Int Surg 2015;**100:**1271–1275
DOI: 10.9738/INTSURG-D-14-00312.1

Case Report

Aggressive Surgical Management for Metastatic Liver Tumors From Squamous Cell Carcinomas: Report of Three Cases

Hironori Hayashi[1], Hiroyuki Takamura[1], Shinichi Nakanuma[1], Jun Kinoshita[1], Isamu Makino[1], Keishi Nakamura[1], Katsunobu Oyama[1], Hisatoshi Nakagawara[1], Tomoharu Miyashita[1], Hidehiro Tajima[1], Itasu Ninomiya[1], Hirohisa Kitagawa[1], Takashi Fujimura[1], Sachio Fushida[1], Takashi Tani[2], Tetsuo Ohta[1]

[1]*Department of Gastroenterologic Surgery, Division of Cancer Medicine, Graduate School of Medical Science, Kanazawa University, Kanazawa, Japan*

[2]*Department of Surgery, Public Central Hospital of Matto Ishikawa, Hakusan, Japan*

The use of hepatectomy for the treatment of metastatic liver tumors (MLTs) arising from squamous cell carcinomas (SCCs) has not been well investigated. The use of hepatectomy for MLTs from SCCs, especially in advanced cases, needs further investigation. Three patients with SCC-derived MLTs underwent hepatectomy. On clinicopathologic examination, the primary lesions were found to be oral cancer, lung cancer, and oropharyngeal cancer, with synchronous metastasis in 2 patients and metachronous metastasis in 1 patient. One case also involved adrenal metastasis, and another involved direct invasion of the diaphragm and lung. In all cases, surgery was performed to eliminate any residual tumor tissue. After the hepatectomy, 1 patient died (22 months postoperatively) of an unrelated disease, 1 remains alive (30 months postoperatively) with a recurrent tumor, and 1 remains alive (60 months postoperatively) without recurrence. For the patients with solitary MLT derived from SCC, hepatectomy gives a chance for a cure. Thus, aggressive hepatectomy is an important modality in the multidisciplinary approach for controlling SCC-derived MLTs.

Key words: Metastatic liver tumor – Squamous cell carcinoma – Hepatectomy

Hepatectomy is a well-established and effective therapeutic modality for liver metastasis from colorectal or neuroendocrine cancers.[1,2] However, the role of hepatectomy for metastatic tumors

Corresponding author: Hironori Hayashi, MD, PhD, Department of Gastroenterologic Surgery, Division of Cancer Medicine, Graduate School of Medical Science, Kanazawa University, 13-1 Takara-machi, Kanazawa, Ishikawa 920-8641, Japan.
Tel.: +81 76 265 2362; Fax: +81 76 234 4260; E-mail: pwrofdrms2000@staff.kanazawa-u.ac.jp

Table 1 Clinical characteristics of the patients

	Case 1	Case 2	Case 3
Age, y/sex	70/male	33/female	62/male
Primary lesion	Oral cancer	Lung cancer	Oropharynx cancer
Synchronous/metachronous	Synchronous	Synchronous	Metachronous
Previous Tx	Resection of primary lesion	Resection of primary lesion	Resection and CRTx of primary lesion
Size, mm/location	50/S8	47/S7/8	65/S7
Tumor number	Solitary	Solitary	Solitary
Other organ involvement	Primary lesion	Lt adrenal gland	Rt diaphragm and lung
Surgical procedure	Partial Hx + resection of primary lesion	Rt hemi-Hx. + Lt adrenal resection	Post. sectionectomy + Rt partial pneumonectomy
Surgical margin	Negative	Negative	Negative
DFS, mo/site of rec	6/liver, lung and primary lesion	60	3/pleural dissemination
Postoperative therapy	CTx → Re-Hx	Adjuvant CTx	RTx
Prognosis	22 mo/died of other disease	60 mo/DFS	30 mo/alive with recurrent tumor

CRTx, chemoradiotherapy; CTx, chemotherapy; DFS, disease-free survival; Hx, hepatectomy; Lt, left; Post., posterior; rec, recurrence; Rt, right; RTx, radiation; Tx, therapy.

arising from noncolorectal and nonneuroendocrine carcinomas is not completely clear.[3,4] The results of a multicenter cohort study provided some insight into patients with squamous cell carcinoma (SCC) liver metastasis who would potentially benefit from hepatectomy.[5] According to the report, long-term survival may be achieved in these patients if they have limited metachronous disease amenable to negative-margin resection. However, the use of hepatectomy for liver metastasis from SCC, especially in advanced cases, needs further investigation. Therefore, in the present report we describe the cases of 3 patients with metastatic liver tumors (MLTs) arising from SCCs, who were treated using an aggressive surgical strategy.

