patient. Another etiology of extensive airway stenosis was the combination of a mass lesion in the right upper lobe and an enlarged lymph node of the tracheal bifurcation (**Fig. 1B**). This type of airway stenosis was observed in four patients. In these patients, the tumor tissue from the lymph node caused airway stenosis at the tracheal bifurcation, and the tumor tissue from the right upper lobe caused airway stenosis through the right main bronchus to the trunks intermedius. **Table 1** shows 12 patients in this study from past to present. Case 1 was treated most recently. The 12 patients comprised five men and seven women with a mean age of 59 years (range, 44–78 years). The primary disease was lung cancer in eight patients, breast cancer in two patients, tracheal cancer in one patient, and thyroid cancer in one patient. All patients exhibited a combination of endoluminal and extraluminal type compression.[1] Both the Hugh–Jones classification (HJ classification) and performance status (PS) improved in nine patients, remained unchanged in two patients, and worsened in one patient (Case 11) after airway stent placement (**Fig. 2**). Case 11 had developed hemoptysis and died of respiratory tract hemorrhage 15 days after the treatment. Treatment-related complication and death was observed in Case 11 only. The mortality rate associated with this treatment was 8.3%. **Figure 3** shows the survival curves after airway stent placement. The median survival period after airway stent placement was 46 days. The 1-month, 6-month, and 1-year survival rates were 58%, 25%, and 13%, respectively. Eleven

Table 1 Characteristics of the patients

Case	Age	Gender	Primary disease	HJ		PS		Treatment site	Initial treatment	Postoperative treatment	Survival time (days)	Outcome	Cause of death
				before	after	before	after						
1	70	male	lung cancer	4	1	4	1	bifurcation to TIM	none	radiotherapy	59	dead	cachexia
2	57	male	lung cancer	3	2	2	1	bifurcation to TIM	none	chemotherapy	227	alive	-
3	50	female	breast cancer	5	2	3	2	bifurcation to TIM	chemotherapy	radiotherapy	40	dead	RF
4	44	male	lung cancer	5	2	3	1	bifurcation to TIM	surgery, chemothrary	none	146	dead	RF
5	78	female	lung cancer	5	5	4	4	bifurcation to TIM	SBRT	none	13	dead	RF
6	56	male	lung cancer	3	2	2	1	bifurcation to TIM	chemoradiotherapy	none	29	dead	RF
7	45	female	lung cancer	4	1	3	1	bifurcation to TIM	chemotherapy	none	14	dead	cachexia
8	74	female	thyroid cancer	4	2	3	2	bifurcation to TIM	surgery	none	25	dead	RF
9	54	female	breast cancer	4	2	2	1	bifurcation to TIM	surgery, chemothrapy	radiotherapy	207	dead	RF
10	67	female	tracheal cancer	5	2	4	1	bifurcation to TIM	chemoradiotherapy	none	745	dead	RF
11	55	female	lung cancer	2	3	1	3	bifurcation to TIM	chemotherapy	none	15	dead	RF
12	61	male	lung cancer	4	4	4	4	bifurcation to LMB	chemoradiotherapy	none	51	dead	RF

HJ: Hugh-Jones classification; PS: performance status; RF: respiratory failure; SBRT: stereotactic body radiotherapy; TIM: truncus intermedius; LMB: left main bronchus

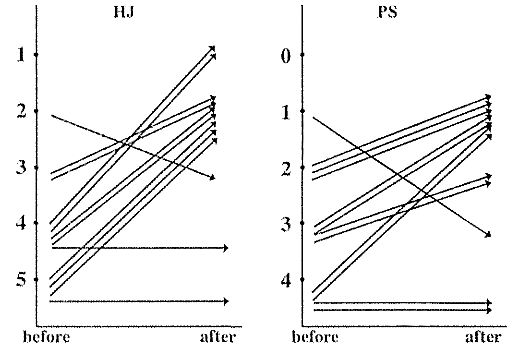

Fig. 2 Hugh–Jones classification (HJ) and Performance Status (PS) before and after airway stent placement.

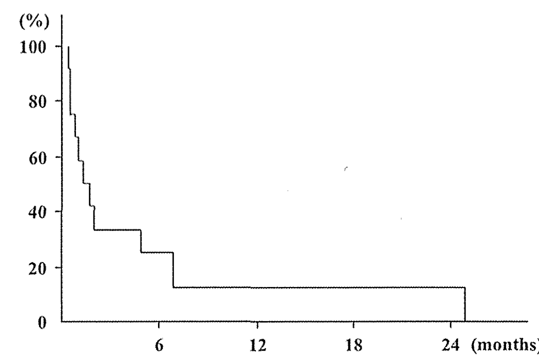

Fig. 3 Overall survival curve after airway stent placement.

patients died of carcinoma during follow up period. Causes of death were respiratory failure in nine patients and cachexia in two patients (**Table 1**).

Discussion

In this study, the median survival period after airway stent placement was 46 days, and our patients had a poorer prognosis than did those in a previous report.[7] One patient (Case 10) who survived for a long period of time, had a tracheal adenoid cystic carcinoma. Because all patients except one had aggressive and advanced carcinoma, the post-treatment prognosis was very poor. As in the present study, the 6-month survival rate after interventional treatment among patients with malignant airway stenosis extending from the trachea to the bronchus was reportedly 20%.[8] However, the respiratory distress decreased after airway stent placement in most patients of the present study. We have shown that airway stenting for extensive malignant airway stenosis may be an effective treatment for select patients. Treatment-related complication and death was observed in only one case. The morbidity rate of airway stenting for malignant airway stenosis is reportedly 20% to 42%,[1,9] and the mortality rate is reportedly 8%.[7] Sequential airway stenting may be an acceptable treatment.

Four patients underwent additional treatment after airway stent placement in this study. Two of these patients had never received initial treatment, and primary lung cancer was diagnosed using the tumor tissue obtained at biopsy during airway stent placement. Case 1 was a 70-year-old male patient who was treated with radiotherapy for primary disease after airway stent placement. Case 2 was a 57-year-old male patient who was treated with four cycles of chemotherapy comprising cisplatin plus pemetrexed after airway stent placement and experienced long-term survival. Airway stent placement plays a role as a bridge procedure to additional anticancer treatment. Airway stenting is recommended for patients with airway stenosis caused by an untreated malignant tumor when no other reliable treatments are available.

