Expandable Metallic Stent for Endobronchial Metastasis from Colorectal Cancer: Reports of 2 Cases

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In recent years, there have been many reports about the efficacy of stenting for central bronchial stenosis. When central bronchial stenosis is due to metastasis of a malignant tumor to the trachea and/or bronchi (endobronchial metastasis: EM), it is classified as "narrow EM" and "broad EM." [1] We managed two patients in whom bilateral stent placement was required for narrow and broad EM arising from colorectal cancer.
Case 1: In September 2011, a 66-year-old man underwent low anterior resection for advanced colorectal cancer associated with unresectable liver metastasis. The liver metastasis became resectable after chemotherapy, with two resection procedures and radiofrequency ablation (RFA) being performed. Thereafter, lung metastasis occurred and a tumor in the left lung was resected. In May 2015, he developed respiratory distress. CT identified multiple lesions protruding into the lumen of the trachea and the left and right main bronchi. There was no evidence of mediastinal relapse or local relapse at the resection margin, and tumors were only detected in the tracheobronchial walls. Accordingly, narrow EM was diagnosed. An expandable metallic stent (EMS) was placed on the right side where stenosis was more severe, and radiation therapy was conducted for the non-stented tumors. The patient died 8 months later.
Case 2: A 69-year-old woman had undergone laparoscopic right hemicolectomy and adjuvant chemotherapy for Stage lllb cancer of the ascending colon. Due to subsequent elevation of tumor markers, PET-CT was conducted and abnormal uptake was seen in the apex of the right lung and right upper abdomen. Both lesions were resected, and omental and lung metastases were diagnosed. She received treatment with UFT / calcium folinate, but relapse occurred at the resection margin in the right lung. At 7 years and 5 months after initial surgery, she complained of respiratory distress at an outpatient visit. CT demonstrated displacement of the trachea and right main bronchus due to enlargement of upper mediastinal lymph nodes. There was also severe stenosis of the right main bronchus due to tumor infiltration. Because there was both infiltration from local recurrence after resection and upper mediastinal lymph node enlargement, broad EM was diagnosed. An EMS was placed at the site of severe stenosis in the right main bronchus. Similar to Case 1, radiation therapy was also conducted, but respiratory distress occurred after 3 months due to tumor re-growth at the stent margin. Accordingly, stent-in-stent placement was performed and her respiratory symptoms improved. However, superior vena cava syndrome occurred 1 month later and the patient died.
We consider that placing an EMS is effective in patients with tracheal stenosis due to EM that is judged to be an oncological emergency.

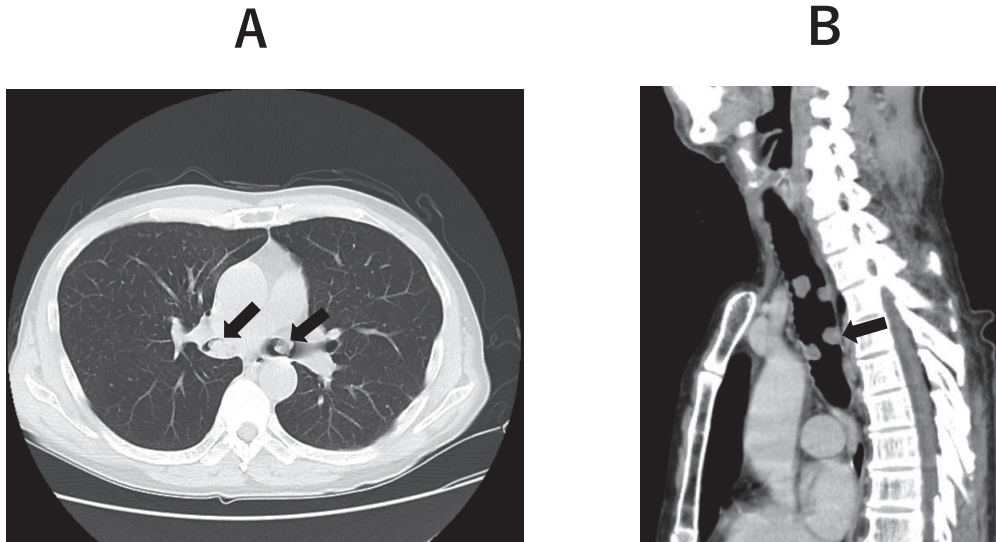Key words: Colorectal cancer, endobronchial metastasis, expandable metallic stent

