Surg Today (2013) 43:556–561
DOI 10.1007/s00595-012-0240-7

CASE REPORT

A case involving long-term survival after esophageal cancer with liver and lung metastases treated by multidisciplinary therapy: report of a case

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Received: 8 October 2010 / Accepted: 16 January 2012 / Published online: 1 July 2012

Abstract A 57-year-old male with lower esophageal cancer underwent subtotal esophagectomy with lymphadenectomy. The histopathological diagnosis was poorly differentiated squamous cell carcinoma, pT2N1M0 pStageIIB. After one course of postoperative adjuvant chemotherapy involving low-dose CDDP/5FU, a PET–CT scan obtained 12 months after surgery revealed a solitary liver metastasis in the S2 area. The patient then underwent five courses of docetaxel chemotherapy (80 mg/body, tri-weekly), and a partial response was observed. We also performed radiofrequency ablation (RFA), after which a complete response was observed. Twenty months after surgery, we detected local liver recurrence in the same position and performed additional RFA. Twenty-four months after surgery, a solitary lung metastasis was detected in the left S2 area and the patient was administered five additional courses of docetaxel therapy. Subsequently, PET–CT revealed growth of lung and liver tumors without recurrence in other areas. Twenty-nine months after surgery, we partially excised metastatic liver and lung tumors, and no subsequent recurrence has since been detected. The prognoses of patients who suffer from esophageal cancer organ recurrence are known to be extremely poor, and optimal therapeutic strategies for treating these patients have not been established. This long-term survival case suggests that multidisciplinary therapy for the treatment of liver and lung recurrence after esophagectomy is effective.

Keywords Esophageal cancer · Organ metastases · Multidisciplinary therapy

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Introduction

Recent advances in surgical techniques, including extensive lymph node dissection and perioperative management, have improved the surgical outcomes of patients with esophageal cancer in Japan [1]. However, patients with advanced disease continue to frequently develop recurrent disease, even after curative resection [1]. Previous studies have shown that two-thirds of patients develop recurrence after radical esophagectomy, and most of these patients have very poor prognoses [2]. In particular, the prognoses of patients with organ recurrence, such as liver and lung metastases, are extremely poor [3] and choosing the optimal treatment, e.g. surgery, radiotherapy or systemic chemotherapy, is often difficult. Aggressive hepatic resection for liver metastases from colorectal cancer has recently been performed and was thus found to improve survival rates [4]. 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 [5, 6]. On the other hand, there is very little information regarding whether patients with liver metastases from esophageal cancer would receive any survival benefits from undergoing hepatic resection.

We herein report the case of a patient with esophageal cancer with non-simultaneous liver and lung metastases who was treated with multidisciplinary therapy consisting

of systemic chemotherapy, radiofrequency ablation (RFA) and resection of the liver and lung metastases that resulted in a long-term survival.

Case report

A 57-year-old male underwent subtotal esophagectomy and three-field lymphadenectomy followed by gastric tube reconstruction for squamous cell carcinoma of the lower thoracic esophagus. A gross examination revealed that the resected tumor was ulcerative, localized and measured 35 × 35 mm in size (Fig. 1a). Microscopic findings showed that the tumor was a poorly differentiated squamous cell carcinoma that had invaded the muscular propria. Additionally, lymph node metastases along the left gastric artery were observed (pT2N[1]M0, Stage IIB) (Fig. 1b). The patient's postoperative recovery was uneventful. He underwent one course of postoperative adjuvant chemotherapy with low-dose cisplatin (CDDP) (10 mg/body/day for 5 days) in addition to 5-FU (250–500 mg/body/day for 5 days), as we previously reported [7].

