


CASE REPORT

Open Access



Hepatectomy for rapidly growing solitary liver metastasis from non-small cell lung cancer: a case report

Hiroyuki Hakoda¹, Yasuharu Sekine², Hideo Ichimura^{2,4,5*} , Kazumitsu Ueda¹, Shigeo Aoki¹, Hideyuki Mishima¹, Akihiro Sako¹, Keisuke Kobayashi², Akiko Sakata³ and Yukio Sato⁴

Abstract

Background: Patients with liver metastasis from non-small lung cancer (NSCLC) usually have multiple metastases at other sites and thus rarely undergo liver surgery. We present a case involving successful resection of rapidly growing liver metastasis from squamous cell carcinoma of the lung.

Case presentation: A 74-year-old man had undergone left lower lobectomy for squamous cell carcinoma of the lung, which was diagnosed pathologically as stage IA. A computed tomography (CT) scan that was taken 12 months after lung resection showed an irregularly shaped mass lesion (size, 8.3 cm) in segment five of the liver. Retrospectively, the mass was identifiable on CT 6 months before this initial recognition. Although the lesion showed rapid growth, positron emission tomography and brain magnetic resonance imaging ruled out the possibility of other metastatic lesions. Therefore, we performed right hepatectomy 14 months after the initial lung surgery. The patient was pathologically diagnosed with liver metastasis from lung cancer and has remained free from recurrence 41 months after the liver surgery, without receiving any adjuvant chemotherapy.

Conclusions: Although there is no reliable clinical indicator for selecting oligo-recurrence, hepatectomy could be an option for solitary liver metastasis from NSCLC for patients who are in good health.

Keywords: Metastatic liver tumor, Hepatectomy, Non-small cell lung cancer, Oligo-metastasis, Oligo-recurrence, Tumor doubling time

Background

Although the recurrences that have been observed after complete resection for non-small cell lung cancer (NSCLC) mostly include multiple organs or sites and are treated with systemic anticancer drugs, oligo-recurrence/metastasis is considered a recurrent mode that could be controlled using a definitive local therapy [1–3]. However, selecting the appropriate patients for definitive local therapy remains an intractable issue.

Since the liver is rarely observed as an oligo-recurrence/metastasis site in patients with NSCLC [1], hepatectomies

for liver metastasis from NSCLC have rarely been reported [4]. We encountered a patient with a rapidly growing solitary liver mass lesion that developed after lung resection for NSCLC and treated the patient using a hepatectomy.

Case presentation

A 74-year-old man had undergone left lower lobectomy for NSCLC (Fig. 1a). The tumor was pathologically diagnosed as squamous cell carcinoma of the lung (1.9 cm in size) without lymph node metastasis (TNM classification 7th edition, pT1aN0M0 and stage IB) (Fig. 1b). He was followed up periodically, and a computed tomography (CT) scan that was taken 1 year after the operation revealed an 8.3 cm, irregularly shaped mass lesion in segment five of the liver (Fig. 1c). Retrospectively, CT performed 6 months

* Correspondence: ichimura@md.tsukuba.ac.jp

²Department of Thoracic Surgery, Hitachi General Hospital, Hitachi, Japan

⁴Department of Thoracic Surgery, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

