

多発肝転移を伴う食道癌に対して同時一括切除と補助化学療法が有効であった1例

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A Case of Esophageal Cancer with Multiple Liver Metastases Treated with Simultaneous Esophagectomy and Hepatic Resections under Adjuvant Chemotherapy

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多発肝転移を伴う食道癌に対して同時一括切除と補助化学療法が有効であった1例

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医学領域 外科学(1)分野

Abstract:

A 66-year-old man who had a chief complaint of pharyngeal discomfort was given diagnosis of abdominal esophageal cancer with synchronous multiple liver metastases. The patient was going to receive systemic chemotherapy with cisplatin. Since hepatic metastases had been progressed after 3 courses of the chemotherapy, the patient was undergone operation for the removal of an abdominal esophageal tumor with simultaneous hepatic lobectomy including liver metastases. The histopathological diagnosis was moderately differentiated squamous cell carcinoma, pT3N1M1, stage IVb (UICC classification). The patient was received 10 courses of postoperative adjuvant chemotherapy with S-1 and docetaxel because the patient's postoperative course was uneventful. The patient died 82 months after surgery from bacterial pneumonia with no signs of recurrence. In our personal experiences, this is the first report of a patient treated with simultaneous esophagectomy and hepatic resection for abdominal esophageal cancer with multiple liver metastases, achieving a disease-free survival exceeding 5 years. It is suggested that an aggressive surgical resection may be the treatment of choice for esophageal cancers with synchronous multiple liver metastases in some cases.

Keywords: esophageal cancer, liver metastasis, simultaneous esophagectomy and hepatic resections, long-term survival

要旨:

症例は 66 歳男性で、咽頭部不快感を主訴に来院し同時性多発肝転移を伴う腹部食道癌と診断された。患者はシスプラチンによる全身化学療法を受けたが、3 コース後に肝転移巣の増悪が認められたため、腹部食道切除術と同時に肝転移を含めた肝葉切除術を施行された。病理学的に腫瘍は中分化扁平上皮癌で pT3N1M1, stage IVb (UICC 分類) と診断された。患者の術後経過は良好で、その後術後補助化学療法として S-1 とドセタキセル併用全身化学療法を 10 コース施行された。患者は術後 82 ヶ月目に細菌性肺炎により死亡したが、その間再発の兆候は認められなかった。我々の調べ得た限りにおいて、多発肝転移を有する腹部食道癌に対して食道・肝同時切除を行い 5 年以上の長期生存が得られた症例の報告は初めてである。積極的な外科的切除が、症例選択によっては同時性肝転移を有する食道癌に対して治療選択肢の一つになり得ることが示唆された。

キーワード: 食道癌, 肝転移, 食道・肝同時切除, 補助化学療法, 長期生存

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Introduction

Hepatic resection for liver metastases in colorectal cancer, both synchronous and metachronous, is the only curative treatment option associated with improved survival⁽¹⁾. Improvements in surgical techniques have led to many cases of challenging hepatectomy being successfully completed⁽²⁾. Furthermore, several recent reports regarding patients with liver metastases from gastric cancer have shown that liver resection prolongs the survival of certain patients without other distant metastases⁽³⁾. However, little information is available regarding whether hepatic resection is beneficial for patients with liver metastases from esophageal cancer, which are rarely eligible for resection and have an extremely poor prognosis⁽⁴⁾. Here we report the case of a patient who was achieving long-term disease-free survival after undergoing simultaneous abdominal esophagectomy with hepatic resections under perioperative chemotherapy for esophageal cancer with synchronous multiple liver metastases.