Twelve months after surgery, a PET–CT scan revealed a solitary liver metastasis measuring 32 × 21 mm in size in the S2 area (Fig. 2a). The patient was then given five courses of systemic chemotherapy with docetaxel (80 mg/body, tri-weekly) to decrease the tumor volume, and a partial response was observed (Fig. 2b). We subsequently performed RFA of the liver metastasis. A CT scan completed 16 months after the operation revealed that the surgery had achieved a complete response according to the Response Evaluation Criteria in Solid Tumors (RECIST) [8]. Twenty months after surgery, we detected a local liver recurrence at the same position (Fig. 2c) and performed additional RFA. Twenty-four months after surgery, a solitary lung metastasis was detected in the left S2 area, and five additional courses of docetaxel chemotherapy (80 mg/body, tri-weekly) were administered. PET–CT subsequently revealed the growth of lung (Fig. 2d) and liver tumors (Fig. 2e) without recurrence in other areas. Considering the extent of these tumors, which existed as solid lesions in the liver and lungs, we decided to perform surgical resection to achieve local control. Twenty-nine months after the operation, we partially excised the metastatic liver and lung tumors. The operative time was 338 min and 136 ml of intraoperative bleeding was observed. The resected liver tumors located at S2 and S4 were 38 × 29 and 12 × 12 mm in size, respectively (Fig. 3a), and the histopathological diagnosis of these tumors was poorly differentiated squamous cell carcinoma (Fig. 3b). The resected lung tumor measured 11 × 6 mm in size (Fig. 3c), and the histopathological diagnosis of this tumor was compatible with that of the lung metastasis from the previous esophageal cancer (Fig. 3d). The patient's postoperative recovery was uneventful. He was discharged 18 days after the operation without any complications, and no further recurrence was detected.

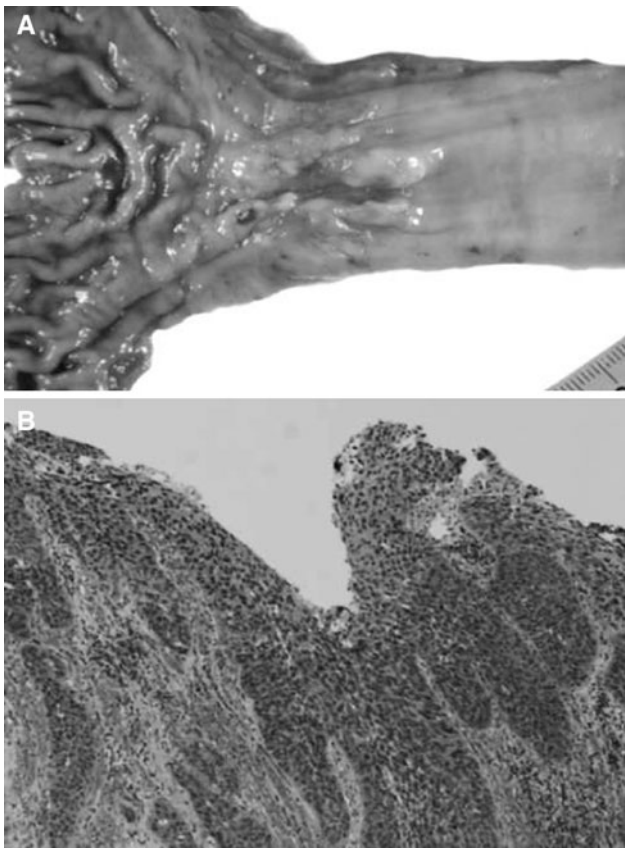

Fig. 1 **a** A resected specimen showed an esophageal tumor measuring 35 × 35 mm in size with ulceration. **b** A pathological diagnosis of poorly differentiated squamous cell carcinoma of the esophagus was made after hematoxylin–eosin staining

Discussion

Although the use of radical esophagectomy with extensive lymph node dissection has improved the outcomes of patients with esophageal squamous cell carcinoma in Japan [1], the distant metastasis rate within 20 months of this procedure has been reported to be 26 %. Patients with distant metastases have very poor prognoses [2, 9]. The most common sites of distant recurrence are the lungs, liver and bones. The incidence of liver metastasis from esophageal cancer has been reported to be between 17 and 35 % with a low long-term survival rate [3]. Optimal therapeutic strategies for treating patients with distant metastases after radical esophagectomy have not yet been fully evaluated.