The HJ classification remained poor and PS persisted in two patients after airway stent placement. Case 5 was a 78-year-old female patient. She was in respiratory failure and required mechanical ventilation upon arrival. Her ventilation did not improve, and she died of respiratory failure 13 days after stent placement. Because pneumonia and long-term mechanical ventilation resulted in organization of her peripheral lung tissue, her respiratory status did not improve after resolution of the airway stenosis. Stent placement should be avoided when nonviable lung tissue is present beyond the obstruction. Case 12 was a 61-year-old male patient. His primary disease was lung cancer. Chest CT showed extensive airway stenosis through the tracheal bifurcation to the left main bronchus caused by an enlarged lymph node of the tracheal bifurcation (**Fig. 4A**). He underwent placement of a silicone Dumon Y stent at the tracheal bifurcation and a Spiral Z-stent at the left main bronchus. Chest roentgenograms showed increased permeability in the left lung field (**Fig. 4B** and **4C**). Although the airway stenosis was resolved, his respiratory status and general condition did not improve. The airway stent might have expanded laterally against the hard tumor tissue at the bronchial bifurcation and pressed against the wall of the pulmonary artery, followed by a decrease in the blood flow on the treatment side (**Fig. 4D**). This ventilation–perfusion imbalance may be a reason for the lack of improvement in respiratory distress after the resolution of airway stenosis. In particular, when airway stenosis extends peripherally, airway stent placement may induce pulmonary arterial compression. However, it is difficult to predict the development of ventilation–perfusion imbalance after airway stent placement.

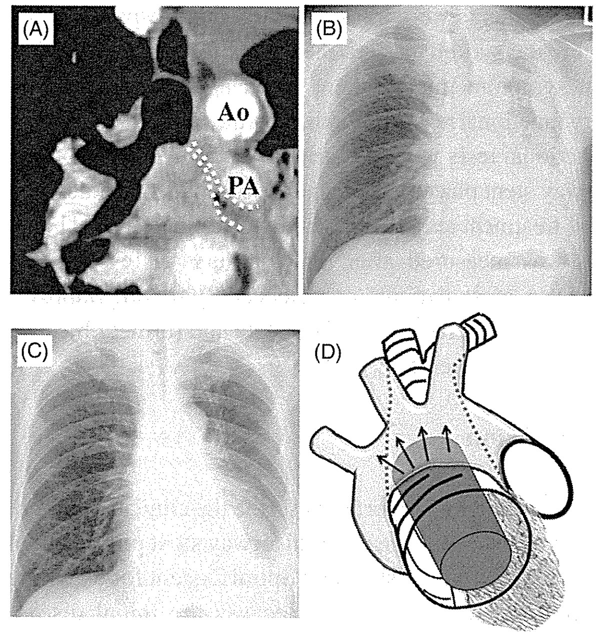

Fig. 4 (**A**) Chest computed tomography showed extensive airway stenosis through the tracheal bifurcation to the left main bronchus, located in immediate proximity to the pulmonary artery. (**B**) Chest X-ray before airway stent placement. (**C**) Silicone Dumon Y stent was placed at the tracheal bifurcation, and the Spiral Z-stent was then placed at the left main bronchus. (**D**) Airway stent expanded laterally against the hard tumor tissue at the bronchial bifurcation and pressed against the wall of the pulmonary artery.

Case 7 was a 45-year-old female patient. She was relieved from respiratory distress and came home after airway stenting. However, she died of rapid progression of cachexia 14 days after airway stent placement. We could not estimate a clinical coarse of the patient before airway stent placement. It is difficult to predict a rapid progression of clinical condition of patients with advanced carcinoma.

There are limitations in this study. The number of patients was extremely small. We could not objectively measure changes in the respiratory status before and after the treatment. The respiratory and general conditions were mainly measured by physical examination. Nine patients underwent stent placement on the day of admission.

Seven patients were transferred to other hospitals within a few days after the treatment, and three patients without symptom improvement could not undergo respiratory functional testing after the treatment. Thus, respiratory functional tests were performed in seven patients before airway stent placement. And only two patients underwent post-treatment respiratory functional testing. Arterial blood gas was measured after the treatment in few patients because most patients experienced symptom improvement. Accumulation of patient data and further objective examination are necessary.

Conclusion

This is the first report to describe the clinical course of patients undergoing sequential airway stent placement of a silicone Dumon Y stent and Spiral Z-stent for extensive malignant airway stenosis. Because the initial disease was advanced and aggressive, the prognosis after sequential airway stent placement was significantly poor. However, respiratory distress decreased after the treatment in most patients; thus, this treatment may be recommended for select patients.

Disclosure Statement

The authors of this manuscript have no relevant financial or other potential conflict of interest.

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CASE REPORT

硬性気管支鏡下に摘出した長期介在気道異物の１例

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丁　奎光[1]；多田弘人[1]

要約 ―― 背景．長期介在気道異物は肉芽形成のため摘出が困難となる．約１年間介在した気道異物を硬性気管支鏡下に安全に摘出できた症例を報告する．症例．68 歳，男性．約１年前に歯科治療中に歯冠を喪失．一時的に咳嗽を認めたが軽快したため放置していた．約１カ月前より乾性咳嗽が出現して持続していた．胸部Ｘ線，胸部 CT で右中間気管支幹内の歯冠と右下葉末梢に無気肺を認めた．軟性気管支鏡下に歯冠の除去を試みたが，肉芽により歯冠は強固に固定されており摘出することはできなかった．そこで，全身麻酔下に硬性気管支鏡を用いて異物除去を施行した．歯冠を鰐口鉗子で把持し硬性気管支鏡ごと回転・牽引することで安全に摘出することができた．翌日には軽快退院し，異物除去４週間後には著明な肉芽組織の減少を認めた．結語．肉芽内に嵌頓するような気道異物を摘出する際には，異物に回転力を伝える必要がある．硬性気管支鏡下異物除去は摘出困難な気道異物に対して有効な手段である．

（気管支学．2014;36:605-610）

索引用語 ―― 気道異物，硬性気管支鏡，肉芽組織

はじめに

気道内に長期間異物が介在すると，肉芽形成のため摘出が困難となる．約１年間介在した気道異物を硬性気管支鏡下に安全に摘出できた症例を報告し，硬性気管支鏡下に気道異物を除去する際の，硬性気管支鏡の特性と手技の工夫について考察する．

症　例

症例：68 歳男性．

主訴：乾性咳嗽．

併存疾患：特記事項なし．

喫煙歴：20 本/日（20～60 歳）．

現病歴：約１年前に歯科治療中に歯冠を喪失．一時的に咳嗽を認めたが軽快したため放置していた．約１カ月前より乾性咳嗽が出現して持続していた．

身体所見：身長 165 cm，体重 72 kg，体温 36.5℃，SpO_2 99％（room air），右下肺野で軽度呼吸音の減弱を認めた．

画像所見：胸部Ｘ線検査（Figure 1A，1B）にて右肺野に歯冠を認めた．胸部 CT 検査では右中間気管支幹内に歯冠が認められ（Figure 1C），右下葉末梢に無気肺を認めた（Figure 1D）．

気管支鏡所見：右中間気管支幹内に歯冠が嵌頓していた（Figure 2A，2B）．歯冠周辺の気道粘膜は浮腫状で著明な肉芽の形成を認めた（Figure 2C，2D）．