INTRODUCTION

Endobronchial metastasis (EM) is a rare condition [2]. EM is considered to arise via (1) direct metastasis to the bronchial wall, (2) direct invasion from metastatic lung tumors, and (3) direct invasion from metastases to the hilar lymph nodes [3]. While (1) is classified as "narrow EM", (2) and (3) are classified as "broad EM." [1] The most frequent primary tumor is breast cancer, followed by colorectal cancer and then renal cancer [2, 3]. Standard treatment options for EM are surgery, radiation therapy, and chemotherapy. Treatment is selected by considering 4 points [4]. Active intervention is necessary to salvage the patient if there

is judged to be oncological emergency due to respiratory distress and choking. Recently, various options have become available to treat EM, such as laser therapy, microwave radiation, and stenting, so the characteristics of each option need to be taken into consideration when choosing among them [5]. We managed patients with narrow EM and broad EM for which stenting was effective, and we report these cases here with a review of the literature.

CASE 1

In September 2011, a 66-year-old man underwent low anterior resection for Stage IV colorectal cancer associated with bowel obstruction and liver metastasis.

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Fig. 1 Chest CT in case 1
A: Sagittal image. Multiple lesions protruding into the trachea (black arrow).
B: Coronal image. Protruding lesion in the main bronchus.

Since the liver tumor was unresectable at that time, he received 7 courses of adjuvant m-FOLFOX6+Bev therapy and 2 courses of FOLFILI+Bev therapy. After reduction of liver tumor volume was observed, partial hepatectomy was conducted twice and radiofrequency ablation (RFA) was also performed. At 2 years and 2 months after initial treatment, CT revealed a metastasis measuring about 10 mm in the lower lobe of the left lung, so the lower lobe was partially resected. Subsequently, an unresectable liver metastasis was detected. NK cell-based immunotherapy was performed, taking the patient's wishes into consideration. Eighteen months later, the patient complained of wet cough with hemosputum, fever, and respiratory distress accompanied by wheezing. CT identified multiple lesions protruding into the lumen of the trachea and the left and right main bronchi (Fig. 1A, B). Laboratory tests showed elevation of CEA to 250.4 ng/dl. Oxygen saturation was reduced to 80% and his symptoms were progressive. Accordingly, it was judged to be an oncological emergency and an expandable metallic stent (EMS) was placed in the trachea and right bronchus under fluoroscopic, tracheal intubation and bronchoscopic guidance (Fig. 2A, B). At the time of intervention, part of the tracheal tumor was expelled. Histopathological examination revealed that the tumor had the same features as the primary colorectal cancer (Fig. 3), while cytokeratin immunohistochemistry was negative for CK7 and positive for CK20. Accordingly, metastasis of colorectal cancer to the trachea was diagnosed. In order to control the tumors at the non-stented parts of the airway, radiation therapy (55 Gy) was performed, followed by best supportive care. The patient died 8 months after stent placement.