Fig. 1 Computed tomography (CT) image of the liver tumor (arrow) in case 1. The ring-enhanced liver tumor at segment 8 is evident.

Case Presentation

Between January 2000 and December 2012, we performed hepatectomies on 3 patients with SCC-derived MLTs (Table 1). The clinicopathologic features of these cases were retrospectively characterized based on patient medical records.

Case 1

A 70-year-old man received a diagnosis of oral cancer and synchronous liver metastasis (diameter, 50 mm) in segment 8 (Fig. 1). He underwent resection of the primary lesion, which resulted in positive margins, and was referred to our department for radical excision of the liver metastasis and residual primary lesion. He underwent partial hepatectomy and primary lesion resection, with negative surgical margins. Six months after the first hepatectomy, recurrence of residual liver, lung, and primary lesions was detected. The patient underwent a second hepatectomy (partial hepatectomy), and the local recurrence was excised. Thereafter, chemotherapy was administered and the tumor was well controlled. However, the patient died of an unrelated disease (a suspected myocardial infarction) 22 months after the first hepatectomy.

Case 2

A 33-year-old woman received a diagnosis of lung cancer and synchronous metastasis in the right lobe of the liver and left adrenal gland (Fig. 2). At 2 months after tumor-free margin resection of the primary lung lesion, she was transferred to our department for

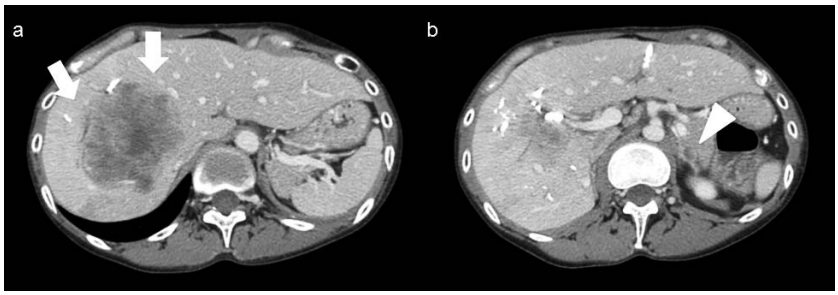

Fig. 2 CT images of the tumors in case 2. A slightly enhanced liver tumor (arrow) is seen in the CT image (a). Moreover, the tumor in the left adrenal gland (arrowhead) is evident (b).

radical excision of the liver metastasis and left adrenal metastasis. She underwent extended right hemihepatectomy and left adrenal gland resection, with negative surgical margins. Moreover, 1 month after the hepatectomy, she received 4 months of adjuvant chemotherapy. Thus far, the patient has exhibited 60 months of recurrence-free survival.

Case 3

A 62-year-old man with a diagnosis of a metastatic liver tumor derived from an oropharyngeal cancer underwent surgical treatment and adjuvant chemoradiotherapy 23 months prior to his referral to our department (Fig. 3). The liver tumor was a 65-mm, solitary lesion in the posterior sector, but it had directly invaded the right diaphragm and lower lobe of the lung. Posterior sectionectomy, along with resection of the locally invaded diaphragm and right lung lower lobe, was performed. However, recurrence was observed 3 months after the hepatectomy as pleural dissemination and adjacent primary lesion. The patient received irradiation for the pleural dissemination, along with systemic chemotherapy. This patient remains alive 30 months after the hepatectomy, with a recurrent tumor that is being closely monitored.

Discussion

Unlike the use of hepatectomy for MLTs arising from colorectal or neuroendocrine cancers,[1,2] the use of hepatectomy for MLTs arising from SCCs is not well established because of the lack of cohort studies assessing its efficacy.[6,7] Pawlik *et al*[5] reported a cohort study involving hepatectomy for SCC-derived MLTs to clarify the significance and advantages of the method. According to their report, long-term survival could be achieved in patients with limited metachronous disease that was amenable to negative-margin resection. However, the use of hepatectomy for advanced MLTs arising from SCCs needs further investigation, because surgical resection represents the only chance for a cure.

In our series, SCC metastasis was not limited to the liver. In case 2, metastasis was noted in the liver and the left adrenal gland. Both lesions were resectable, and thus negative surgical margins could be obtained. The recurrence-free clinical course of this patient suggests the importance of adjuvant chemotherapy for patients with resectable metastatic tumor, including MLT. The use of adjuvant chemotherapy after curative resection of the tumor has also been demonstrated to be beneficial for lung SCCs[8,9] and SCCs from other primary lesions.[10–12] Thus, for patients with tumors limited to the primary lesion and liver metastasis, a combination therapy involving hepatectomy for the MLT and surgical or other curative therapy for the primary lesion, as well as adjuvant chemotherapy, is believed to yield a good prognosis.