血液検査所見：白血球 10670/mm^3，CRP 2.03 mg/dl と炎症所見の上昇を認めた．

治療経過：軟性気管支鏡下に生検鉗子，キュレット鉗子，バスケット鉗子を用いて歯冠の除去を試みたが，肉芽により歯冠は強固に固定されており摘出することはできなかった．そこで，全身麻酔下に硬性気管支鏡を用いて異物除去を施行する方針とした．

手術所見：全身麻酔下に硬性気管支鏡を挿入した．硬性気管支鏡は Dumon-Harrell universal bronchoscope（EFER, La Ciotat, France）を使用した．5 mm の直視鏡を挿入し，中間気管支幹内に嵌頓する歯冠を確認した．鰐口鉗子で把持して牽引したが，肉芽内からの摘出は容易ではなかった．鰐口鉗子を把持し回転させながら硬性気管支鏡ごと牽引することで歯冠は肉芽内から移動し始め（Figure 3），歯冠を把持した状態で硬性気管支鏡ごと気道外に摘出した．再度硬性気管支鏡を挿入し，歯冠除去後の気道粘膜からの出血に対してはボスミン加生理食塩水の散布を施行した．

術後経過：術翌日に軽快退院となった．気道異物除去後４週間目の気管支鏡所見では気道の開存は良好で，肉芽組織の著明な縮小を認めた（Figure 4）．

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受付日：2014 年３月 12 日，採択日：2014 年６月４日．

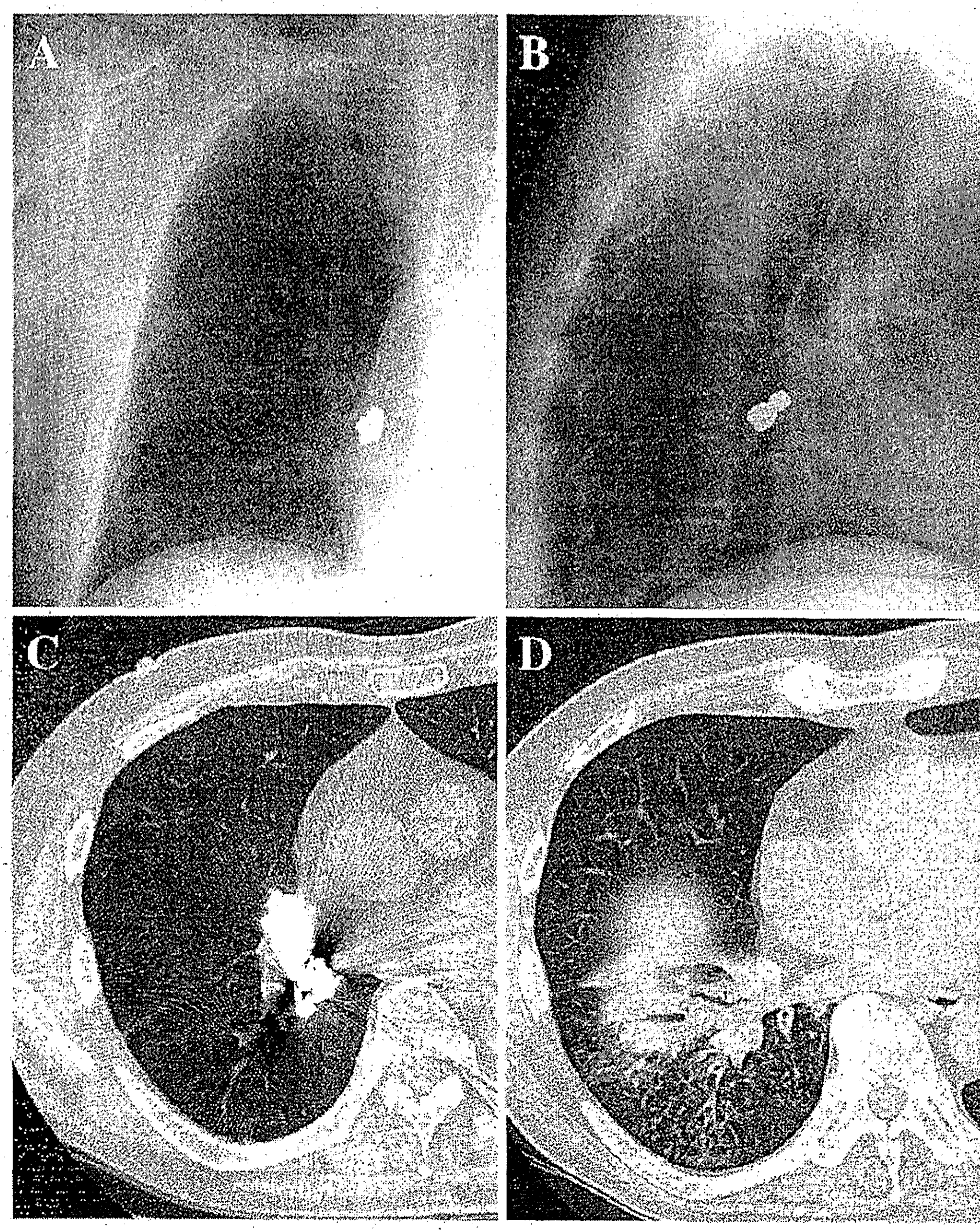

Figure 1. **A, B:** Chest radiography revealed a foreign body in the right lung field. **C, D:** Chest CT showed a metal crown in the right truncus intermedius that had induced atelectasis in the right lower lobe.

考　察

我々は硬性気管支鏡下に摘出した長期介在気道異物症例を報告した．気道異物症例の28%は誤嚥当日に摘出される．一方で1カ月以上の長期介在例は気道異物症例の16%と報告されている[1]．異物が嵌頓し固定してしまえば症状は消失する．異物発見時に無症状の症例が24%あり，固定による症状の消失が異物の長期介在につながると考えられる[2]．気道内に異物が介在することにより異物周囲の反応性炎症が始まり，4〜5週間後には増殖性肉芽病変が形成される[3]．気道内に2年間辺縁が平滑な石が介在した場合，周囲の気道粘膜に肉芽形成はなかったと報告されており[4]，増殖する肉芽の程度は異物の形状によるところが大きいと考えられる．歯冠は辺縁が複雑な形状