CASE 2

In November 2007, laparoscopic right hemicolectomy was performed in a 69-year-old woman for cancer of the ascending colon. The surgical diagnosis was Stage IIIb. As adjuvant chemotherapy, she received 6 courses of IFL therapy, followed by treatment with oral UFT/UZEL. At 20 months after the initial treatment, laboratory tests indicated that tumor markers were elevated (CEA was 5.5 ng/dl and CA19-9 was 44.8 ng/dl). Both markers continued to increase gradually. Three months later, abdominal ultrasound detected a tumor mass measuring 20 mm in diameter. PET-CT was conducted, revealing uptake by a mass 8 mm in diameter at the apex of the right lung and another lesion 18 mm in diameter located within the omentum of the upper right abdomen. Since no other sites of abnormal uptake were observed, partial omentectomy and partial resection of the right upper lobe were conducted. At both sites, metastasis from ascending colon cancer was diagnosed. Considering the patient's social circumstances, oral administration of UFT / calcium folinate was initiated. At 3 years and 2 months after initial surgery, follow-up CT revealed relapse at the resection margin in the right lung. Five years and 4 months after initial surgery, the patient complained of respiratory distress. Oxygen saturation was 96%. CT demonstrated severe circumferential stenosis of the right main bronchus caused by displacement of trachea due to enlargement of right upper mediastinal lymph nodes. In addition, a pericardium effusion and a small pleural effusion were observed (Fig. 5A, B). Due to reduction of respiratory sounds in the right lung accompanied by stridor, this was considered to be an oncological emergency. An EMS was placed from the trachea to the right main bronchus under fluoroscopic, tracheal intubation and bronchoscopic guidance, after which her symptoms improved (Fig. 6A, B). In order to control tumors at the non-stented sites, radiation therapy (total dose: 55 Gy) was also conducted. Three months after stent placement, the patient again developed respiratory distress and was brought to hospital by ambulance. Tumor re-growth was observed at the stent margin, so a stent-in-stent procedure was performed. However, the patient developed superior vena cava syndrome and died at 4 months after placement

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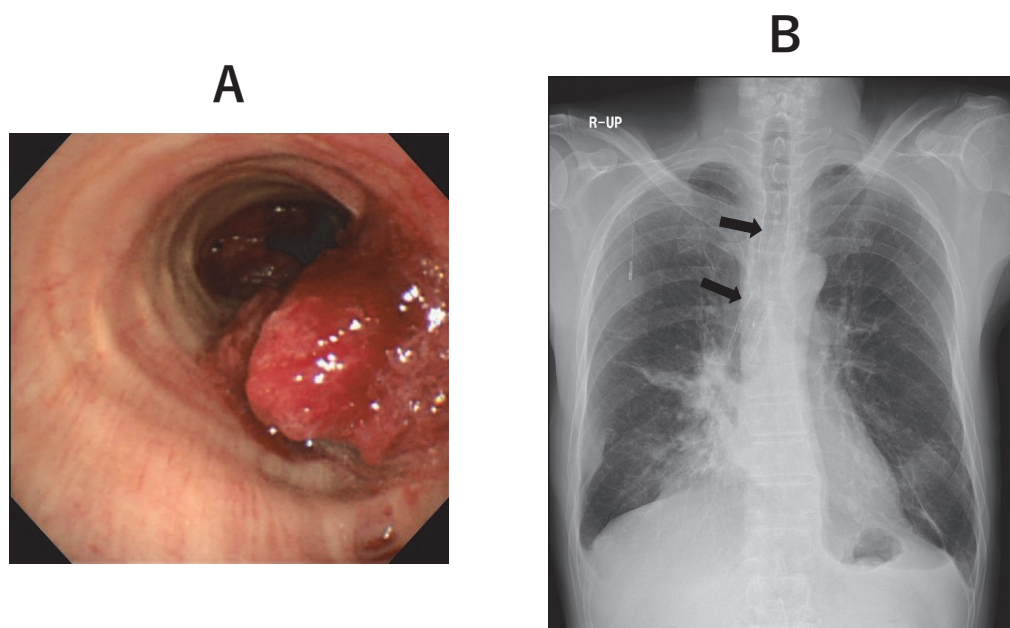
Fig. 2 Bronchoscopy and chest X-ray film in case 1
A: Tracheal lumen prior to stent placement: Scattered tumor masses protruding into the trachea.
B: Chest X-ray film after stent placement: Stent expansion is good and the airway lumen is maintained.
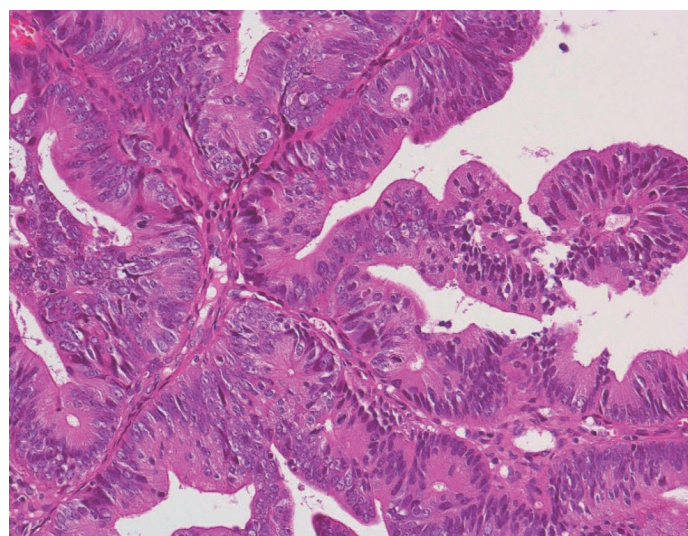