Another type of MLT progression involves local extension and invasion to adjacent organs, as indicated in one of the present cases. In this case,

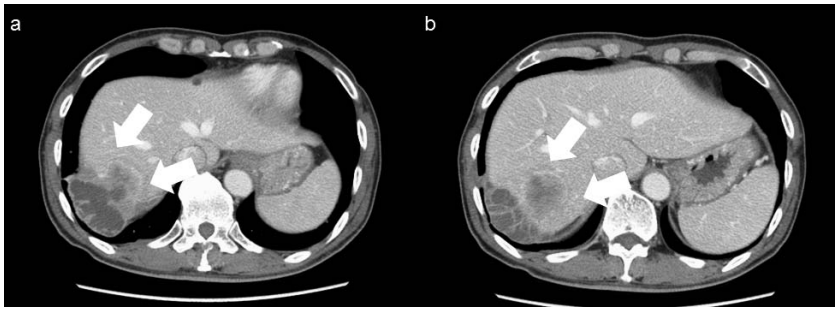

Fig. 3 CT image of the liver tumor (arrow) in case 3. The ring-enhanced liver tumor is evident in the posterior sector (b), and has directly invaded the diaphragm and lung (a), as shown.

the tumor invaded the right lung from the right lateral sector via the diaphragm. In such cases, the risk of peritoneal and pleural dissemination is unavoidable because of tumor progression. Furthermore, the treatment modality used for peritoneal and pleural dissemination is important because these cases have a high risk of recurrence. In our series, pleural dissemination was treated with irradiation because irradiation has been suggested to be effective for SCCs with disseminated lesions.[13,14] In contrast, peritoneal dissemination is difficult to treat with irradiation because of the morbidities associated with intestinal injury. In such cases, other modalities, such as systemic chemotherapy, are preferred.[15] The most important therapeutic strategy for SCC metastasis involves the use of a multidisciplinary treatment approach, including surgery in combination with chemotherapy or irradiation. Nevertheless, hepatectomy for SCC-derived MLTs is a useful option because liver tumor progression is directly related to tumor-associated mortality.

Intrahepatic recurrence after hepatectomy of SCC liver metastasis should also be aggressively treated, and this may involve the use of repeat hepatectomy, if possible. Repeat hepatectomy is a safe, feasible, and effective therapeutic modality in patients with adequate preserved hepatic reserve.[16] Thus, recurrence in the residual liver is not a contraindication for surgery, even if the tumor is an SCC-derived MLT, as in one of the cases in this study. If the hepatic reserve is sufficient for tumor-free margin hepatectomy, repeat surgery is the best modality for tumor control, because an MLT may be a life-threatening lesion.

In our series, all of the patients had solitary MLTs. This seems to be important for predicting the biologic behavior of the resected tumor. The number of metastatic liver lesions is significantly related to the prognosis in patients with other types of primary lesions, such as colorectal adenocarcinoma.[17,18] Similarly, solitary hepatic metastasis of urothelial carcinoma, gastric cancer, and breast cancer is a good prognostic factor.[19–21] Thus, in our SCC patients the presence of a solitary MLT after hepatectomy was a good prognostic feature.

An important problem, according to the clinical outcome of our series, is selection bias. Such bias was unavoidable because the determination of surgical indications was influenced by the tumor status. In our series, the patients were referred to our department from various departments that were initially responsible for treating the primary lesions, including dental surgery, respiratory surgery, and otorhinolaryngology. Thus, the treatment of SCC liver metastases depends on a decision by the doctor in charge regarding the possibility of a posthepatectomy cure. Therefore, knowing and disseminating information regarding the curability of SCC liver metastases are very important.

The selection of appropriate patients for hepatectomy after the diagnosis of SCC-derived MLTs is critical. Although most patients develop recurrent lesions, as mentioned above, surgical resection represents the only chance for a cure. Thus, to achieve negative resection margins, it is very important to have an aggressive surgical strategy that includes metastasectomy and extended resection of the adjacent invaded organs in order to eliminate residual tumor tissue. Additionally, effective adjuvant therapies appear to be useful for preventing recurrence after aggressive surgery.

In summary, aggressive surgery is an important therapeutic modality for patients with advanced SCC liver metastasis. Moreover, good clinical judgment and cautious selection of patients are essential for determining the surgical indications for SCC-derived MLTs. The consideration of an aggressive surgical strategy is an important factor when deciding the therapeutic strategy, although accumulation of further cases is needed to determine the characteristics of SCC liver metastases that are amenable to this strategy.