Full list of author information is available at the end of the article

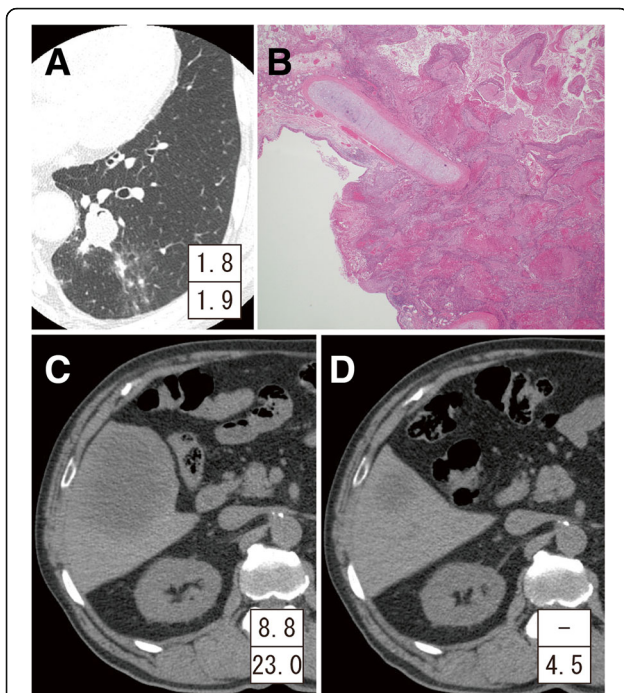


Fig. 1 **a** Chest computed tomography (CT) shows 1.8-cm nodule in the left lower lobe of the lung. **b** The pathological image shows squamous cell carcinoma of the lung (hematoxylin-eosin stain). **c** The abdominal CT taken 12 months after lung resection shows an 8.3-cm mass in the right liver. **d** CT taken 6 months after lung resection shows a 3.1-cm low-density lesion in the liver. Insets in **a**, **c**, and **d** show serum levels of tumor markers at the time (upper: carcinoembryonic antigen [CEA]; lower: cytokeratin 19 fragment [CYFRA])

prior showed a 3.1 × 2.9 cm low-density lesion at the identical site (Fig. 1d). Since 18-fluoro-2-deoxyglucose (¹⁸F-FDG) positron emission tomography and enhanced brain magnetic resonance imaging (MRI) ruled out any metastatic lesions other than the one in the liver, the patient was referred to a gastroenterological surgeon. Liver MRI demonstrated a well-defined mass, which was hypointense relative to the liver parenchyma on T1-weighted images (Fig. 2a) and hyperintense on T2-weighted images (Fig. 2b). The hepatic mass exhibited clear hypointensity in the late dynamic and hepatobiliary phases on ethoxybenzyl diethylenetriaminepentaacetic acid-MRI (Fig. 2c). Moreover, MRI showed that the mass had increased to 9.6 cm in diameter within a 1-month interval. Although serum levels of carcinoembryonic antigen (CEA; cut-off value, 3.4 ng/ml) and cytokeratin 19 fragment (CYFRA; cut-off value, 3.5 ng/ml) were both within the normal range at the time of lung resection, both CEA and CYFRA levels increased to 11.0 ng/ml and 23.0 ng/ml, respectively, along with enlargement of the hepatic mass (CEA and CYFRA levels at each time point are indicated in Figs. 1 and 2).