Fig. 3 Histopathological findings in case 1
Tracheal tumor (HE staining, magnification: x200).

of the initial stent.

DISCUSSION

Endobronchial metastasis (EM) is a collective term for endobronchial tumors caused by lung metastases [2]. EM can occur via 3 routes, which are (1) direct metastasis to the bronchi, (2) metastasis from a metastatic lesion in the lung parenchyma, and (3) infiltration or compression of the bronchi by metastasis to the hilar lymph nodes [3]. While (1) is classified as "narrow EM", (2) and (3) are classified as "broad EM." [1] The reported prevalence of EM in metastatic lung cancer varies widely from 4 to 36% [2]. [6-8], In recent reports, the term EM is also used to include tracheal or

bronchial metastases that are found by bronchoscopy [9]. Based on review of clinical course and morphology of the metastatic lesions, Case 1 had a lung metastasis that was relatively small (10 mm in diameter) and it was completely resected. Subsequent imaging studies did not demonstrate relapse in the mediastinum/ hilar nodes and or at the resection margin, but isolated lesions developed in the tracheal wall. Accordingly, this patient was considered to have "narrow EM." In Case 2, the time until occurrence of EM was longer, but diagnostic imaging revealed relapse at the resection margin and metastasis to the mediastinal lymph nodes. Therefore, she was diagnosed as having "broad EM." EM due to colorectal cancer is uncommon, with
