Surgical resection of liver metastasis of leiomyosarcoma

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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 originates 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 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
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) | 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                                    | 0¹                      | Liver, left kidney                  | 24 (Dead)                      |
| 3   | 50      | F   | Ileocecal resection                   | 4                           | None                                    | 0¹                      | 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 carcinoma               | 11 (Alive)                     |
| 10  | 50      | M   | Retroperitoneal mass excision         | 4                           | None                                    | 5                       | None                                | 8 (Alive)                      |

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

¹Period from resection of primary lesion(retroperitoneal) to diagnosis of liver metastasis. ²Patients 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)⁴ | Number of liver mass | Location of liver metastasis | Liver cirrhosis/ fatty liver | Mean SUV of liver mass⁵b | 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           | 7                    | 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                     |

SUB, standardized uptake values; IORFA, intraoperative radiofrequent ablation.

⁴Maximum diameter of the metastatic mass in the liver. ⁵On 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 radioreistant [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. Akiwari 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.

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