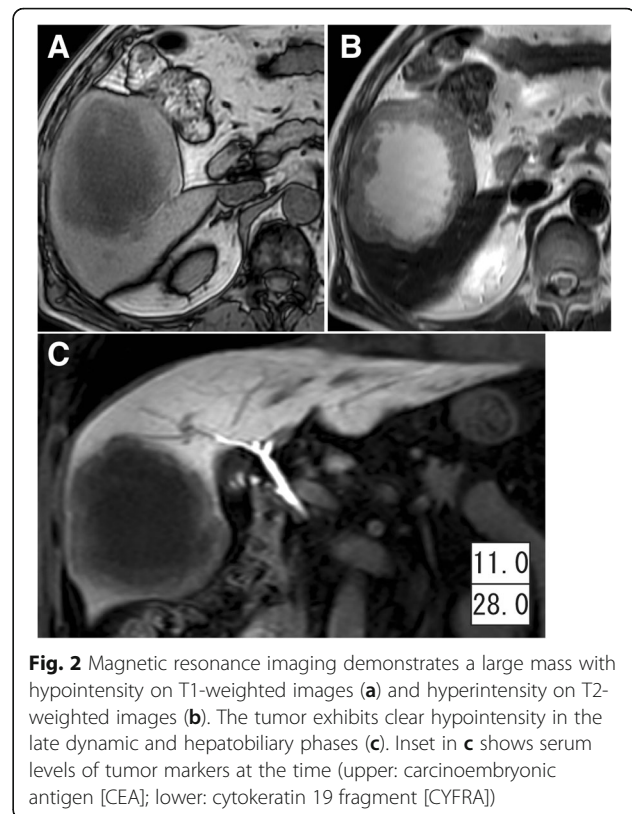


Fig. 2 Magnetic resonance imaging demonstrates a large mass with hypointensity on T1-weighted images (**a**) and hyperintensity on T2-weighted images (**b**). The tumor exhibits clear hypointensity in the late dynamic and hepatobiliary phases (**c**). Inset in **c** shows serum levels of tumor markers at the time (upper: carcinoembryonic antigen [CEA]; lower: cytokeratin 19 fragment [CYFRA])

Since his general condition was good and his major organ functions were tolerable to general anesthesia, the patient underwent right hepatectomy 14 months after the lung resection at the primary site. Intraoperatively, a huge mass was detected in the right liver, but no other metastatic sites were identified. The postoperative course was uneventful, and the patient was discharged on postoperative day 10.

The macroscopic examination of the cut specimen showed an irregular, grayish mass that measured 10 × 8 × 5.5 cm, with massive central necrosis (Fig. 3a). The pathologic examination confirmed metastatic squamous cell carcinoma of the lung (Fig. 3b). He did not receive adjuvant chemotherapy and was free from recurrence 41 months after the hepatectomy.

Discussion

Here, we performed a right hepatectomy for a rapidly growing giant liver metastasis from NSCLC, and the patient did not present recurrence 41 months after the hepatectomy and 54 months after the lung resection. Although the liver is not a common recurrence site [3], and reported cases of hepatectomies for liver metastases from NSCLC are rare [4], we recommended surgical resection to this patient. Since the tumor showed substantial growth after we overlooked the liver lesion 6 months before the initial recognition

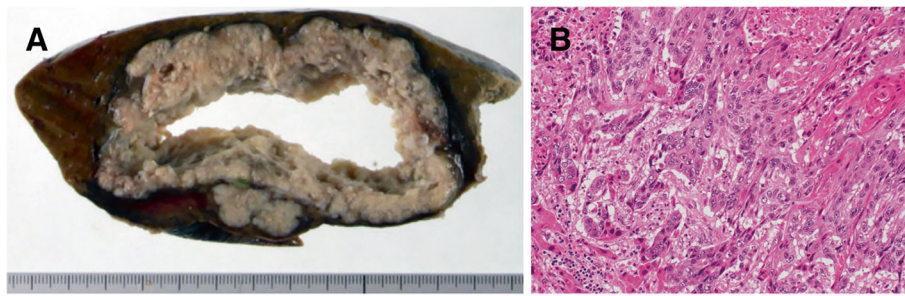
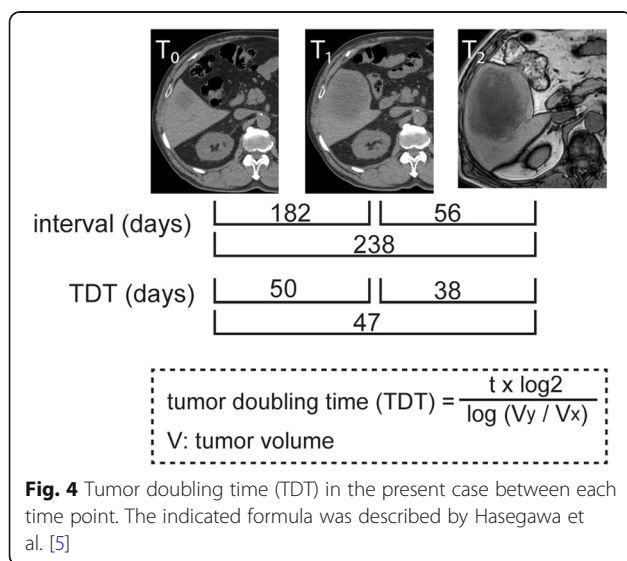