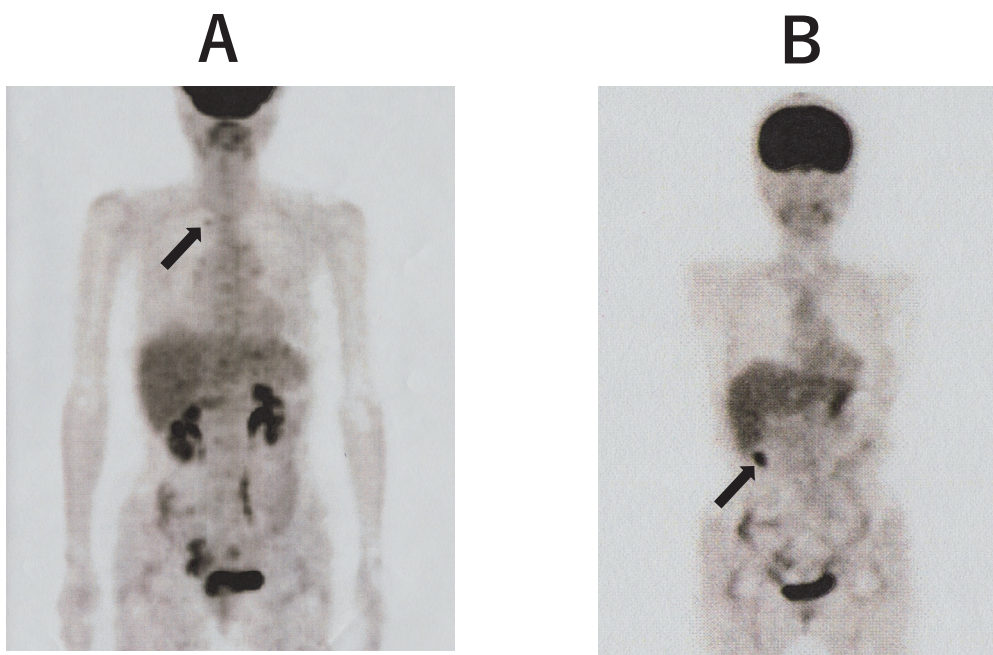
Fig. 4 PET-CT in case 2
A: Increased uptake at the apex of the right lung.
B: Increased uptake in the upper right abdomen.
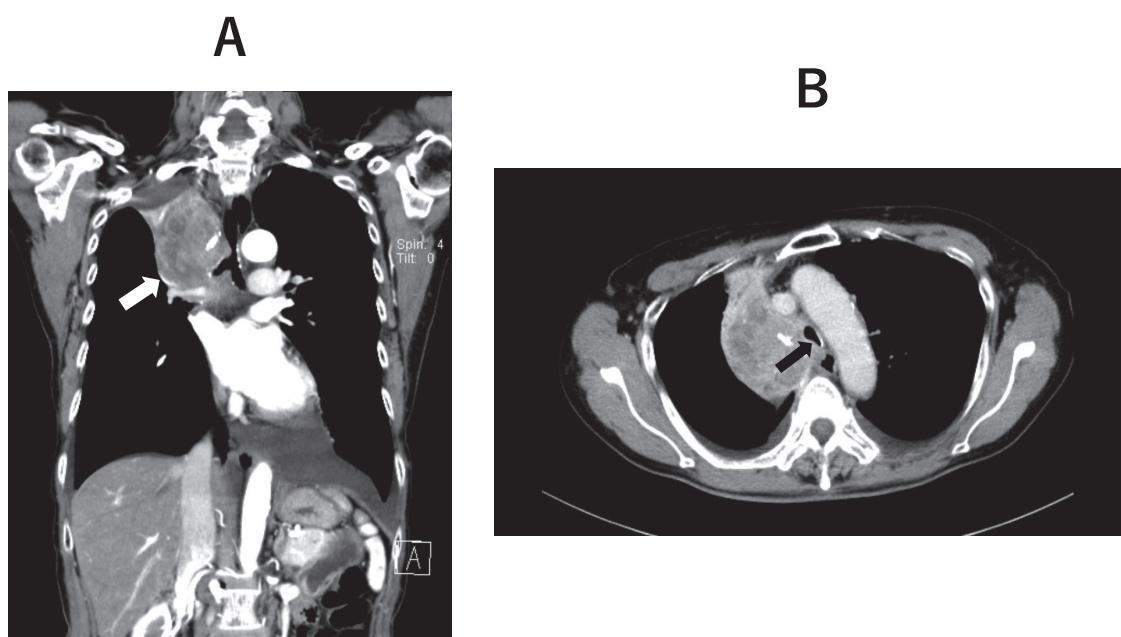
Fig. 5 Chest CT in case 2
A: Coronal image. The trachea is compressed by enlarged upper mediastinal lymph nodes. The lumen of the right main bronchus is narrowed by tumor infiltration (white arrow).
B: Sagittal image. The trachea is displaced dorsally by enlarged upper mediastinal lymph nodes (black arrow).

rectal cancer only accounting for 11-29% and thus being relatively rare [10, 11]. Using "rectal cancer" and "tracheal metastasis" as search terms, a PubMed literature search was conducted for the period from 1983 to 2016. This search identified reports with detailed information about 10 patients [12-21]. Two patients were mentioned in the literature of the Japan Medical Abstracts Society [9, 22], so this is the third patient in Japan. With regard to sex difference, one report suggested a higher frequency of EM in females [10], but there are differences among reports. Accordingly, accumulation of more patients appears to be required.

The mean time from onset of colorectal cancer to detection of EM was 59.4 months (range: 1-112 months). In our patients, the time was 44 months and 62 months. The prognosis after detection of EM is poor and the median survival time was only 8.7 months (range: 2-14 months) [23]. In the present