Case Report

A 66-year-old man had been receiving outpatient treatment for 10 months at otorhinolaryngology department of another hospital for a chief complaint

of dysphagia. He was referred to the surgical department in Tsuruga Medical Center in December 2007 for further examination and treatment. Esophagogastroduodenoscopy and upper gastrointestinal contrast radiography showed an ulcerative tumor in the abdominal esophagus exposing the cardia (Figs.1a, b) and biopsy revealed moderately differentiated squamous cell carcinoma (SCC). Abdominal computed tomography (CT) showed a low-density tumor in the esophagogastric junction with several enlarged lymph nodes along the small curvature of the stomach. CT also showed multiple low-density areas of 30 mm in diameter at the widest points in Couinaud's segments 2 (S2), 4 (S4), and 6 (S6) of the liver (Fig2a, b, c). Laboratory data, including complete blood count, blood chemistry, and urinalysis, were all within the normal ranges with the exception of increased serum levels of SCC antigen (10.0 ng/ml; normal range, 0–1.5) and cytokeratin 19 fragment antigen (CYFRA 1–21; 2.4 ng/ml; normal range, 0–2.0). After we obtained informed consent from the patient, the patient was received the chemotherapy with a regimen of once administration of cisplatin at 60 mg/m² every three weeks from late December to February 2008. Hepatic metastases had been progressed after three times administrations of cisplatin. In April, the patient was

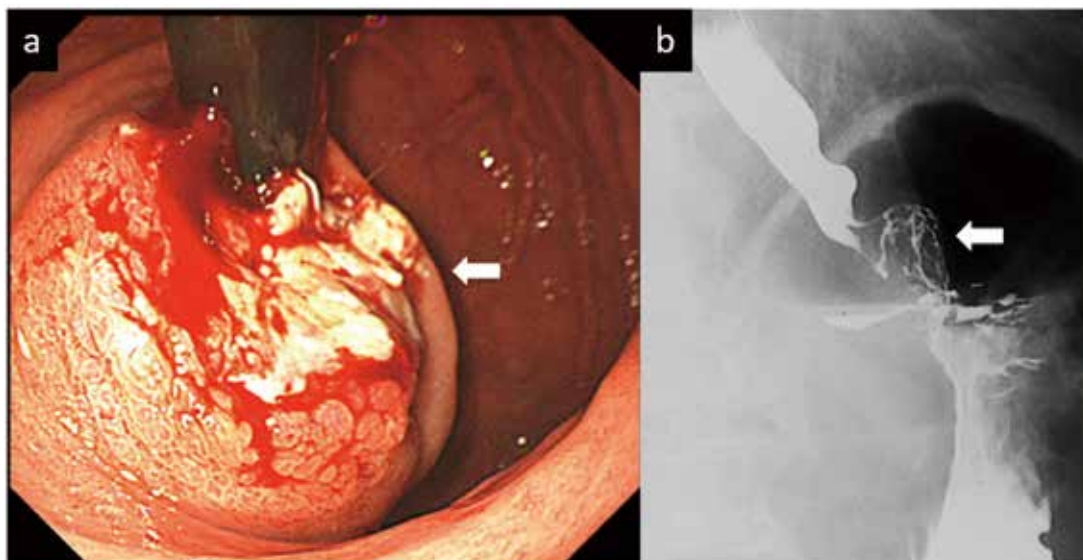


Fig. 1: Esophagogastroduodenoscopy (a) and upper gastrointestinal contrast radiography (b) showing an ulcerative tumor (arrows) in the abdominal esophagus exposing the cardia

