Surgical resection of liver metastasis of leiomyosarcoma

Yong Woon Kim¹, Jae Hoon Lee², Jeoung Eun Kim³, Jihoon Kang³

¹Division of General Surgery, Department of Surgery, Asan Medical Center, Seoul;

²Division of Hepatobiliary & Pancreas Surgery, Department of Surgery, Asan Medical Center, Seoul;

³Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Purpose: Intra-abdominal leiomyosarcoma is an uncommon malignant tumor, and its standard treatment is surgical resection. However, there is no generally preferred treatment for its metastatic mass, especially in the liver.

Methods: According to the sarcoma registry, 476 patients were diagnosed as leiomyosarcoma and received treatment in Asan Medical Center, Seoul, Korea. And from 2003 to 2015, surgical resections of liver metastases were performed in 10 patients with leiomyosarcoma. The characteristics and short-term results were documented.

Results: Of the 10 patients, the median age was 48 years and the median survival period was 34.2 months. The mean period from primary resection to liver metastasis was 12.9 months. Six patients had a single metastatic mass, and four had multiple nodules. One patient had an additional distant metastasis outside of the liver. Eight patients had a partial hepatectomy, and the others were treated using segmentectomy or lobectomy. Two patients (20%) died during follow-up. Four patients showed metastasis to other organs after surgical resection of the liver.

Conclusion: Intra-abdominal leiomyosarcoma with liver metastasis is a very rare disease. Long-term survival can be achieved after surgical resection and should be considered for all patients.

Keywords: Leiomyosarcoma, Liver metastasis, Hepatectomy

INTRODUCTION

Intra-abdominal leiomyosarcomas are often diagnosed as an incidentally discovered abdominal mass. They are generally asymptomatic until they grow large enough to compress the surrounding organs or structures. The standard treatment for these lesions is complete surgical resection, with or without adjuvant chemotherapy (CTx) [1]. However, there is no general consensus on the treatment for the metastasis of leiomyosarcoma to the liver, nor the frequency of liver metastasis. Intra-abdominal leiomyosarcoma origins primarily in the gastrointestinal tract (stomach, small bowel, and colon), the genitourinary tract (uterus, bladder, prostate, and

kidney), and the retroperitoneum (inferior vena cava) [2]. We present our experiences with the complete resection of metastatic liver masses of intra-abdominal leiomyosarcoma from 2003 to 2015.

METHODS

According to the sarcoma registry, 476 patients were diagnosed as leiomyosarcoma and received treatment in Asan Medical Center, Seoul, Korea. And from February 2003 to November 2015, 10 patients with liver metastasis of intra-abdominal leiomyosarcoma were treated with surgical resection and confirmed by pathology. All 10 patients underwent complete surgical resection, and two of these cases had surgery for primary and metastatic lesions at the same time.

The surgical procedure was chosen according to the location of the metastatic mass. We retrospectively reviewed the patient characteristics, survival periods, pathologic findings, and disease progressions, including metastasis to other organs after hepatectomy.

RESULTS

Among our 10 patients with liver metastasis of leiomyosarcoma,

Received: Sep 27, 2017 Accepted: Oct 26, 2017

Correspondence to: Jae Hoon Lee

Division of Hepatobiliary and Pancreas Surgery, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea

Tel: +82-2-3010-1521, Fax: +82-2-3010-6701

E-mail: hbbsurgeon@gmail.com

Copyright © Korean Society of Surgical Oncology

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

the median age was 48 years (range, 38–60 years) at the diagnosis of liver metastasis (Table 1). There were three males and seven females. Five patients had primary lesions in the retroperitoneum, and the other patients had them in the pancreas, small bowel, and stomach. All patients had resection surgery for the primary lesion and two had surgery for the primary lesion and liver metastasis at the same time. Each patient was diagnosed by computed tomography (CT) scan. Four patients had CTx after primary surgery, and

two of them had radiotherapy (RTx) simultaneously. The regimens of CTx and RTx are documented in Table 1. The median survival period was 34.2 months (range, 8–170 months) and the mean period from primary resection to liver metastasis was 12.9 months (range, 0–38 months). Five patients were diagnosed with additional metastasis on follow-up (patients 1, 2, 3, 6, and 9). One patient (patient 1) had additional partial hepatectomy 40 months later due to metastasis and had wide local excisions of metastatic masses in