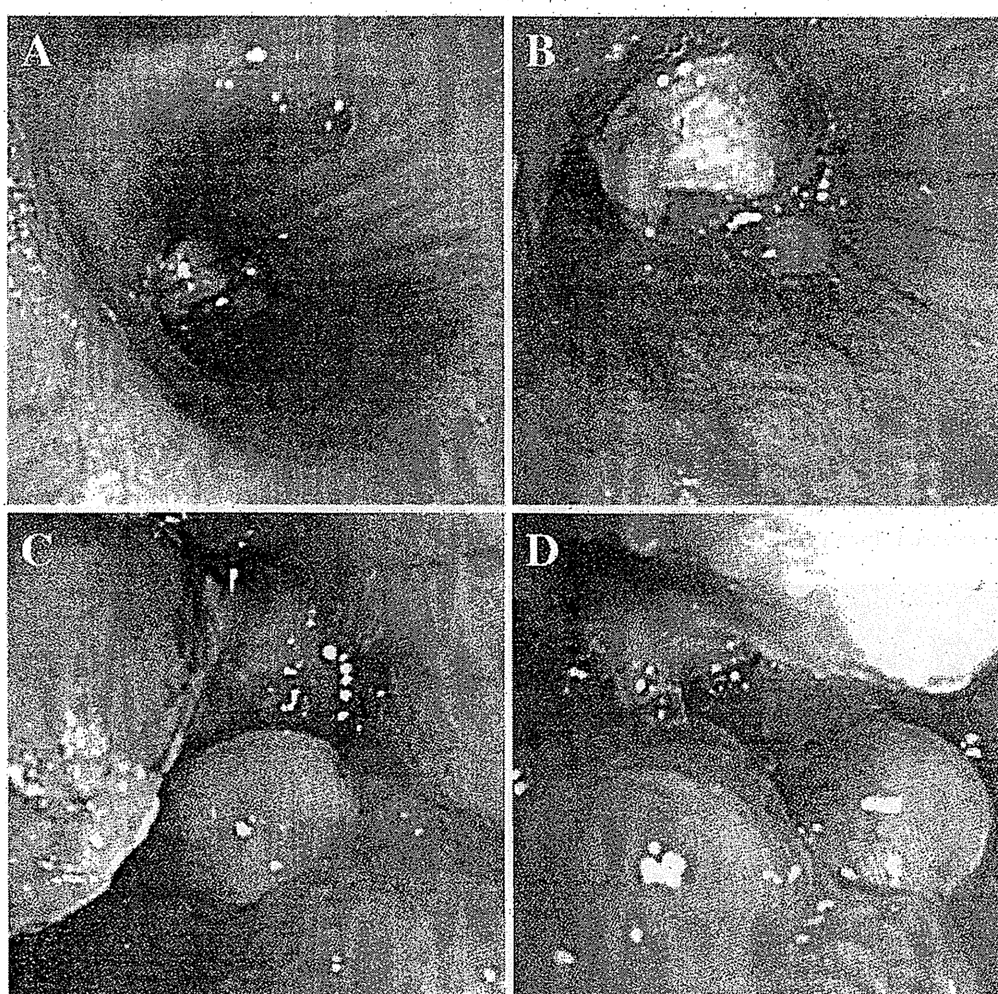

Figure 2. A, B: A flexible bronchoscopic examination showed a metal crown in the right truncus intermedius. C, D: Severe granulation tissue was noted surrounding the metal crown in the right truncus intermedius. The metal crown was incased in the granulation tissue.

をしており，約1年の介在中に著明な肉芽が形成されていた．歯冠は増生した肉芽内に嵌頓した状態で発見された．自験例のように歯冠などの比較的大きな異物が1年間も気道に介在し，内視鏡下に摘出できた詳細な報告はない．

一般的に軟性気管支鏡下に摘出不可能な気道異物は5%未満である[3]．したがって気道異物が疑われたとき，まずは軟性気管支鏡下に観察および摘出を試みるべきである．軟性気管支鏡下に摘出ができなかったときに硬性気管支鏡下での摘出が選択される．硬性気管支鏡の長所は以下の点が挙げられる．中枢気道では安定した広い視野が確保できる．強い把持力のある大きな鉗子を使うことができる．手指の微妙な力の変化が直接鉗子の先端に伝わるため，微細な操作が可能．出血を含めた大量の分泌物に対応可能．一方で短所は以下の点である．全身麻酔が必要．除去可能な異物は区域支までとされている[5]．

しかし，硬性気管支鏡を用いて透視下に鉗子を挿入することで亜々区域支内の異物が除去可能であったとの報告も認められる[6]．もっとも報告例はB^9末梢の異物で直線的に鉗子が挿入しやすい部位と考えられ，一般的には上葉や亜区域支内の異物では軟性気管支鏡が有利と考えられる．自験例においても軟性鏡下による気道異物を試みたが摘出できず，硬性気管支鏡下での摘出を施行した．軟性気管支鏡下でも確実に把持できればある程度の牽引力が異物に伝わると考えられる．しかし異物が肉芽内に嵌頓しているような場合では，嵌頓を解除しなければ異物は受動しない．そのために最も必要な力線は長軸方向ではなく短軸方向，つまり回転力と考えられる．軟性鏡

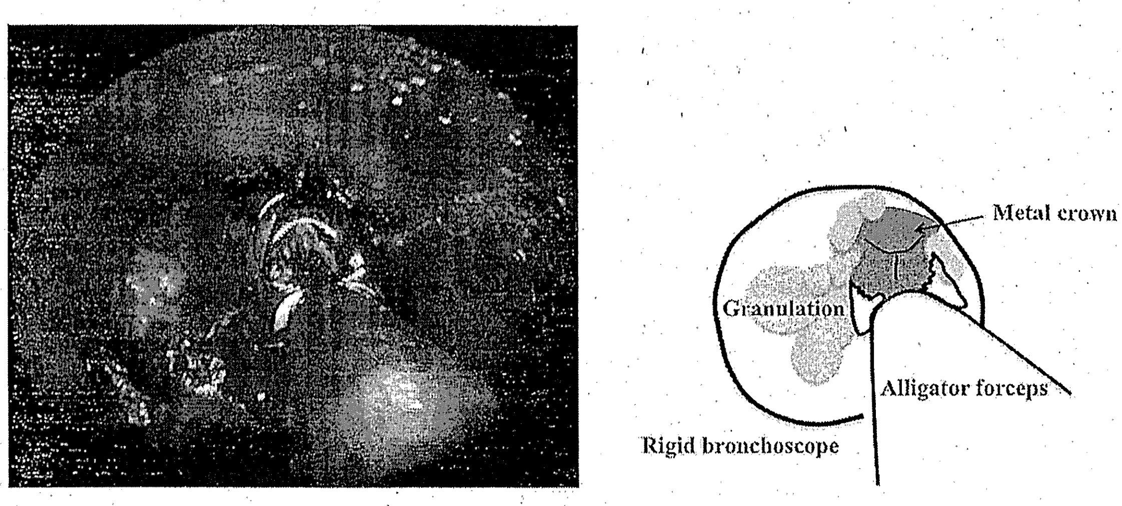

Figure 3. We grasped the metal crown with alligator forceps and swung it back and forth, exerting sufficient torque to release it from the granulation tissue.

