

CASE REPORT

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## Development of severe complications caused by stent placement followed by definitive radiation therapy for T4 esophageal cancer

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**Abstract** Esophageal stenting in previously irradiated patients is known to cause more severe complications than those in patients who were not irradiated. But there are few reports regarding the results of stent placement before radiation therapy. Three patients with stage T4 esophageal cancer with direct invasion to the trachea and/or aorta underwent radiation therapy after stent placement. Two of the three patients had received systemic chemotherapy before radiation therapy. Fifty-one to 66Gy of radiation therapy was administered 15 to 66 days after the stent placement. The initial response to radiation therapy was no change (NC) or progressive disease (PD). All patients died of bleeding or pneumonia caused by perforation at the site of the stents 17 to 79 days after the radiation therapy. It is strongly suggested that even in patients with locally advanced esophageal cancer with severe dysphagia, radiation therapy should precede stent placement, because the consequences of radiation therapy after stent placement are devastating, and radiation therapy alone can, potentially, resolve the symptoms.

**Key words** Esophageal cancer · Radiation therapy · Stent · Case report

### Introduction

The number of people who died of esophageal cancer in Japan in 1997 was 9599, which is 3.49% of the deaths from

cancer. Although the standard treatment for advanced esophageal cancer has been esophagectomy with regional lymph node dissection, the number of patients who receive definitive radiation therapy (RT) has been increasing, with encouraging results for concurrent chemoradiation.<sup>1,2</sup>

Esophageal stents were developed in the 1970s, and they were made of plastic until 1990. Since Domschke et al.<sup>3</sup> first reported the self-expandable metallic stent (SEMS) in 1990, the SEMS has been widely used for malignant esophageal stenosis.<sup>4</sup>

There are many reports of the combination of RT and stent placement for esophageal cancer.<sup>5–8</sup> Most of them have concluded that stent placement in patients who have been irradiated causes more severe complications than those in patients who have not been irradiated. However, there are few reports regarding stent placement before RT.<sup>9,10</sup>

We herein report the consequences in three patients who underwent stent placement followed by definitive RT.

### Case reports

We reviewed the medical records of 69 consecutive patients with primary esophageal cancer who received RT from 1992 to 1996. Stents were placed before definitive RT in 3 of them (4.3%). (Two of the three patients were sent from other hospitals to receive RT, and were sent back to the hospitals after the RT. Their medical records and films in other hospitals are not available now.)

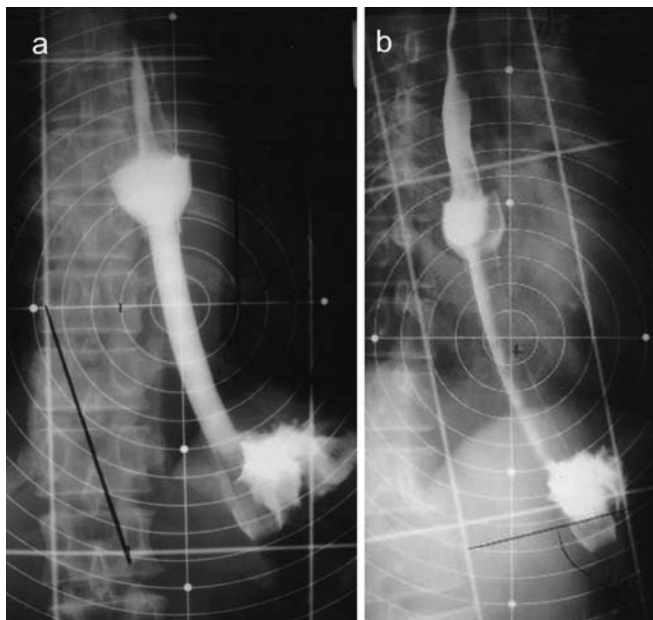
#### Case 1

A 61-year-old man with progressive dysphagia was diagnosed with squamous cell carcinoma in the lower third of the thoracic esophagus. After esophageal dilation, and the intubation of a plastic esophageal prosthesis for severe dysphagia, he was referred for definitive RT. His International Union Against Cancer (UICC) stage was T4N1M0 stage