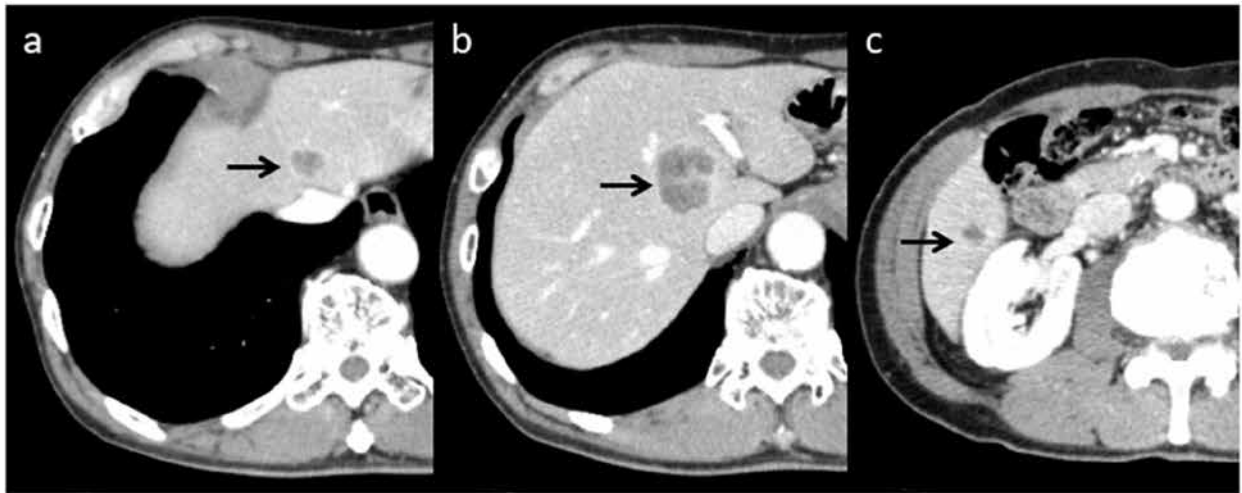


Fig. 2: A contrast-enhanced abdominal computed tomography scan showing multiple low-density areas (arrows) measuring 30 mm in diameter at their widest points in the S2 (a), S4 (b), and S6 (c) liver segments

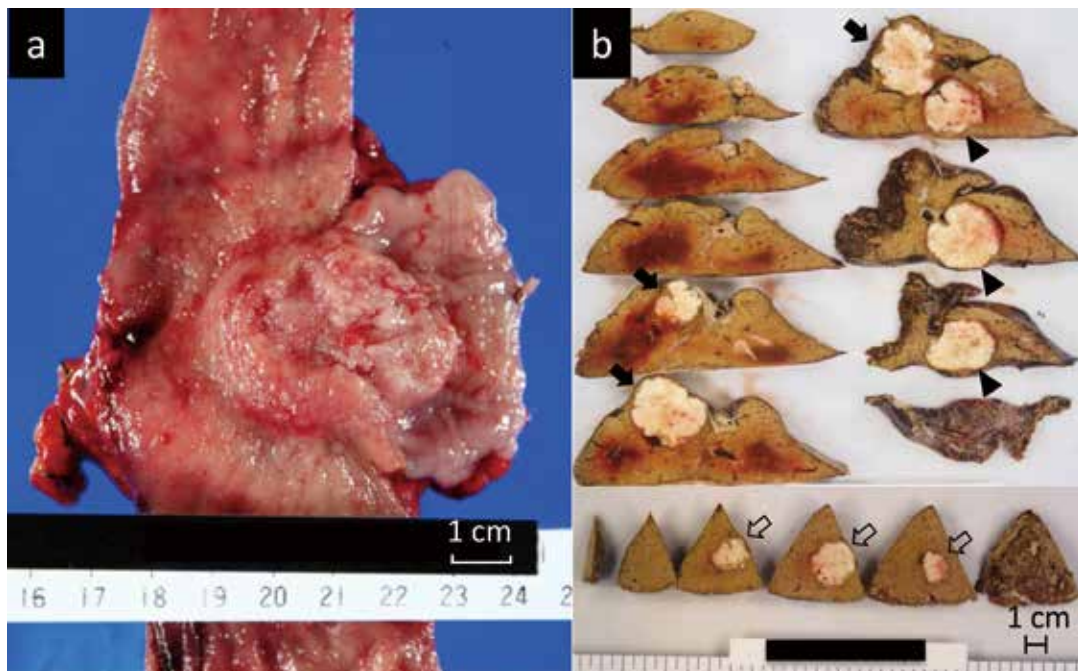


Fig. 3: Macroscopic findings showing (a) a 5.5 × 3.3-cm tumor with ulceration in the specimen resected from the esophagus and cardia and (b) tumors in the S4 (closed arrows), S2 (arrowheads), and S6 (open arrows) liver segments with diameters of 4.0 cm, 3.7 cm, and 2.0 cm, respectively

undergone lower esophagectomy with regional lymph node dissection combined with esophagogastric anastomosis reconstruction for the esophageal tumor. Directly after that, the patient was given left hepatic lobectomy and partial hepatic resection of S6 without open thoracotomy for the liver tumor. The time required for the operation was 6 h 8 min and intraoperative blood loss was 970 ml.