Recently, docetaxel, a taxane, was demonstrated to show significant activity against various solid tumors,

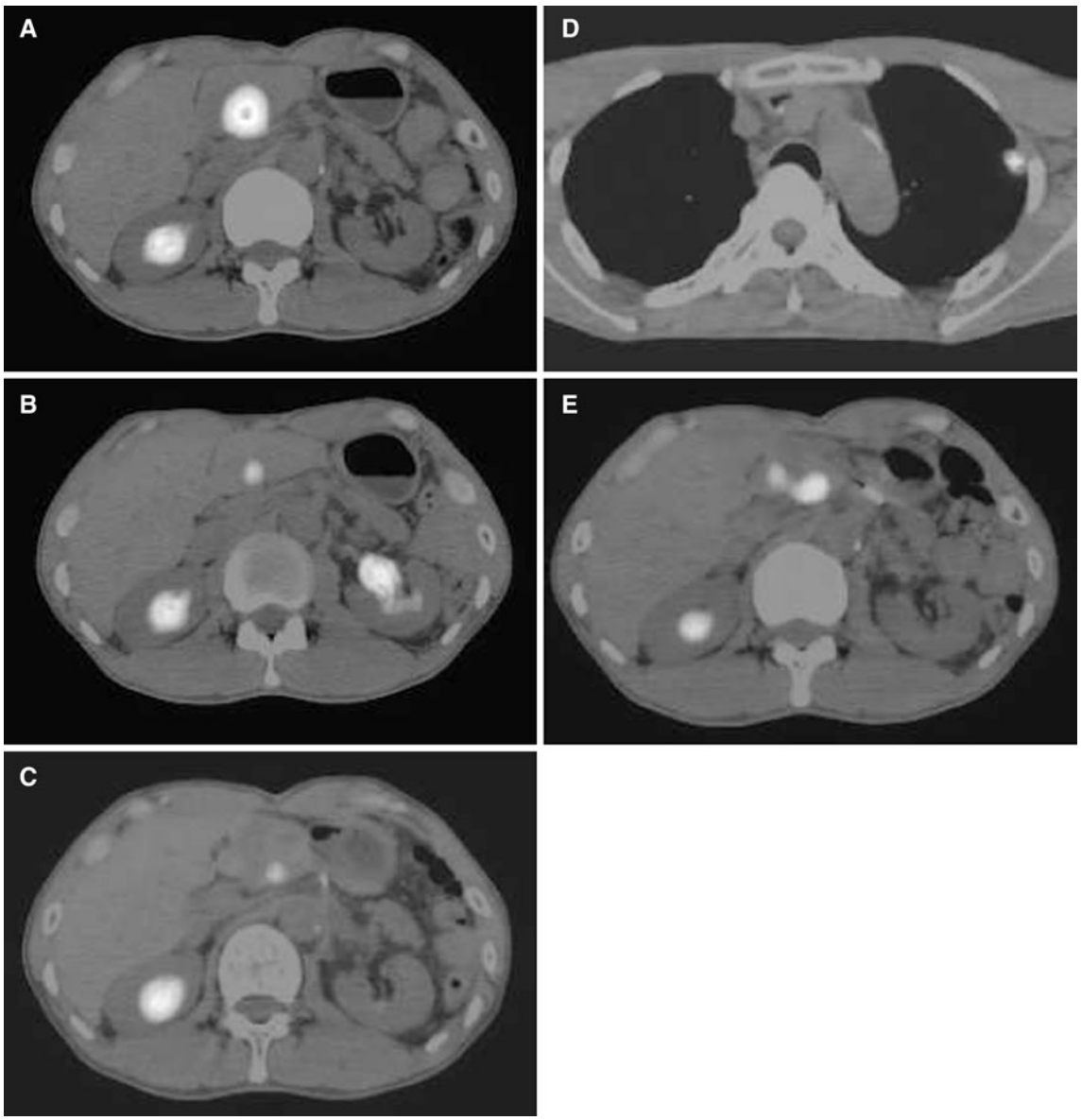

Fig. 2 PET–CT scan findings. **a** High uptake by a solitary liver tumor in the S2 area 12 months after esophagectomy. **b** Sixteen months after esophagectomy, the liver metastasis had decreased in size after treatment with systemic docetaxel chemotherapy. **c** At 20 months after esophagectomy (just before the second RFA). Lung (**d**) and liver (**e**) metastases at 28 months after esophagectomy (just before resection)

including non-small cell lung carcinomas, breast cancer, head and neck cancer, gastric cancer and others [10–12]. Muro et al. [13] reported the results of a Japanese Phase II study on the use of single-agent docetaxel (70 mg/m^2 every 3 weeks) in patients with metastatic esophageal cancer. In that study, the overall response rate was 20.4 % and the median survival time was 8.1 months. Similar results were also observed in patients with esophageal adenocarcinoma. Furthermore, several combination therapies with docetaxel have been studied in patients with esophageal cancer [14–16]. In particular, the combination of docetaxel, 5-FU and cisplatine (DCF) has been reported to be effective in treating patients with esophageal cancer [15, 16], gastric cancer [11] or head and neck cancer [12]. Patients treated with DCF therapy require hospitalization because of the need for continuous intravenous infusion and the potential for severe side effects. In this case, the patient did not wish to be hospitalized. Therefore, we chose to administer single-agent docetaxel chemotherapy in the outpatient clinic, and a partial response was observed.