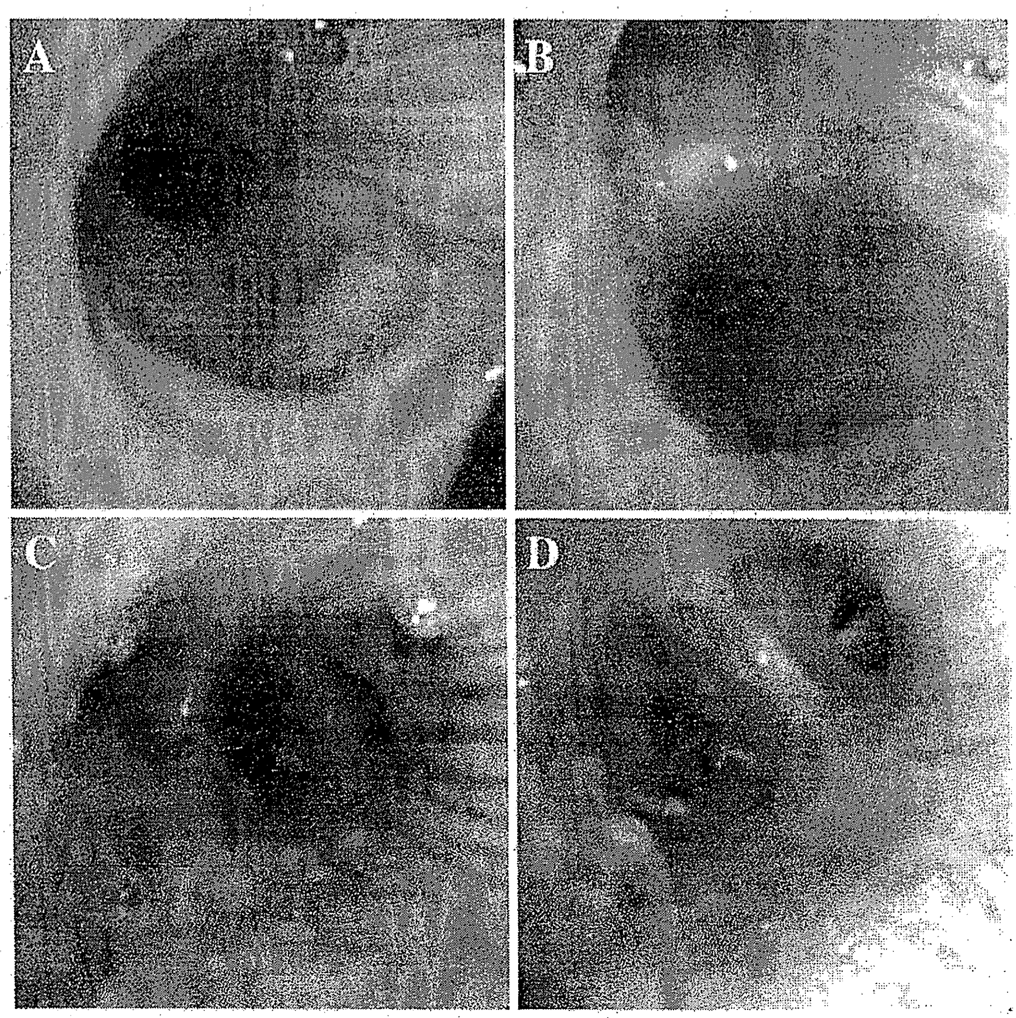

Figure 4. The patient was reevaluated four weeks later. The examination showed that the amount of granulation tissue had decreased significantly.

下に鉗子で異物を把持できたとしても，鉗子のワイヤー部分を介して強い回転力を伝えることは不可能である．自験例では硬性鏡下に鉗子で歯冠を強く把持し，さらに強い回転力を直接伝えられたことが体外への摘出に最も有効に作用したと考えられる．一方で，歯冠は中間気管支幹内の肉芽内に嵌頓していたため，硬性気管支鏡下に中間気管支幹内の異物を把持し回転させる際には，鉗子の操作部と内視鏡のカメラヘッドが接触して鉗子のみを回転させることはできない．一時的に換気を止めた状態で硬性気管支鏡ごと回転させる必要があった．内視鏡画像は歯冠を把持した鉗子に占拠され，さらに画像自体が回転してしまうため内視鏡画像による内腔の観察は困難であった．そこで，透視下に硬性気管支鏡と気道の向きを確認しながら，鉗子で歯冠を把持した状態で硬性気管支鏡ごと回転・牽引することで，安全に摘出することができた．

まとめ

硬性気管支鏡下に長期介在気道異物を摘出することができた．肉芽内に嵌頓するような気道異物を摘出する際には，異物に回転力を伝える必要がある．硬性気管支鏡下異物除去は，肉芽形成を来しているような摘出困難な気道異物に対して極めて有効と考えられる．

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Removal of a Long-term Lodged Bronchial Foreign Body Using a Rigid Bronchoscope

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ABSTRACT —— *Background.* Granulation tissue prevents the removal of foreign bodies lodged in bronchial tissue for relatively long periods. We herein report the case of a patient with a bronchial foreign body lasting for one year. We were able to remove the object safely using a rigid bronchoscope. *Case.* A 68-year-old man had lost a metal crown during dental therapy one year previously. He presented to our institute complaining of a persistent cough that had started one month prior to his visit. Chest radiography revealed a foreign body in the right lung field. Chest computed tomography showed a metal crown in the right truncus intermedius that had induced atelectasis in the right lower lobe. Because the metal crown was fixed in granulation tissue, we were unable to remove it using a flexible bronchoscope. We therefore chose a rigid bronchoscope to remove the foreign body under general anesthesia. During the procedure, we grasped the metal crown with alligator forceps and swung it back and forth, exerting sufficient torque to release it from the granulation tissue. We then pulled the crown away from the tissue and removed it. The patient was discharged the following day. A follow-up visit four weeks later showed that the amount of granulation tissue had decreased significantly. *Conclusions.* Sufficient torque must be exerted to remove bronchial foreign bodies fixed in granulation tissue. We successfully removed the foreign object in this case using a rigid bronchoscope.

