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# Case Report



## Favorable Outcome of Repeated Salvage Surgeries for Rare Metastasis to the Ligamentum Teres Hepatis and the Upper Abdominal Wall in a Stage IV Gastric Cancer Patient

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Gastric cancer with peritoneal metastases is typically a devastating diagnosis. Ligamentum teres hepatis (LTH) metastasis is an extremely rare presentation with only four known cases. Herein, we report salvage surgery of successive metastases to the abdominal wall and LTH in a patient originally presenting with advanced gastric cancer with peritoneal metastasis, leading to long-term survival. A 72-year-old man with advanced gastric cancer underwent curative-intent distal gastrectomy with D2 lymph node dissection for gastric outlet obstruction. During this procedure, three small peritoneal metastases were detected in the lesser omentum, the small mesentery, and the mesocolon; however, intraoperative abdominal lavage cytology was negative. We added cytoreductive surgery for peritoneal metastasis. The pathological diagnosis of the gastric cancer was tubular adenocarcinoma with pT4aN1pM1(PER/P1b)CY0 stage IV (Japanese classification of gastric carcinoma/JCGC 15th), or T4N1M1b stage IV (UICC 7th). Post-operative adjuvant chemotherapy with S-1 (TS-1)+cisplatin (CDDP) was administered for 8 months followed by S-1 monotherapy for 4 months. At 28 months after the initial surgery, a follow-up computed tomography (CT) detected a small mass beneath the upper abdominal wall. The ass showed mild avidity on <sup>18</sup>F-fluorodeoxyglucose positron-emission (FDG-PET) CT. Salvage resection was performed for diagnosis and treatment, and pathological findings were consistent with primary gastric cancer metastasis. At 49 months after the initial gastrectomy, a new lesion was detected in the LTH with a similar level of avidity on FDG-PET CT as the abdominal wall metastatic lesion. We performed a second salvage surgery for the LTH tumor, which also showed pathology of gastric cancer metastasis. There has been no recurrence up to 1 year after the LTH surgery. With multidisciplinary treatment the patient has survived almost 5 years after the initial gastrectomy. Curative-intent gastrectomy with cytoreductive surgery followed by adjuvant chemotherapy for advanced gastric cancer with localized peritoneal metastasis might have had a survival benefit in our patient. Successive salvage surgeries for oligometastatic lesions in the abdominal wall and the LTH also yielded favorable outcomes.

Key words: gastric cancer, peritoneal metastasis, ligamentum teres hepatis, oligometastasis, salvage surgery



astric cancer (GC) is the fifth most common malignancy and the third leading cause of can-

cer-related death worldwide [1]. In Japan, GC is the second most common cancer and second most frequent cause of mortality, Cancer Statistics. Cancer Information

Service, N.C.C., Japan (Vital Statistics of Japan, Ministry of Health, Labour and Welfare), CANCER STATISTICS IN JAPAN 2022 <a href="https://ganjoho.jp/public/qa\_links/">https://ganjoho.jp/public/qa\_links/</a> report/statistics/2022\_en.html> (accessed April, 2022). Peritoneal metastasis (PM) frequently accompanies advanced GC and suggests a very poor prognosis [2]. Treatment of GC with PM has not been well established; however, multimodal treatment for oligometastatic disease is becoming more common [3]. Recently, Yamaguchi et al. showed the efficacy of postoperative chemotherapy after curative-intent surgery, even for advanced GC with localized PM or positive peritoneal lavage cytology [4]. In this report, we describe a rare case of repeated salvage surgeries for rare ligamentum teres hepatis (LTH) and abdominal wall metastases in a patient who initially had stage IV GC with localized PM and had been treated with curative-intent gastrectomy with macroscopic complete resection of PM (i.e., cytoreductive surgery) and adjuvant chemotherapy. The metachronous recurrences in the upper abdominal wall

and LTH were completely resected. No recurrence or distant metastasis was observed 12 months after the last salvage surgery for LTH metastasis, and the patient was still surviving 4 years and 11 months after the initial gastrectomy.