Fig. 3 **a** A macroscopic image of the cut specimen shows an irregular, grayish mass measuring 10.0 cm with massive central necrosis. **b** The microscopic image of the liver mass shows squamous cell carcinoma

and the new metastatic lesion did not emerge during the 6-month interval, we considered that the liver metastasis could be an oligo-metastasis. Retrospectively, we verified whether our presumption based on an unintentional 6-month observation was supported by the tumor doubling time (TDT) [5]. In this case, the TDT ranged from 38 to 50 days (Fig. 4). If the patient had other clinically unrecognizable metastatic lesions that were 2 mm in diameter and could grow to a recognizable 1 cm diameter, this increase would take 116 days, since the TDT is 50 days. Although 6 months is longer than this 116-day interval, we can assume that a single metastatic cell from this patient would require 30 times the TDT ($30 \times 50 = 1500$ days) bio-mathematically [6] to become a nodule with a diameter of 1 cm. Thus, our presumption that this case truly involves oligo-metastasis is not fully supported by the TDT model. To select appropriate patients with oligo-recurrences/metastases for definitive local therapy, other clinical indicators, such as circulating tumor cells, should be developed [7].

We reviewed hepatectomy cases from the literature available in English and Japanese for reports of metachronous liver metastases from NSCLC, excluding patients who were diagnosed with liver metastasis concurrently with lung cancer, and found 21 cases, including the present one (Table 1) [8–17]. Among these patients, there is a case who is not truly oligo-recurrence because of multiple abdominal lymph node metastases [8]. Moreover, Nagashima et al. [17] mentioned that they did not report two other patients who underwent hepatectomies and did not survive. Although it is impossible to rule out selection and publishing biases in our review of reported cases, the median survival time of all cases after hepatectomy is 24.3 months, and the median interval between initial lung surgery and hepatectomy is 11 months (mean 15 months, range 1.6–48 months). The interval is not significantly different between post-hepatectomy survival and mortality cases (mean 16.8 and 11.4 months, Mann-Whitney *U* test: $p = 0.40$). Squamous cell carcinoma was the dominant histologic type, and this finding is consistent with Hishida et al.'s observation [1], which showed that oligo-recurrence was non-adenocarcinoma histology dominant. On survival analyses, cases of pathological stage I lung cancer showed better post-hepatectomy prognosis than those of pathological stage II or more (2-year survival rate 87.5% and 50.0%, respectively). Moreover, cases with squamous cell carcinoma showed better post-hepatectomy prognosis than those with non-squamous histologies (2-year survival rate 87.5% and 55.6%, respectively). Tumor angiogenesis varies between histologic types [18], and this might affect the recurrent mode and prognosis after definitive local therapy for recurrence.



Conclusion

We report on a patient who underwent hepatectomy for liver metastasis from NSCLC and remained recurrence free at 41 months after liver surgery. Although we

Table 1 Reported cases of hepatectomy for metachronous liver metastases from non-small cell lung cancer