(*JJSRE.* 2014;36:605-610)

KEY WORDS —— Bronchial foreign body, Rigid bronchoscope, Granulation tissue

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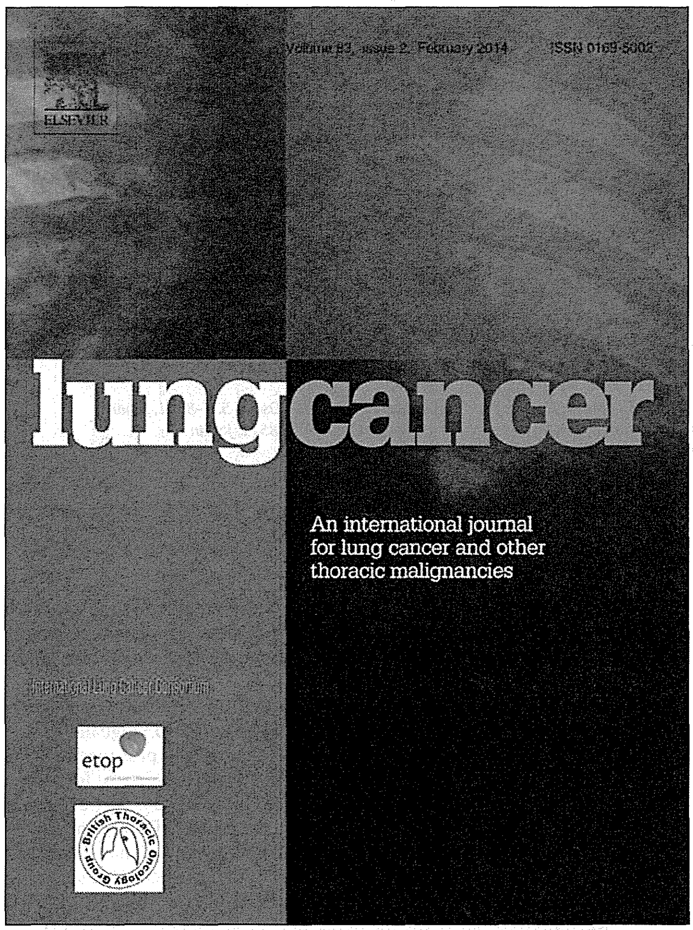
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Case report

Bilateral ovarian metastasis of non-small cell lung cancer with *ALK* rearrangement

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ABSTRACT

The discovery of a distinct subtype of non-small cell lung cancer (NSCLC) positive for rearrangement of the anaplastic lymphoma kinase gene (*ALK*) has had a substantial impact on personalized therapy for this disease. The clinical features associated with metastasis in individuals with *ALK* rearrangement-positive NSCLC remain to be fully characterized, however. We now describe a case of ovarian metastasis from NSCLC with *ALK* rearrangement. A 39-year-old woman underwent a right middle lobectomy for acinar-type adenocarcinoma of the lung (pT2aN2M0, stage IIIA). Fluorescence in situ hybridization (FISH) analysis of the resected tumor tissue revealed the presence of an *ALK* rearrangement. Twenty months later, a large intrapelvic mass was detected in the patient at follow-up. She underwent both left salpingo-oophorectomy and right ovarian cystectomy. Histological examination of the ovarian tumors showed acinar adenocarcinoma, and FISH analysis revealed the presence of *ALK* rearrangement, confirming a diagnosis of *ALK* rearrangement-positive NSCLC with ovarian metastasis. Although the ovary is an uncommon site for metastasis from lung cancer, physicians should be aware of the possibility for such metastasis during follow-up for female patients with *ALK* rearrangement-positive NSCLC. Further investigation is warranted to clarify the incidence of ovarian metastasis in NSCLC patients with *ALK* rearrangement.

1. Case presentation

A 39-year-old woman who smoked one pack per day underwent a right middle lobectomy for adenocarcinoma of the lung (pT2aN2M0, stage IIIA) in August 2009. Mutation analysis of the resected tissue revealed that the tumor was wild type for the epidermal growth factor receptor gene (*EGFR*). Fluorescence in situ hybridization (FISH) analysis of the tumor tissue with break-apart probes for the anaplastic lymphoma kinase gene (*ALK*) revealed the presence of an *ALK* rearrangement, however, and subsequent reverse transcription and polymerase chain reaction analysis confirmed the presence of transcripts for the fusion gene. The patient received four cycles of combination therapy with cisplatin and vinorelbine as postoperative adjuvant chemotherapy. One year later, multiple asymptomatic brain metastases were detected, and the patient underwent whole-brain radiotherapy followed by gamma knife radiosurgery. At 20 months after lung resection, a large intrapelvic mass was detected on follow-up examination by positron emission tomography-computed tomography (PET-CT) (Fig. 1A). The maximum standardized uptake value (SUV_{max}) was relatively high at 12.2. Magnetic resonance imaging (MRI) revealed a multilobulated ovarian tumor (15 by 10 cm), which was suspected to be a tumor of the left ovary because of a negative beak sign for the adjacent uterus to the right (Fig. 1B). The patient underwent both left salpingo-oophorectomy (Fig. 1C) and right ovarian cystectomy. Half of the excised left ovarian tumor was cystic, filled with old blood, whereas the remaining half comprised heterogeneous, slightly yellow and white solid tissue with small cysts that showed displacing growth. Microscopic examination of both ovaries revealed acinar adenocarcinoma with a morphology similar to that of the lung cancer diagnosed 20 months earlier (Fig. 2A and B). FISH analysis also showed the presence of *ALK* rearrangement in the ovarian tumor tissue (Fig. 2C). The pathological and molecular findings thus supported a diagnosis of *ALK*

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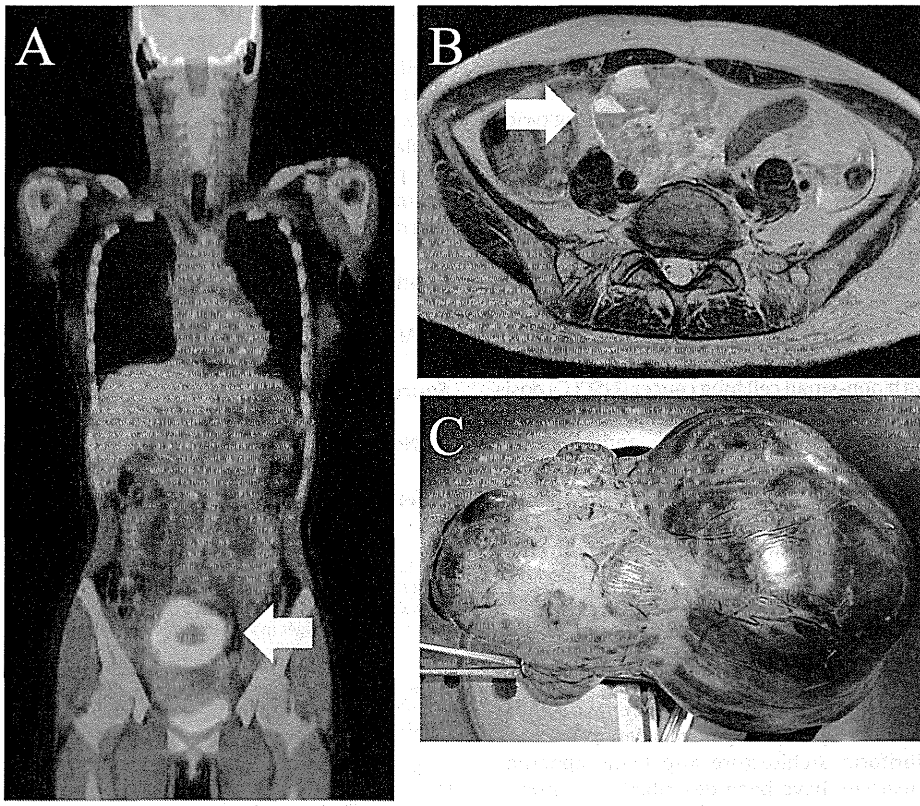

Fig. 1. Ovarian metastasis of lung cancer. (A) PET-CT showing the large intrapelvic mass (arrow) of the patient. (B) Pelvic MRI revealing an ovarian tumor (arrow) with solid and cystic portions that displaced the uterus to the right with a negative beak sign. (C) The excised left ovarian tumor.