References

1. Tzeng CW, Aloia TA. Colorectal liver metastases. *J Gastrointest Surg* 2013;**17**(1):195–201
2. Pathak S, Dash I, Taylor MR, Poston GJ. The surgical management of neuroendocrine tumour hepatic metastases. *Eur J Surg Oncol* 2013;**39**(3):224–228
3. Weitz J, Blumgart LH, Fong Y, Jarnagin WR, D'Angelica M, Harrison LE *et al*. Partial hepatectomy for metastases from noncolorectal, nonneuroendocrine carcinoma. *Ann Surg* 2005; **241**(2):269–276
4. Yamada H, Katoh H, Kondo S, Okushiba S, Morikawa T. Hepatectomy for metastases from non-colorectal and non-neuroendocrine tumor. *Anticancer Res* 2001;**21**(6A):4159–4162
5. Pawlik TM, Gleisner AL, Bauer TW, Adams RB, Reddy SK, Clary BM *et al*. Liver-directed surgery for metastatic squamous cell carcinoma to the liver: results of a multi-center analysis. *Ann Surg Oncol* 2007;**14**(10):2807–2816
6. Theodosopoulos TK, Marinis AD, Dafnios NA, Vassiliou JG, Samanides LD, Carvounis EE *et al*. Aggressive treatment of metastatic squamous cell carcinoma of the rectum to the liver: a case report and brief review of the literature. *World J Surg Oncol* 2006;**4**:49

7. Tokar M, Bobilev D, Zalmanov S, Geffen DB, Walfisch S. Combined multimodal approach to the treatment of metastatic anal carcinoma: report of a case and review of the literature. *Onkologie* 2006;**29**(1–2):30–32
8. Naim Younes R, Gross JL, Abrao FG, Rodrigues Pereira J. Impact of adjuvant chemotherapy in completely resected stage IIIA non-small cell lung cancer. *Minerva Chir* 2013;**68**(2):169–174
9. Ou W, Sun HB, Ye X, Zhang BB, Yang H, Fang Q *et al*. Adjuvant carboplatin-based chemotherapy in resected stage IIIA-N2 non-small cell lung cancer. *J Thorac Oncol* 2010;**5**(7):1033–1041
10. Ku GY, Ilson DH. Adjuvant (postoperative) therapy for esophageal cancer. *Thorac Surg Clin* 2013;**23**(4):525–533
11. Kupets R, Le T, Le T, Bentley J, Farrell S, Fortier MP *et al*. The role of adjuvant therapy in endometrial cancer. *J Obstet Gynaecol Can* 2013;**35**(4):375–379
12. Rades D, Ulbricht T, Hakim SG, Schild SE. Cisplatin superior to carboplatin in adjuvant radiochemotherapy for locally advanced cancers of the oropharynx and oral cavity. *Strahlenther Onkol* 2012;**188**(1):42–48
13. Czito BG, Meyer J. Radiation therapy in anal and rectal cancer. *Surg Oncol Clin N Am* 2013;**22**(3):525–543
14. Yang H, Diao LQ, Shi M, Ma R, Wang JH, Li JP *et al*. Efficacy of intensity-modulated radiotherapy combined with chemotherapy or surgery in locally advanced squamous cell carcinoma of the head-and-neck. *Biologics* 2013;**7**:223–229
15. Hainsworth JD, Fizazi K. Treatment for patients with unknown primary cancer and favorable prognostic factors. *Semin Oncol* 2009;**36**(1):44–51
16. Nakamura S, Sakaguchi S, Nishiyama R, Suzuki S, Yokoi Y, Baba S *et al*. Aggressive repeat liver resection for hepatic metastases of colorectal carcinoma. *Surg Today* 1992;**22**(3):260–264
17. Zou L, Zhang G, Tang T, Lian R, Wang W. Retrospective analysis of clinical and pathologic risk factors in liver resection for hepatic colorectal metastases. *J Cancer Res Ther* 2013; **9**(suppl):S178–S182
18. Feroci F, Fong Y. Use of clinical score to stage and predict outcome of hepatic resection of metastatic colorectal cancer. *J Surg Oncol* 2010;**102**(8):914–921
19. Abe T, Kitamura H, Obara W, Matsumura N, Tsukamoto T, Fujioka T *et al*. Outcome of metastasectomy for urothelial carcinoma: a multi-institutional retrospective study in Japan. *J Urol* 2014;**191**(4):932–936
20. Kodera Y, Fujitani K, Fukushima N, Ito S, Muro K, Ohashi N *et al*. Surgical resection of hepatic metastasis from gastric cancer: a review and new recommendation in the Japanese gastric cancer treatment guidelines. *Gastric Cancer* 2014;**17**(2):206–212
21. van Walsum GA, de Ridder JA, Verhoef C, Bosscha K, van Gulik TM, Hesselink EJ *et al*. Resection of liver metastases in patients with breast cancer: survival and prognostic factors. *Eur J Surg Oncol* 2012;**38**(10):910–917