Hepatic resection is the only curative treatment available for colorectal metastases and recent reports have shown that this procedure improves long-term survival rates and achieves low mortality and morbidity in selected patients

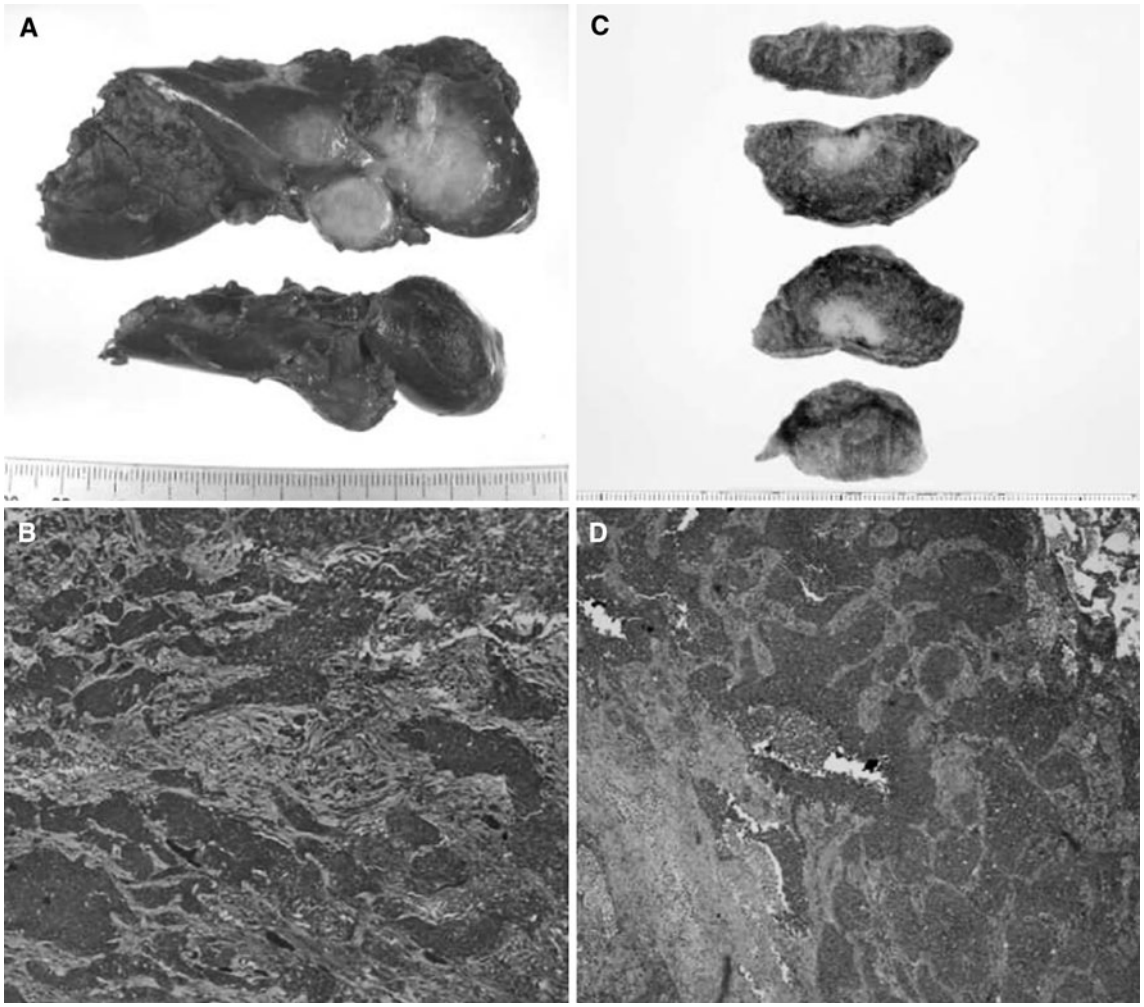

Fig. 3 **a** Resected specimens showed that the liver metastases at S2 and S4 measured 38 × 29 and 12 × 12 mm in size, respectively. **b** A pathological diagnosis of poorly differentiated squamous cell carcinoma was made after hematoxylin–eosin staining. **c** The resected lung tumor measured 11 × 6 mm in size. **d** The pathological diagnosis made after hematoxylin–eosin staining was compatible with that of the lung metastasis from the previous esophageal cancer

[4]. Furthermore, several reports have shown that liver resection prolongs survival in patients with isolated liver metastases of gastric cancer [5, 6]. A few case reports exist regarding hepatic resection for esophageal liver metastases [17, 18]. Likewise, pulmonary resection has become the standard therapy for various metastatic malignancies in the lungs [19, 20]. Chen et al. [21] analyzed five patients with pulmonary metastases from esophageal carcinoma who underwent complete pulmonary resection and concluded that patients with solitary pulmonary metastases are good candidates for this treatment and show favorable prognoses. Although the accumulation of cases is required to provide more evidence, the results of these case reports and the outcome of our patient, who survived more than 30 months after undergoing radical esophagectomy, suggest that hepatic and pulmonary resections are effective treatments for metastases from esophageal or colorectal cancer. While the effectiveness of and indications for local therapies remain controversial, our treatment strategy for isolated liver or lung metastases is to perform aggressive local treatments such as RFA and surgery after the reduction of tumor volume to a controllable size using systemic chemotherapy. In the present case, we detected a liver metastasis measuring 32 × 21 mm in size 12 months after esophagectomy. We first administered systemic chemotherapy with docetaxel to reduce the tumor volume. The tumor was subsequently reduced to 18 × 17 mm in size and no other metastatic lesions were detected. We performed RFA, which is known to be effective against liver metastases measuring <3 cm [22].

RFA is a safe and minimally invasive technique that can be repeatedly performed and provides good local control of target lesions equivalent to that achieved with surgical resection. A previous report showed that RFA can be applied as an effective local therapy for esophageal recurrence and metastases [23]. In the present case, a solid liver