No.	Author	Age	Sex	Primary lesion		Stage	Histological type	Adjuvant therapy	Time interval (months)	Liver metastases			Treatment for recurrences	Outcome (months)
				Management	Metastasis					Location	Size (cm)	Number		
1	Di Carlo	69	F	L	NA	AD	-	48	S7	5	1	P	-	Alive (36)
2	Takagi	46	M	L	NA	Pleo	-	10	S6	10	1	S	CT	Dead (12)
3	Nagashima	71	M	L	IB	AD	-	6	S5/S6	2.5/0.4	2	P	-	Alive(62)
4	Nikkumi	60	M	L	IB	SQ	RT	12	S7	7	1	P	Surg	Alive (73)
5	Kim	55	M	Pn*	IA	SQ	-	7	caudate	NA	1	S	-	Alive (60)
6	Ercolani	52	M	L	NA	AD	CT	24	S6	5	1	S	-	Dead(36)
7	Ercolani	60	F	L	NA	AD	CT	18	NA	6	1	L	-	Alive (NA)
8	Ileana	56	M	L*	IIIA	LCNEC	-	24	NA	NA	3	L	CT	Alive(21)
9	Ileana	70	F	CCRT	IIIB	AD	-	9	NA	3	1	NA	CT	Dead (55)
10	Ueda	77	M	L	IIA	LA	CT, RT	8	S8	5	1	S	-	Alive (6)
11	Ueda	65	F	L	IIIA	AD	CT, RT	20	S7	2	1	S	-	Dead (20)
12	Higaki	77	M	P	IB	SQ	-	10	S2	1	1	S	RT, BI, CT	Alive(33)
13	Watanabe	71	M	L	IA	AD	-	11	S6	3.5	1	P	EGFRTKI	Alive (6)
14	Ishige	NA	M	Surg	IIIA	SQ	-	1.6	NA	4.5	1	S	RT	Dead(15.2)
15	Ishige	NA	M	Surg	IB	SQ	-	15	NA	4	4	P	CT	Alive(23.4)
16	Ishige	NA	M	Surg	IIIA	SQ	CT	8	NA	4	1	S	CT	Dead(24.5)
17	Ishige	NA	M	Surg	IA	SQ	-	7	NA	2.3	3	S	NA	Alive(30.2)
18	Ishige	NA	M	Surg	IB	SQ	CT	13	NA	3	1	P	CT	Alive(26.2)
19	Ishige	NA	F	Surg	IB	AD	-	42	NA	1.9	4	P	-	Alive(24)
20	Ishige	NA	M	Surg	IB	LA	-	7.4	NA	7.5	1	S	-	Dead(16.5)
21	Present case	74	M	L	IB	SQ	-	14	S5	9.6	1	L	-	Alive (41)

NA not available, AD adenocarcinoma, SQ squamous cell carcinoma, LA large cell carcinoma, LCNEC large cell neuroendocrine carcinoma, Pleo pleomorphic carcinoma, CT chemotherapy, RT radiotherapy, CCRT concurrent chemoradiotherapy, time interval the interval of time between primary lesion treatment and hepatectomy, P partial resection, S segmentectomy or sectionectomy, Surg surgery, I lobectomy, Pn pneumonectomy, BI bronchoscopic intervention, EGFRTKI epidermal growth factor receptor tyrosine kinase inhibitor
 Italic font indicates the pathological stage
 *Induction therapy was administered

do not have a reliable clinical indicator for selecting oligo-recurrent cases, hepatectomy provides an option for patients with solitary liver metastasis from NSCLC. Based on our review of reported cases, patients with pathological stage I NSCLC and squamous cell carcinoma who undergo hepatectomies demonstrate better post-hepatectomy prognoses.

Abbreviations

NSCLC: Non-small cell lung cancer; TDT: Tumor doubling time

Acknowledgements

Not applicable

Funding

None.

Availability of data and materials

The dataset supporting the conclusions of this case report is included within the article.

Authors' contributions

KU carried out the surgery, and YSek, KK, SA, HM, and ASako cared for the patient postoperatively and/or at outpatient clinic. KU and HH prepared and drafted the manuscript. HI and HH corrected and finalized the manuscript. ASako took pathological images. YSat comprehensively supervised this case report. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details

¹Department of Surgery, Hitachi General Hospital, Hitachi, Japan.

²Department of Thoracic Surgery, Hitachi General Hospital, Hitachi, Japan.

³Department of Pathology, Hitachi General Hospital, Hitachi, Japan.

⁴Department of Thoracic Surgery, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan. ⁵Department of Thoracic Surgery, Faculty of Medicine, University of Tsukuba, Hitachi Medical Education and Research Center, 2-1-1 Jyounan, Hitachi, Ibaraki 317-0077, Japan.