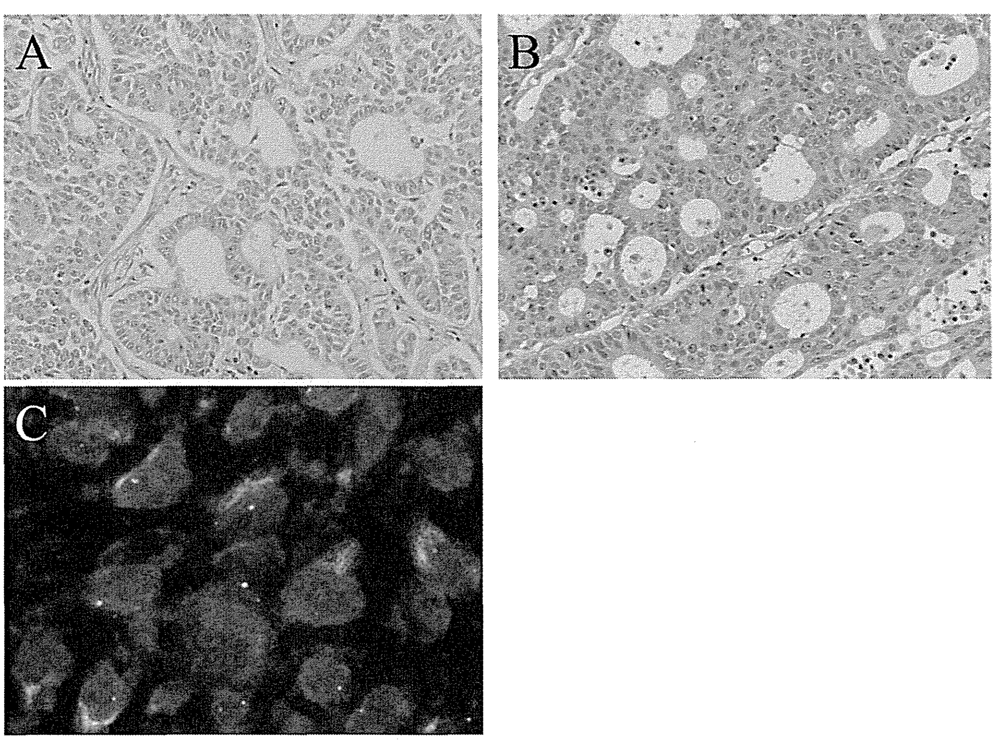

Fig. 2. Tumor histology and FISH analysis. (A) Hematoxylin–eosin staining of the lung adenocarcinoma showing a predominant acinar pattern. Original magnification, 100×. (B) Hematoxylin–eosin staining of the excised left ovarian tumor, revealing adenocarcinoma with a predominant acinar pattern similar to that of the lung cancer. Original magnification, 100×. (C) FISH analysis of the ovarian adenocarcinoma with break-apart probes (red and green fluorescence) for *ALK*. A pattern typical for *ALK* translocation is apparent. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

rearrangement-positive lung cancer with ovarian metastasis. Four months after resection of the ovarian metastases, right bony pelvic and cervical spine metastases were detected on follow-up PET-CT. Radiotherapy was performed for the bone metastasis and was followed by oral administration of crizotinib at a dose of 250 mg twice daily. The patient has shown no evidence of progression on regular follow-up for 4 years after the initial surgery for her primary lung cancer.

2. Discussion

ALK translocation was recently identified as a targetable oncogenic driver. Crizotinib, the first clinically available ALK tyrosine kinase inhibitor, has shown marked and durable efficacy for the treatment of patients with non-small cell lung cancer (NSCLC) positive for *ALK* rearrangement [1]. The incidence of *ALK* rearrangement is only 3–5% in unselected NSCLC patients [2], and the clinical features of metastasis in such patients remain to be fully characterized. We now present the first reported instance of ovarian metastasis in a patient with NSCLC positive for *ALK* rearrangement. About 5–10% of malignant ovarian tumors are metastases from other sites, with primary lung cancer accounting for only 0.4% of metastatic ovarian tumors [3]. The ovary is thus an uncommon location for metastasis from lung cancer. A review of 32 cases of lung cancer that metastasized to the ovary revealed that 14 of these cancers were small cell carcinoma, 11 were adenocarcinoma, and 5 were large cell carcinoma [3]; the most common histological subtype of adenocarcinoma was acinar, with a cribriform architecture also being apparent in some tumors. Such features have been described as a prominent histological type for NSCLC positive for *ALK* rearrangement [4,5]. Women with metastatic ovarian adenocarcinoma from the lung were found to have a mean age of 46 years [3], with disease onset at a young age also being a prominent characteristic of *ALK* rearrangement-positive NSCLC [4]. Further investigation is thus warranted to clarify whether *ALK* rearrangement is associated with a distinct metastatic behavior of NSCLC—in particular, metastasis to the ovary. Physicians should be aware of the possibility for such metastasis when performing follow-up examinations for female patients with NSCLC positive for *ALK* rearrangement.

Conflicts of interest

All authors have no conflict of interest to disclose.

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ORIGINAL ARTICLE

Prognosis associated with surgery for non-small cell lung cancer and synchronous brain metastasis

Takashi Kanou · Jiro Okami · Toshiteru Tokunaga · Ayako Fujiwara · Daisuke Ishida · Hidenori Kuno · Masahiko Higashiyama

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Abstract
Purpose Several reports have described extended survival after aggressive surgical treatment for non-small cell lung cancer (NSCLC) and synchronous brain metastasis. This retrospective analysis assesses the prognostic factors in this population.
Methods We reviewed retrospectively the medical records of 29 patients with synchronous brain metastasis from NSCLC, who underwent surgical treatment in our institution between 1980 and 2008. All patients underwent chest surgery to remove the primary lesion. The impact of several variables on survival was assessed.
Results The median follow-up period was 9.6 months and the 5-year survival rate from the time of lung cancer resection was 20.6 %. Univariate analysis demonstrated that the carcinoembryonic antigen (CEA) level, primary tumor size, and the presence of lymph node involvement were predictive of overall survival ($p < 0.05$). Multivariate analysis also identified those factors to be independent favorable prognostic factors.
Conclusions Although the survival of patients with brain metastasis from non-small cell lung cancer remains poor, surgical resection may benefit a select group of patients, particularly those with a normal CEA level, small tumor size, and node-negative status.