tumor was safely treated with two lots of RFA without complications. A complete response was evaluated after the first RFA according to RECIST [8]. Twenty months after surgery, we detected a second liver metastasis at the same position. We selected to perform additional RFA because the procedure is easy to repeat and has a low rate of morbidity and complications [24].

The effectiveness of and indications for postoperative adjuvant chemotherapy after local treatment for liver or lung metastases of esophageal cancer remain controversial. Tokairin [25] et al. reported that five patients, who did not undergo postoperative adjuvant chemotherapy after surgical resection for liver metastases of esophageal cancer, had good outcomes. Regarding gastric cancer, several papers have reported that postoperative adjuvant chemotherapy after hepatic resection for liver metastases is not a significant prognostic factor [5, 6]. Therefore, in the present case, we did not perform postoperative adjuvant chemotherapy after local treatment, such as RFA, liver resection or lung resection.

Arterial infusion chemotherapy via the hepatic artery is considered to be effective for treating liver metastases. However, Nakajima et al. reported that placing a catheter and infusing highly concentrated anti-cancer drugs into a common hepatic artery, feeding a reconstructed stomach roll via the right gastroepiploic artery and the right gastric artery results in necrosis or ulceration of the stomach roll caused by feeding artery thrombosis or aneurysm. The authors conclude that the use of hepatic artery infusion in patients with reconstructed stomach rolls should be restricted [26]. For this reason, we chose systemic chemotherapy over arterial infusion chemotherapy in the present case.

In conclusion, we herein presented the long-term survival case of a patient with esophageal cancer with liver and lung metastases who was treated with multidisciplinary therapy consisting of systemic chemotherapy, RFA and surgical resection. In general, the prognoses of patients with organ metastases and esophageal cancer recurrence are extremely poor. However, the outcome of the present case highlights the potential of multidisciplinary therapy to prolong the survival of patients with esophageal cancer organ metastases.

Conflict of interest Daisuke Iitaka and other co-authors have no conflicts of interest to report.

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