#### **Case Presentation**

A 72-year-old man was referred to our hospital due to gastric outlet obstruction. He was diagnosed with advanced GC in the antrum by endoscopy with biopsy; computed tomography (CT) (Fig. 1A, 1B) also identified a synchronous left renal cell cancer. Tumor markers, such as CEA and CA 19-9, were not elevated, and the preoperative radiological examination showed no evidence of unresectable GC. Elective surgery was planned; however, during the procedure, three 2-mm masses were discovered in the lesser omentum, the small mesentery, and the posterior lobe of the transverse mesocolon and confirmed as peritoneal metasta-

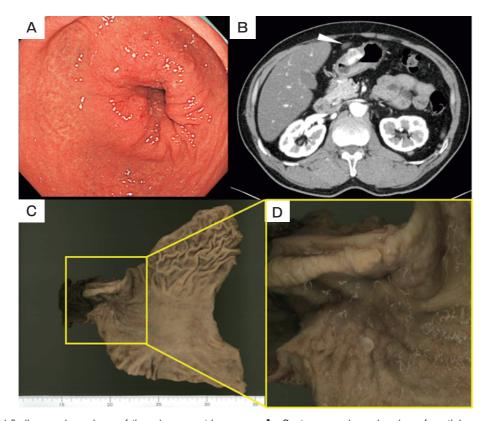


Fig. 1 Clinical findings and specimen of the primary gastric cancer. A, Gastroscopy showed a circumferential mass in the antrum of the stomach; B, Contrast CT showed enhanced gastric wall thickening in the lower stomach (white arrowhead); C, D, The primary gastric cancer specimen.

ses using intraoperative rapid pathological diagnosis (P1b/Japanese classification of Gastric Carcinoma/ JCGC 15th). Intraoperative abdominal lavage cytology, however, was negative (CY0). We performed standard distal gastrectomy with dissection of the regional lymph nodes (D2) and macroscopic complete resection for the peritoneal metastases primarily to address the gastric outlet syndrome and to prevent bleeding from the tumor. Left partial nephrectomy was performed simultaneously for the renal tumor. Examination of the specimen resected from the antrum revealed a  $40 \times 39$  mm type 3 GC (Fig. 1C, 1D). The pathological diagnosis was moderately differentiated (tub2 > por2) adenocarcinoma with pT4aN1pM1 (PER/P1b) stage IV (JCGC 15th), or T4N1M1b stage IV (UICC 7th). The surgical margins of the GC and the resected peritoneal masses were negative (R0), and the their Her2 status was negative (1+/immunohistochemistry test). The renal cell cancer was an early-stage clear cell carcinoma.

Post-operative adjuvant chemotherapy comprising S-1 (TS-1; Taiho Pharmaceutical Co. Ltd.; Tokyo, Japan)+cisplatin (CDDP) was administered for 8

months; for the next 4 months this regiment was reduced to S-1 monotherapy due to the adverse effect of general fatigue. Follow-up contrast computed tomography (CT) 28 months after the surgery, or 16 months after cessation of adjuvant chemotherapy, detected a 10-mm mass beneath the upper abdominal wall. There was no elevation of tumor markers at the time (Fig. 2A). <sup>18</sup>F-fluorodeoxyglucose positron-emission (FDG-PET) CT showed mild avidity with an early SUVmax of 1.94 (Fig. 2B). Salvage tumorectomy was performed for diagnosis and treatment since the abdominal wall lesion appeared to be a solitary lesion (Fig. 2C) and could cause pain if chemotherapy failed. Multidisciplinary discussion also intended recycling platinum-based regimen was preserved at this point. The pathological findings of the tumor were consistent with metastasis of the primary GC (Fig. 2D). Intensive follow-up was continued without systemic chemotherapy since this metastasis could have been due to tumor implantation from the previous gastrectomy, rather than the peritoneal metastasis.