Received: 20 February 2019 Accepted: 24 April 2019

Published online: 02 May 2019

References

- Hishida T, Yoshida J, Aokage K, Nagai K, Tsuboi M. Postoperative oligo-recurrence of non-small-cell lung cancer: clinical features and survival. *Eur J Cardiothorac Surg*. 2016;49:847–53.
- Yano T, Okamoto T, Fukuyama S, Maehara Y. Therapeutic strategy for postoperative recurrence in patients with non-small cell lung cancer. *World J Clin Oncol*. 2014;5:1048–54.
- Sonobe M, Yamada T, Sato M, Menju T, Aoyama A, Sato T, et al. Identification of subsets of patients with favorable prognosis after recurrence in completely resected non-small cell lung cancer. *Ann Surg Oncol*. 2014;21:2546–54.
- Ishige F, Takayama W, Chiba S, Hoshino I, Arimitsu H, Yanagibashi H, et al. Hepatectomy for oligo-recurrence of non-small cell lung cancer in the liver. *Int J Clin Oncol*. 2018;23:647–51.
- Hasegawa M, Sone S, Takashima S, Li F, Yang ZG, Maruyama Y, et al. Growth rate of small lung cancers detected on mass CT screening. *Br J Radiol*. 2000; 73:1252–9.
- Schwartz M. A biomathematical approach to clinical tumor growth. *Cancer*. 1962;14:1272–94.
- Radwan N, Phillips R, Ross A, Rowe SP, Gorin MA, Antonarakis ES, et al. A phase II randomized trial of Observation versus stereotactic ablative Radiation for OLigometastatic prostate CancEr (ORIOLE). *BMC Cancer*. 2017; 17:453.
- Watanabe H, Kurumiya Y, Mizuno K, Sekoguchi E, Kobayashi S, Hiramatsu Y. A case of surgical resection of solitary liver metastasis from lung cancer. *Geka*. 2017;79:383–7 in Japanese.
- Higaki N, Nakane S, Uemura H, Okada K, Miyake Y, Murakami M, et al. Advanced lung cancer with recurrence of liver and tracheal metastases responsive to multimodality therapy - a case report. *Gan To Kagaku Ryoho*. 2014;41:2047–9 in Japanese.
- Ueda J, Yoshida H, Mamada Y, Taniai N, Mineta S, Yoshioka M, et al. Surgical resection of solitary metastatic liver tumor arising from lung cancer: a case series. *Hepatogastroenterology*. 2012;59:2307–9.
- Ileana E, Greillier L, Moutardier V, Barlesi F. Surgical resection of liver non-small cell lung cancer metastasis: a dual weapon? *Lung Cancer*. 2010;70: 221–2.
- Kim KS, Na KJ, Kim YH, Ahn SJ, Bom HS, Cho CK, et al. Surgically resected isolated hepatic metastasis from non-small cell lung cancer: a case report. *J Thorac Oncol*. 2006;1:494–6.
- Ercolani G, Ravaioli M, Grazi GL, Cescon M, Varotti G, Del Gaudio M, et al. The role of liver resections for metastases from lung carcinoma. *HPB (Oxford)*. 2006;8:114–5.
- Nikkuni K, Makino S, Shimizu T, Nishimura A, Kawachi Y, Shimizu T. A long-term and recurrence-free survivor after repeated surgical resection of liver metastases from lung cancer. *J Jpn Surg Assoc*. 2005;66:1308–11 in Japanese.
- Takagi K, Watanabe Y, Watanabe Y, Mado K, Iijima R, Shimamura M, et al. Resection of liver metastasis from lung cancer: case report. *Nihon Univ J Med*. 2004;46:85–90.
- Di Carlo I, Grasso G, Patane D, Russello D, Latteri F. Liver metastases from lung cancer: is surgical resection justified? *Ann Thorac Surg*. 2003;76:291–3.
- Nagashima A, Abe Y, Yamada S, Nakagawa M, Yoshimatsu T. Long-term survival after surgical resection of liver metastasis from lung cancer. *Jpn J Thorac Cardiovasc Surg*. 2004;52:311–3.
- Yuan A, Yang PC, Yu CJ, Lee YC, Yao YT, Chen CL. Tumor angiogenesis correlates with histologic type and metastasis in non-small-cell lung cancer. *Am J Respir Crit Care Med*. 1995;152:2157–62.

Submit your manuscript to a SpringerOpen[®] journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► [springeropen.com](https://www.springeropen.com)