Table 1. Characteristics of the study patients

No.	Age (yr)	Sex	Surgical procedure for primary lesion	Size of primary tumor (cm)	Adjuvant treatment after primary surgery	Period to liver metastasis (mo) ^{a)}	Additional metastasis after hepatectomy	Overall survival period (mo)
1	42	F	Distal pancreatectomy and splenectomy	18	CTx (cisplatin+ifosfamide, 6 cycles), RTx (58 Gy/29 fx)	16	Lung, thigh, arm	170 (Alive)
2	38	M	Small bowel resection and anastomosis	3.5	None	0 ^{b)}	Liver, left kidney	24 (Dead)
3	50	F	Ileocecal resection	4	None	0 ^{b)}	Liver	14 (Dead)
4	41	F	Retroperitoneal mass excision	19	None	14	None	20 (Alive)
5	51	F	Retroperitoneal mass excision	18	CTx (cyclophosphamide+vincristine+doxorubicin+dacarbazine, 4 cycles)	6	None	18 (Alive)
6	43	F	Retroperitoneal mass excision	17.5	CTx (ifosfamide+doxorubicin, 6 cycles)	19	Rectum, peritoneum, small bowel mesentery	19 (Alive)
7	60	F	Laparoscopic wedge resection of stomach	3.5	None	38	None	40 (Alive)
8	69	F	Retroperitoneal mass excision	4.1	None	19	None	18 (Alive)
9	38	M	Small bowel resection and anastomosis	8.2	CTx (ifosfamide+etoposide+cisplatin, 4 cycles), RTx (5,000 cGy/25 fx)	12	Peritoneal carcinomatosis	11 (Alive)
10	50	M	Retroperitoneal mass excision	4	None	5	None	8 (Alive)

F, female; CTx, chemotherapy; RTx, radiotherapy; M, male.

^{a)}Period from resection of primary lesion(retroperitoneal) to diagnosis of liver metastasis. ^{b)}Patients underwent surgical resection of the primary lesion and liver metastasis at the same time.

Table 2. Characteristics of the liver metastases in the study cohort

No.	Size (cm) ^{a)}	Number of liver mass	Location of liver metastasis	Liver cirrhosis/fatty liver	Mean SUV of liver mass ^{b)}	Surgical procedure	Microscopic resection margin
1	2.5	1	Segment 6	Negative/Negative	Not tested	Partial hepatectomy	Negative
2	3	2	Segments 7 and 4	Positive/Negative	No hypermetabolism	Partial hepatectomy	Negative
3	2.5	7	Segments 1, 2, 3, 6, and 8	Negative/Negative	1.7	Partial hepatectomy	Positive
4	1.6	2	Segments 3 and 4	Negative/Negative	1.8	Partial hepatectomy	Negative
5	0.9	1	Segment 7	Negative/Negative	1.8	Right hepatectomy	Negative
6	2.8	1	Segment 3	Negative/Negative	1.8	Left lateral sectionectomy	Negative
7	2	1	Segments 7 and 8	Negative/Negative	Not tested	Partial hepatectomy+IORFA	Negative
8	2.6	1	Segment 6	Negative/Negative	1.8	Partial hepatectomy	Negative
9	3	1	Segment 6	Negative/Negative	Not tested	Partial hepatectomy	Negative
10	3	2	Segments 3 and 6	Negative/Negative	Not tested	Partial hepatectomy	Negative

SUV, standardized uptake values; IORFA, intraoperative radiofrequency ablation.

^{a)}Maximum diameter of the metastatic mass in the liver. ^{b)}On whole body positron emission tomography-computed tomography scan.

the left thigh twice, 14 months and 45 months after the last hepatectomy. This patient received radiation therapy postoperatively. Another patient (patient 2) was diagnosed with a 7.5 cm sized liver metastasis and a 1.5-cm-sized kidney metastasis 21 months after the surgery, with no additional treatment. One patient (patient 3) was diagnosed with multiple liver metastases 10 months after surgery. Additional CTx was planned but canceled due to severe cytopenia. And another patient (patient 6) was diagnosed simultaneously with upper rectal, peritoneal, and small bowel mesenteric metastasis with liver metastasis and had left lateral sectionectomy of the liver with pelvic mass excision at the same time. This patient had adjuvant CTx after surgery.

Two of the study patients (20%) died during postoperative follow-up (patients 2, 3). The other eight cases remained alive at the time of review and receive annual checkups in the outpatient department.

We also tested for the tumor markers carcinoembryonic antigen and carbohydrate antigen 19-9, but they showed no predictive value either before or after hepatectomy.

The mean size of metastatic masses was 2.39 cm (range, 0.9–3 cm) (Table 2). Six patients had a single liver metastatic mass and four had multiple masses (patient 3 had seven metastatic masses). The liver status was clear in every case, with no liver cirrhosis or fatty liver, with the exception of one patient with liver cirrhosis due to hepatitis B virus. Six patients underwent a whole-body positron emission tomography-CT scan, with a mean standardized uptake value of 1.7 to 1.8. Eight of them underwent partial hepatectomy, and others were treated with right hepatectomy and left lateral sectionectomy. Patient 7 had a partial hepatectomy for a lesion at segment 8 and an intraoperative radiofrequent ablation for a lesion at segment 7. This was because the location of the lesion at segment 7 was difficult to approach. Among our 10 patients, only one case had a microscopically positive resection margin. There were no complications after hepatectomy in this series and the mean hospital stay was 8.4 days.