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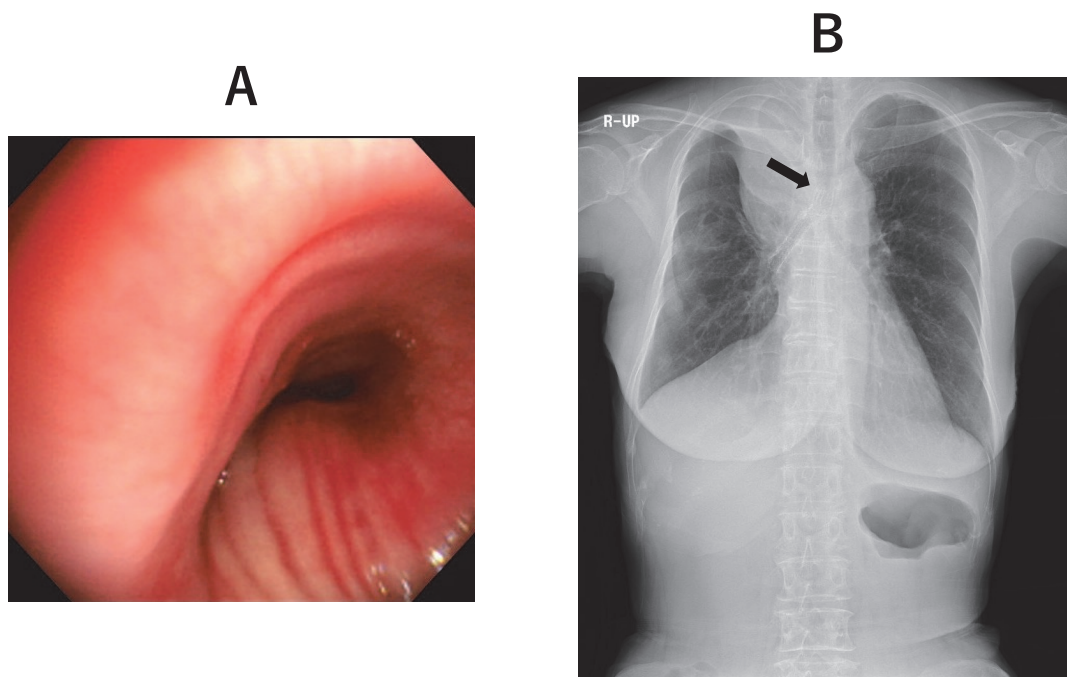
Fig. 6 Bronchoscopy and chest X-ray film in case 2
A: Tracheal lumen prior to stent placement: The trachea is compressed in the dorsal direction.
B: Chest X-ray film after stent placement: Stent expansion is good and the airway lumen is maintained.

two cases, the time was 3 and 6 months. Since the prognosis is poor once EM occurs, if the interval for routine follow-up was set differently, we might have been able to conduct more aggressive therapy for EM such as early surgical intervention, radiation therapy, and chemotherapy. This is considered to be an area for improvement in the management of colorectal cancer.

The treatment strategy for EM is selected by considering the following 4 points: (1) the presence or absence of other remote metastasis, (2) the status of the primary tumor, (3) the feasibility of complete resection of EM lesions, and (4) whether treatment of symptoms is needed [4]. Both of our patients presented here were considered to have an oncological emergency because they presented with respiratory distress accompanied by stridor and choking due to tracheal stenosis on diagnostic imaging. Accordingly, intervention was selected that prioritized securing the airway in both patients. Airway interventions can include laser therapy, microwave irradiation, and stenting [5]. To perform laser therapy and microwave therapy, dedicated equipment is needed [24]. Therefore, it was considered that these options were not suitable for an emergency situation, and stenting with an EMS was chosen [25, 26]. Stent placement for airway stenosis was first conducted by Wallace in 1986, using an EMS designed for vascular stenting in the trachea and bronchi. Since then, airway stenting has become an accepted procedure [27]. The Ultraflex stent that we used is made of memory metal and is flexible. It can be inserted into curved structures and is resistant to infection. Moreover, this stent is not easily damaged or detached by events such as paroxysmal coughing.

CONCLUSION

Tracheal stenosis caused by EM arising from colorectal cancer is a rare condition. We inserted an EMS to treat EM due to colorectal cancer presenting as an oncological emergency in two patients, and improved both their quality of life and performance status. In addition to presenting the clinical course of these patients, we provided a review of the literature.

ABBREVIATIONS

Endobronchial metastasis (EM), expandable metallic stent (EMS), radiofrequency ablation (RFA)

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