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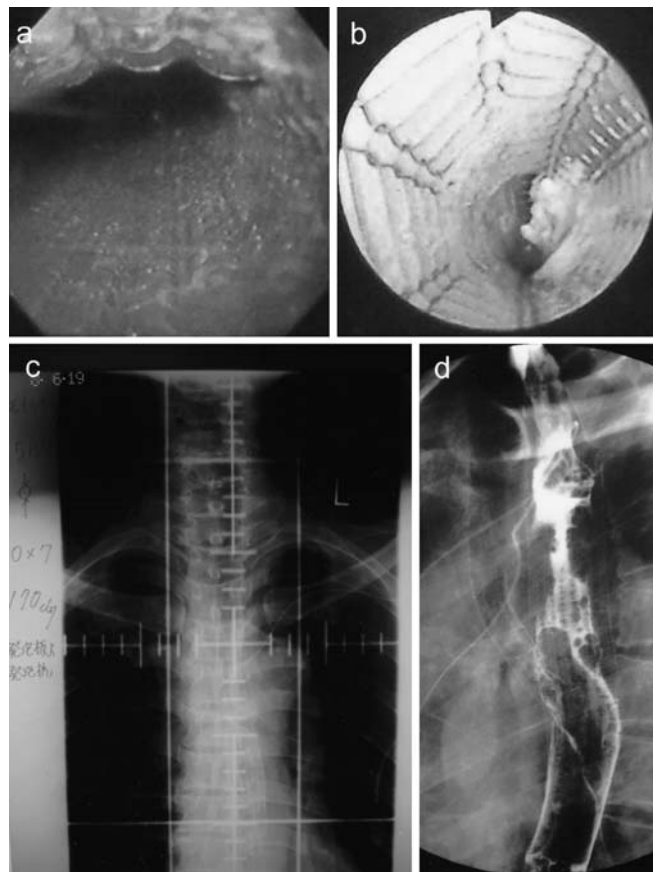


**Fig. 1a,b.** Radiation fields. **a** Large field (2 Gy/day). **b** Targeted field (1.2 Gy/day)

III, with direct invasion to the descending aorta (T4), and paraaortic and cardiac lymph node (N1) swelling. The RT was 68Gy in total. Daily fractionations were 2.0Gy and 1.2 Gy (field-in-field) (accelerated hyperfractionation) (Fig. 1). The primary tumor showed partial response to RT, but the swelling of the paratracheal lymph nodes got worse. Dysphagia recurred 2 months after the RT. The patient felt that his prosthesis was uncomfortable and wished to remove it. While he was waiting for the operation, he died due to hematemesis. Autopsy revealed a fistula from the esophagus to the left atrium at the upper end of the prosthesis. Squamous cell carcinoma was not detected.

#### Case 2

A 64-year-old man with progressive dysphagia and dyspnea was diagnosed with a keratinizing type of squamous cell carcinoma in the middle and lower thirds of the thoracic esophagus. His UICC stage was T4N1M1 stage IVB with tracheal invasion (T4) and paraesophageal lymph node (N1) and deep cervical lymph node (M1) swelling. He underwent stent placement both in the esophagus (Fig. 2a) and in the trachea (Fig. 2b) for palliation. The esophageal stent was a covered nitinol stent (UltraFlexR; Boston Scientific, Natic, MA, USA). He underwent intratumoral injection of ethanol and systemic chemotherapy (cisplatin [CDDP], 50mg/body, twice), with no response. Thus, he was referred for RT, and was scheduled to receive 60Gy of RT, consisting of a 1.7-Gy fraction daily (Fig. 2c). However, esophago-bronchial fistula occurred during RT (Fig. 2d). The RT was interrupted at 25.5 Gy for 20 days for preoperative evaluation for immediate salvage surgery, and was terminated at 51 Gy due to deterioration of the fistula. Esophagectomy was not indicated. He underwent place-



**Fig. 2.** **a** Esophageal stent. **b** Tracheal stent. **c** Radiation therapy (RT) field. **d** Esophago-bronchial fistula

ment of another stent in the trachea for dyspnea, but he died due to pneumonia. Autopsy revealed a 5-cm esophago-bronchial fistula at the site of the esophageal stent. Macroscopic tumor did not remain.