DISCUSSION

Soft tissue sarcoma of the intra-abdominal organ is a rare malignant tumor and leiomyosarcoma is its most common histologic type [3]. Regardless of the histologic type, however, surgical resection is considered standard therapy [1]. There have been few studies of distant metastases that occur after the complete resection of a primary leiomyosarcoma. There is no generally accepted treatment for this either, especially for a liver metastasis, although surgery remains the mainstay, because leiomyosarcoma is relatively chemoresistant and radioresistant [4]. There have been few case

reports of primary or metastatic leiomyosarcoma of liver [5]. Faraj et al. [4] reported five cases of liver resection for metastatic colorectal leiomyosarcoma, with a median survival of 47 months. Akwari et al. [6] reported 108 cases of intestinal leiomyosarcoma, but with no mention of the management of these metastases. McGrath et al. [7] analyzed 51 cases of primary gastrointestinal sarcoma (virtually all were leiomyosarcomas.) and their prognostic factors, but reported no data related to metastasis. There have been many other reports of intra-abdominal or gastrointestinal leiomyosarcoma, but few that have analyzed its characteristics and the management of its metastasis. Notably, much of the reported evidence casts doubt on the benefits of adjuvant CTx after surgical resection [2]. There is also no general consensus on the frequency of liver metastasis. There has been one report of 65 patients with hepatic metastasis of soft tissue sarcoma among which 62% of all visceral sarcomas had metastasized to the liver [8]. There have been no randomized trials of surgical resection with and without postoperative radiation therapy. In this situation, the efficacy of other adjuvant therapies is unclear, if there are no severe complications after surgery. We therefore still consider surgical resection to be the optimal treatment option for resectable metastatic masses. There have been no perioperative complications or mortality among the 10 study patients, and the relatively minor range of the operations may have contributed to the quality of the recovery, because eight of our patients (80%) had only a partial hepatectomy.

We expected that surgical resection would improve the survival of our leiomyosarcoma patients, making it a treatment of choice for metastatic lesions. In addition, liver resection has been shown previously to prolong survival in such cases [9]. When a metastatic mass can be completely resected with curative surgery, a hepatectomy should be considered. Among our 10 study cases, eight patients (80%) remained alive at the time of writing and five patients (50%) had no additional metastases after the surgical resection of the first liver metastasis. Among these five patients, three had a metastasis to other organs but were still living and receiving CTx, RTx, or both. Thus, we contend that there is a role for CTx and RTx in such cases. This requires further study however.

There were some limitations to this study of note. A liver metastasis from an intra-abdominal leiomyosarcoma is so rare that a randomized controlled trial was not really possible. Thus, we performed a retrospective study, and a multi-center study should be considered in the future. And because there is only small series of surgical resection cases, we couldn't compare the clinical outcomes of liver metastasis between surgical group and non-surgical group statistically.

According to our sarcoma registry, 476 patients were diagnosed as leiomyosarcoma and received treatment in our institution. Pri-

mary site of their tumor was various and they also received various treatment including surgery, CTx, or radiation therapy. Five-year survival of overall leiomyosarcoma patients was 66.9%.

In conclusion, the surgical resection of a liver metastasis from an intra-abdominal leiomyosarcoma is a possible treatment of choice, although this remains to be clinically confirmed.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Raut CP, Pisters PW. Retroperitoneal sarcomas: Combined-modality treatment approaches. *J Surg Oncol* 2006;94:81-7.
2. McLeod AJ, Zornoza J, Shirkhoda A. Leiomyosarcoma: computed tomographic findings. *Radiology* 1984;152:133-6.
3. Lawrence W Jr, Donegan WL, Natarajan N, Mettlin C, Beart R, Winchester D. Adult soft tissue sarcomas: a pattern of care survey of the American College of Surgeons. *Ann Surg* 1987;205:349-59.
4. Faraj W, El-Kehdy J, Nounou GE, Deeba S, Fakhri H, Jabbour M, et al. Liver resection for metastatic colorectal leiomyosarcoma: a single center experience. *J Gastrointest Oncol* 2015;6:E70-6.
5. Baek I, Kim JH, Lee MS, Baik GH, Hahn T, Park HJ, et al. A case of primary leiomyosarcoma of the liver. *Korean J Hepatol* 2002;8:481-5.
6. Akwari OE, Dozois RR, Weiland LH, Beahrs OH. Leiomyosarcoma of the small and large bowel. *Cancer* 1978;42:1375-84.
7. McGrath PC, Neifeld JP, Lawrence W Jr, Kay S, Horsley JS 3rd, Parker GA. Gastrointestinal sarcomas: analysis of prognostic factors. *Ann Surg* 1987;206:706-10.
8. Jaques DP, Coit DG, Casper ES, Brennan MF. Hepatic metastases from soft-tissue sarcoma. *Ann Surg* 1995;221:392-7.
9. Chen H, Pruitt A, Nicol TL, Gorgulu S, Choti MA. Complete hepatic resection of metastases from leiomyosarcoma prolongs survival. *J Gastrointest Surg* 1998;2:151-5.