Macroscopically, the esophageal and cardia specimen involved a 5.5 × 3.3 cm tumor with ulceration (Fig.3a). The resected liver tumors located at S2, S4, and S6 had diameters of 4.0, 3.7, and 2.0 cm, respectively (Fig.3b). Microscopically, the esophageal tumor was moderately differentiated SCC (Fig.4a), growing into the adventitia with lymph node metastasis along the left gastric artery.

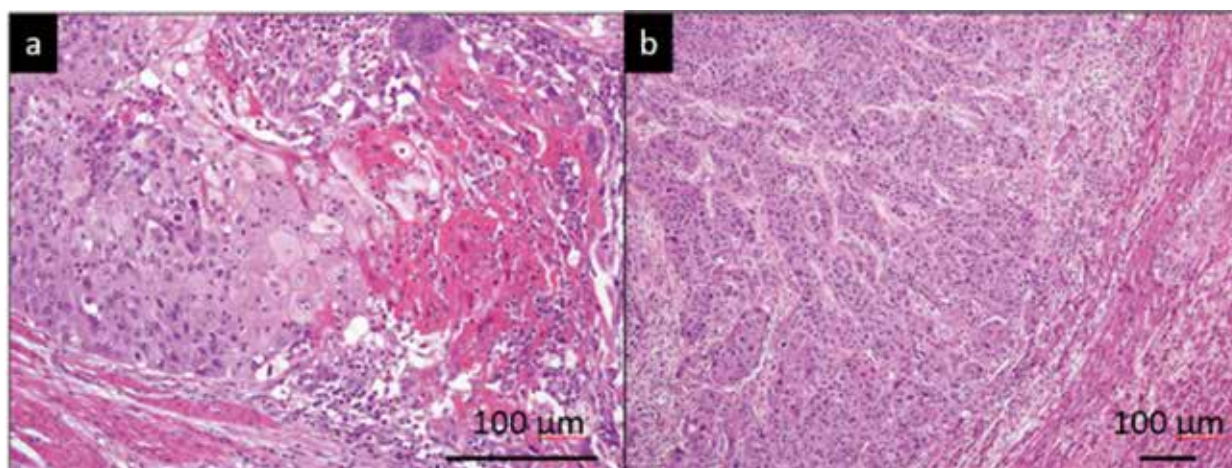


Fig. 4: Microscopic findings showing (a) moderately differentiated squamous cell carcinoma, accompanied by keratinization in the esophageal tumor (hematoxylin and eosin, $\times 400$) and (b) squamous cell carcinoma in the liver tumors that metastasized from the esophageal cancer (hematoxylin and eosin, $\times 200$)

Histology of the liver tumors revealed metastatic lesions from the esophageal cancer (Fig.4b). Pathologic stage was finally classified as T3N1M1, stage IVb according to the UICC classification. A hospitalization period was five weeks. In May 2008, the patient was started to receive daily oral administration of tegafur/gimeracil/oteracil (S-1) at 80 mg/m^2 for two weeks and docetaxel at 40 mg/m^2 on the first day as an adjuvant chemotherapy at an outpatient department, because the patient's postoperative course was uneventful. Since the patient developed grade 3 leukopenia, anorexia, and stomatitis after finishing a course, we reduced dose of docetaxel to 30 mg/m^2 and extended the duration of the chemotherapy. He had completed additional 10 courses of the chemotherapy until February 2009. Serum levels of SCC antigen and CYFRA 21-1 have been maintained normal levels since returning to normal levels immediately after surgery. He died 82 months after the surgery from bacterial pneumonia with no signs of recurrence.