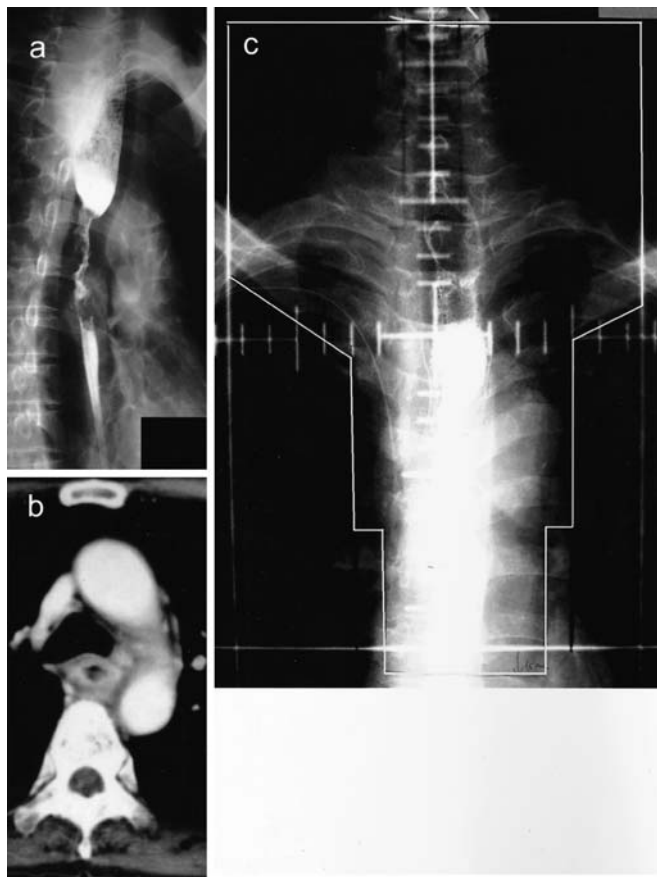
#### Case 3

A 58-year-old man with dysphagia and vomiting was diagnosed with a moderately differentiated squamous cell carcinoma in the middle and lower thirds of the thoracic esophagus (Fig. 3a,b). His UICC staging was T4N1M1 stage IVB, with tracheal, bronchial, and superior vena cava (SVC) invasion (T4), and paraesophageal lymph node (N1) and cervical lymph node (M1) swelling. He received neoadjuvant chemotherapy consisting of CDDP and 5-fluorouracil (FU), and showed a partial response (PR). He then underwent surgery; however, the tumor was unresectable due to tumor invasion to the trachea and SVC. He underwent placement of an uncovered nitinol stent (UltraFlexR; Boston Scientific) in the esophagus for palliation, and was referred for RT (Fig. 3c). He received 66Gy of RT, consisting of 2-Gy fractions daily. But an esophago-tracheal fistula occurred after RT, and he died of pneumonia. Autopsy was not performed.

Types of stents, radiation dose, and the consequences are summarized in Table 1.

**Table 1.** Types of stents, radiation dose, and consequences

Case no.	Type of stent	Radiation therapy (RT)	Interval from stent placement to RT (days)	Interval from RT to death (days)
Case 1	Prosthesis	68 Gy / 1.2 + 2.0 Gy b.i.d.	20	79
Case 2	Covered nitinol metallic stent	51 Gy / 1.7 to 2 Gy	66	17
Case 3	Uncovered nitinol metallic stent	66 Gy / 2 Gy	15	60

**Fig. 3.** a Barium study. b Enhanced computed tomography (CT). c RT field

## Discussion

Stent placement has been shown to be effective in palliating dysphagia due to esophageal cancer,<sup>6</sup> but there are many reports of complications caused by the combination of a stent and RT.<sup>5,7,9</sup> The reason for the increased risk of complications in patients with prior radiation and/or chemotherapy is likely multifactorial. The expansive force of an expandable stent may cause complications such as bleeding, perforation, fistula formation, and chest pain.<sup>8</sup> Radiation-induced vasculitis may also cause esophageal perforation and tracheoesophageal fistulas.<sup>5</sup>

There are opinions that stent placement before RT may improve the patient's nutritional condition and quality of life (QOL), and therefore be beneficial for subsequent RT.<sup>6</sup> However, there are few reports regarding the safety and

effectiveness of such a treatment. Although it is difficult to clearly distinguish the complications reported here from the natural courses of esophageal cancer, the three patients reported here died less than 3 months after the end of RT, and the RT in these patients apparently had no substantial benefit.

In addition to the factors mentioned above, fragility of the existing tumor may be contributory to toxicities observed in these patients. Stent placement can even weaken the effect of RT by obstructing vessels with expansive pressure, which causes tumor hypoxia. Although new types of esophageal stent with improved flexibility and biocompatibility are available now, patients who underwent RT before stent placement experienced substantially fewer complications than those who underwent RT after stent placement.<sup>10</sup> To prevent the complications of stent placement, especially longterm ones, retrievable expandable nitinol stents<sup>11</sup> may be useful for malignant esophageal strictures. However, there are few reports that support this possibility.<sup>12</sup>

In case 1, the plastic prosthesis and accelerated hyperfractionated RT may have caused complications such as the patient's uncomfortable feelings and the fistula from the esophagus to the left atrium. Plastic prostheses are reported to cause more severe complications than self-expandable metallic stents.<sup>13,14</sup> Accelerated hyperfractionated RT for esophageal cancer causes more complications in the heart and lung than once-a-day RT.<sup>15</sup>

There are many reports regarding the results of chemoradiation for locally advanced esophageal cancer. One report indicated that more than 80% of patients with T4M0 or T4M1LYM achieved a complete response (CR) or PR. Dysphagia in the responders was alleviated without stent placement. There were long term survivors even in advanced stages, and the 5-year survival rate of patients with T4 was 14%.<sup>2</sup>

Some reports indicate that patients with unresectable esophageal cancer (ranging from T2N1M0 to T4N2M1) who received concurrent radiation and chemotherapy before being treated with a mesh stent experienced prolonged survival compared with patients of equal tumor staging who were not treated with the stents.<sup>16</sup>

There are many reports regarding esophageal stenting for malignant esophageal stenosis. They indicate that esophageal stenting provides excellent palliation with few severe complications in the short-term.<sup>17</sup> But the median survival after stenting is reported to be less than 4 months.<sup>18</sup>

These findings suggest that concurrent chemoradiation should be given first for patients with inoperable esophageal

cancer with severe dysphagia, and esophageal stents should be reserved for nonresponders.