Keywords Lung cancer · Brain metastasis · Synchronous · Resection

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Introduction

The prevalence of metastatic disease at presentation in patients with non-small cell lung cancer (NSCLC) ranges from 11 to 36 % [1]. The central nervous system (CNS) is a frequent and devastating site of metastasis development in NSCLC patients. Brain metastasis occurs in 30–50 % of patients with NSCLC and confers a poor prognosis and quality of life [2–4]. The long-term survival of NSCLC patients with brain metastasis is generally rare; however, this has been achieved in selected patients following surgical treatment of both the primary lesion and brain metastases [5]. Aggressive thoracic treatment in the form of lung resection, the absence of nodal disease, and a histology of adenocarcinoma have commonly been described as indicative of a better prognosis [6–11]. Moreover, the modalities for treating metastatic brain tumors, such as stereotactic radiosurgery (SRS), have improved in recent years [11]. However, the significance of and indications for aggressive bifocal treatment of lung cancer with synchronous brain metastasis remain controversial. In recent years, the risk of thoracic surgery has diminished, and the benefits of surgical treatment have been discussed not only for patients with brain metastasis but also for those with pulmonary metastasis and elderly patients [12, 13].

We review retrospectively our experience of treating patients aggressively for both lung and brain tumors, aiming to identify the clinical factors predictive of survival, to select the best candidates for this surgery.

Patients and methods

The subjects of this retrospective single-center study were patients with synchronous brain metastatic NSCLC who received bifocal treatment with curative intent. We reviewed the medical charts and follow-up data of patients with histologically proven NSCLC, treated at Osaka Medical Center for cancer and cardiovascular disease between January, 1980 and December, 2008. Of more than 4,000 patients who underwent pulmonary surgical resection for NSCLC, we selected 29 with brain metastases diagnosed based on the presence of lesions on magnetic resonance imaging or computed tomography, performed at the time of diagnosis. All patients underwent chest surgery for the primary lesion and were considered to be potentially cured, with the exception of brain tumors. All these patients also underwent treatment for the metastatic brain tumors, in the form of surgical resection only ($n = 12$, 41 %), surgical resection + radiation therapy ($n = 12$, 41 %), or SRS only ($n = 5$, 18 %). Patients with any other synchronous distant metastases, such as liver, bone or adrenal metastases, were excluded from the study cohort. We did not perform pulmonary resection for clinical N2 disease, and such patients were also excluded from this study.

In our institution, the operability criteria for brain metastasis were determined by cranial nerve surgeons. Our inclusion criteria for craniotomy were as follows: a surgically accessible tumor location and distinct negativity for cancer in other distant regions. The inoperability criteria included the following: no potential for the patient to live for more than a few months and the likelihood of craniotomy resulting in severe neural disorder. After 2004, the indication for stereotactic radiosurgery (SRS) was a tumor size of <3 cm. To prevent intracranial recurrence, whole brain radiation therapy (WBRT) was generally delivered postoperatively to patients who underwent craniotomy for metastatic brain tumors. However, several patients did not receive WBRT due to their poor performance status. The timing of treatment for brain tumors was dependent on the patient's symptoms. Patients with symptoms caused by brain metastases received treatment for the brain tumors before undergoing thoracic surgery.

The tumors were classified and staged according to the 7th edition of the TNM classification of malignant tumors [14]. The thoracic stage and nodal status were evaluated based on the findings of chest CT performed before surgery. Positron emission tomography integrated with CT (PET/CT) was performed when required. Patients with suspected clinical N2 disease were excluded from our study cohort. No patient underwent mediastinoscopy because the indication for this procedure at our institution was imaging findings of positive mediastinal lymph nodes.

Follow-up was based on outpatient visits and correspondence with the primary physicians. Follow-up for the primary disease was performed using CT or PET/CT every 3–6 months, in general. Because of the need to evaluate bone metastases, bone scans were performed before PET/CT. Follow-up for brain metastasis was conducted using CT (until 1990) or MRI (since 1990), generally every 6 months. When we detected recurrence during follow-up, systemic chemotherapy was generally given. Pain caused by bone metastasis was treated palliatively with radiation therapy. If the patient was found to have an activating epidermal growth factor receptor (EGFR) mutation, we administered EGFR-tyrosine kinase inhibitor (TKI) as the treatment for recurrence. Only two patients in this series received TKI therapy as treatment against recurrence.

Descriptive statistics were generated with respect to the patients, tumors, and treatment characteristics of the patient population. The Kaplan–Meier method was used to estimate survival, which was calculated from the date of the first pathologic diagnosis to the date of the last follow-up as the end point. Survival curves were compared using the log-rank test. Statistical comparisons were made using the X^2 test. Univariate and multivariate analyses (SPSS V11.5; SPSS, Chicago, Illinois) were performed to identify prognostic factors in the patient population. A p value of <0.05 was considered significant. For the multivariate analysis, a Cox's proportional hazards regression model was used to

Table 1 Clinical and pathological characteristics of the 29 patients with synchronous brain metastasis from non-small cell lung cancer (NSCLC)

Gender (male/female)	25/4
Age (years)	60.5 ± 10.8
Distribution of treatment date (~90/91–99/2000 ~)	5/8/16
CEA level before pulmonary resection (ng/ml)	4.6 ± 33.2
Histologic classification	
(Ad/others)	19/10
Primary lesion	
Tumor size (cm)	4.5 ± 42.7
Operation (lobe/pneumo)	27/2
Clinical T (T 1/2/3/4)	8/14/4/3
Clinical N (N 0/1)	19/10
Pathological T (T 1/2/3/4)	7/12/7/3
Pathological N (N 0/1/2)	15/4/10
Brain lesion	
Number of brain meta (1/2/3/4/5)	15/6/3/2/3
Treatment for meta (Res/Res + WBRT/SRS)	12/12/5
Symptoms before Tx (yes/no)	25/4
Sequence of treatment	
Pulmonary first/brain first	9/20
Chemotherapy (perioperative chemotherapy/none)	18/11
Cause of death (brain meta/others)	5/24

CEA carcinoembryonic antigen, *Ad* adenocarcinoma, *Res* resection *WBRT* whole brain radiotherapy, *SRS* stereotactic radiosurgery, *Tx* treatment