Discussion

The incidence of liver metastasis from esophageal cancer has been reported to be in the range of 17–35%⁽⁵⁾. Quint et al.⁽⁴⁾ reported that 31% of liver metastases from esophageal cancer originated in the lower esophagus and that 10% of cases were SCC, as in the present case. The

prognosis of such patients is bitter, especially in those with synchronous metastatic conditions. Liver metastasis from esophageal cancer is rarely eligible for resection because the primary lesion of esophageal cancer is typically widespread and involves the lymph nodes, and the curability rate is poor. Although multimodal therapy for liver metastasis from esophageal cancer, consisting of intra-arterial chemotherapy or radiofrequency ablation therapy, has been reported, long-term survival after them cannot be achieved^(5,6).

Improvements in the safety of liver surgery due to patient selection, intraoperative techniques, and perioperative management have continued to expand the extent and indications for hepatic resection⁽²⁾. The increased safety of hepatic resection with acceptably low rates of morbidity and mortality has encouraged esophageal surgeons to perform aggressive esophagectomy with simultaneous hepatic resection including liver metastasis from esophageal cancer. However, the success rate in these reports has been quite low. Three cases of simultaneous hepatic resection and esophagectomy for metastatic esophageal cancer have been reported^(7,9). Hanazaki et al.⁽⁷⁾ reported lower esophagectomy with extended hepatic left lobectomy for 2 metastatic lesions performed via laparotomy. Yamamoto et al.⁽⁸⁾ and Mudan et al.⁽⁹⁾ reported transthoracic

esophagectomy with hepatic subsegmentectomy for solitary liver metastasis. The patients reported by Hanazaki et al.⁽⁷⁾ and Yamamoto et al.⁽⁸⁾ developed multiple liver recurrences at 6 and 7 months, respectively following surgery. Three patients indicating effectiveness of the surgical and chemotherapeutic treatment for esophageal cancer with liver metastasis survived for 18, 15, and 29 months, respectively⁽⁷⁻⁹⁾. In the present case, as surgical resection was the only remaining curative option, we performed aggressive surgical treatment after obtaining sufficient informed consent. Since the esophageal cancer was limited to the lower esophagus, both abdominal esophagectomy with regional lymphadenectomy and hepatic resections could be performed without thoracotomy, and all lesions were successfully resected with negative surgical margins. The postoperative course was uneventful without any complications such as liver dysfunction, and good postoperative progress led to an early introduction of adjuvant chemotherapy.

The effectiveness of and indications for postoperative adjuvant chemotherapy after local treatment for liver metastases of esophageal cancer remain controversial. Favorable antitumor effects of chemotherapy with docetaxel and S-1 in esophageal cancer were recently reported⁽¹⁰⁻¹³⁾. Docetaxel normally plays a key role as second-line chemotherapy for platinum-refractory patients with advanced esophageal cancer^(11,12). In contrast, a novel oral S-1 therapy comprising tegafur, gimeracil, and oteracil potassium has been developed to improve the tumor-selective toxicity of 5-FU⁽¹³⁾. We selected a docetaxel/S-1 regimen for adjuvant chemotherapy because of its high activity, high tolerability, low side-effect profile, and suitability for administration in an outpatient setting. Upon administration, chemotherapy toxicity was indeed tolerable, and the patient could maintain a satisfactory level of normal social activities during outpatient treatment. Therefore, adjuvant docetaxel/S-1 therapy can be considered effective because of its contribution to maintaining quality of life

in patients with metastatic esophageal cancer.

In our personal experiences, this is the first report of a patient with simultaneous hepatic resection and esophagectomy for metastatic esophageal cancer to achieve a disease-free survival exceeding 5 years. Repeated examinations with modalities such as systemic CT and 18F-fluorodeoxyglucose positron emission tomography have revealed no signs of recurrence, strongly suggesting that surgery and adjuvant chemotherapy with S-1 and docetaxel achieved locoregional disease control and eradication of possible invisible tumor dissemination, respectively.

Taken together, simultaneous hepatic resection appears to be an effective treatment in selective cases for not only metastases from gastric and colorectal cancer, but also liver metastasis from esophageal cancer, unless unresectable metastases are confined to the liver. Aggressive surgery with adjuvant chemotherapy may provide a survival advantage and is the treatment of choice for esophageal cancer with liver metastases.

Conflict of interest

None declared

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