In conclusion, we encountered three patients with advanced esophageal cancer who received RT after esophageal stenting. All three patients died early, of perforation at the stent site. Even in patients with locally advanced esophageal cancer with severe dysphagia, RT should precede stent placement, because the consequences of RT after stent placement are devastating, and RT alone can, potentially, resolve the symptoms.

## References

1. Cooper JS GM, Herskovic A, Macdonald JS, et al. (1999) Chemoradiotherapy of locally advanced esophageal cancer: long-term follow-up of a prospective randomized trial (RTOG 85-01). Radiation Therapy Oncology Group. *JAMA* 281:1623–1627
2. Ohtsu A, Boku N, Muro K, et al. (1999) Definitive chemoradiotherapy for T4 and/or M1 lymph node squamous cell carcinoma of the esophagus. *J Clin Oncol* 17:2915–2921
3. Domschke W, Foerster EC, Matek W, et al. (1990) Self-expanding mesh stent for esophageal cancer stenosis. *Endoscopy* 22:134–136
4. Furukawa K, Kato H (1999) Stenting for airway and esophageal stenosis. *J Jpn Bronchoesophagol Soc* 51:345–353
5. Kinsman KJ, DeGregorio BT, Katon RM, et al. (1996) Prior radiation and chemotherapy increase the risk of life-threatening complications after insertion of metallic stents for esophagogastric malignancy. *Gastrointest Endosc* 43:196–203
6. Song HY, Do YS, Han YM, et al. (1994) Covered, expandable esophageal metallic stent tubes: experiences in 119 patients. *Radiology* 193:689–695
7. Abe T, Tangoku A, Hayashi H, et al. (1999) Esophageal perforation and mediastinal abscess following placement of a covered self-expanding metallic stent and radiation therapy in a cancer patient. *Surg Endosc* 13:1044–1046
8. Raijman I, Siddique I, Lynch P (1997) Does chemoradiation therapy increase the incidence of complications with self-expanding coated stents in the management of malignant esophageal strictures? *Am J Gastroenterol* 92:2192–2196
9. Alberts AS, Burger W, Greeff F, et al. (1992) Severe complications of 5-fluorouracil and cisplatin with concomitant radiotherapy in inoperable non-metastatic squamous cell oesophageal cancer after intubation – early termination of a prospective randomised trial. *Eur J Cancer* 1005–1006
10. Song HY, Lee DH, Seo TS, et al. (2002) Retrievable covered nitinol stents: experiences in 108 patients with malignant esophageal strictures. *J Vasc Interv Radiol* 13:285–293
11. Song HY, Jung HY, Park SI, et al. (2000) Covered retrievable expandable nitinol stents in patients with benign esophageal strictures: initial experience. *Radiology* 217:551–557
12. Song HY, Park SI, Jung HY, et al. (1997) Benign and malignant esophageal strictures: treatment with a polyurethane-covered retrievable expandable metallic stent. *Radiology* 203:747–752
13. Takagi Y, Aoki T, Osaka Y, et al. (2001) Comparison of plastic prostheses and self-expandable metallic stents in the treatment of malignant esophageal stenosis. *Jpn J Thorac Cardiovasc Surg* 49:641–645
14. Knyrim K, Wagner HJ, Bethge N, et al. (1993) A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. *N Engl J Med* 329:1302–1307
15. Kikuchi Y, Kita M, Hamajima N, et al. (2000) The clinical trial on the effectiveness of multiple fractions per day irradiation. *J Jpn Soc Ther Radiol Oncol* 12:389–393
16. Ludwig D, Dehne A, Burmester E, et al. (1998) Treatment of unresectable carcinoma of the esophagus or the gastroesophageal junction by mesh stents with or without radiochemotherapy. *Int J Oncol* 13:583–588
17. Neil AC, Percival OB, Hiran CF, et al. (2001) Results of expandable metal stents for malignant esophageal obstruction in 100 patients: short-term and long-term follow-up. *Ann Thorac Surg* 71:1797–1802
18. Peter DS, Wim CJH, Mark B, et al. (2001) A comparison of three types of covered metal stents for palliation of patients with dysphagia caused by esophagogastric carcinoma: a prospective, randomized study. *Gastrointest Endosc* 54:145–153