Twenty-one months after the salvage surgery to the

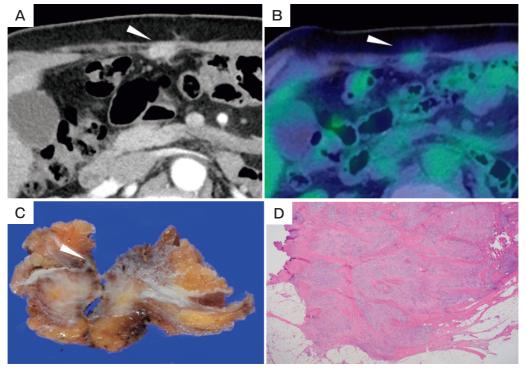


Fig. 2 Clinical and pathological findings of metastasis to the abdominal wall (white arrowhead shows abdominal wall metastasis). A, Contrast CT showed the irregular mass beneath the rectal fascia; B, On FDG-PET CT, the mass had mild avidity; C, The tumor specimen; D, Histopathological examination confirmed it as a metastasis from the initial gastric cancer.

abdominal wall metastasis, and 49 months after the initial gastrectomy, a new 10-mm mass was detected in the LTH (Fig. 3A-D) with a similar level of avidity on FDG-PET CT as the previous abdominal metastatic lesion (early SUVmax, 2.34; Fig. 3E). The tumor markers were not elevated and again, no other distant metastatic lesion was found. The tumor was suspected as a metas-

tasis considering the previous findings of metastasis to the abdominal wall, but it was difficult to clinically determine whether it originated from the stomach or the kidney. Therefore, we performed a second salvage surgery for the LTH tumor rather than perform systemic chemotherapy. The LTH was surgically resected (Fig. 4A, 4B) and pathologically diagnosed as metasta-

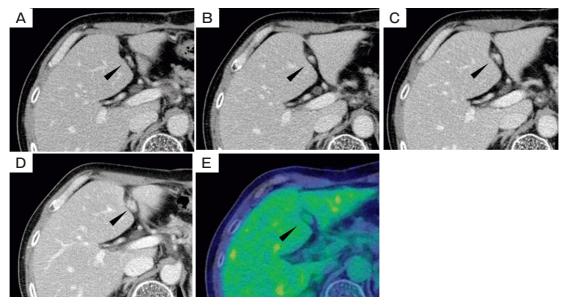


Fig. 3 Serial contrast CT and additional PET/CT findings of the lesion of the ligamentum teres hepatis (black arrowhead shows the LTH). Contrast CT at 23, 39, 40 and 50 months after the gastrectomy (A-D) The additional PET-CT (E).

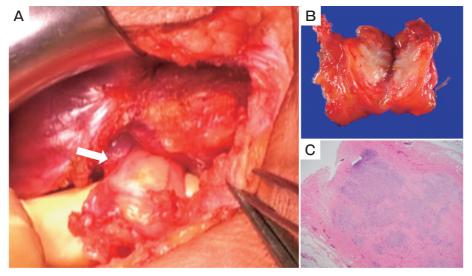


Fig. 4 Clinical and pathological findings of metastasis to the ligamentum teres hepatis (white arrow shows the mass in the LTH). A, Intraoperative findings of the LTH mass; B, The tumor specimen; C, Histopathological examination revealed it as a metastasis from the initial tubular adenocarcinoma in the stomach.

sis from the GC (Fig. 4C). Mild lymphovascular invasion was found in the tumor, but vascular invasion was absent (ly1, v0). No recurrence has occurred up to 1 year after the LTH surgery. The patient has survived for almost 5 years after the initial gastrectomy with multidisciplinary treatment.

## Discussion

This is the first successfully treated case of metachronous LTH and abdominal wall metastasis from a case initially diagnosed as stage IV GC, which had been treated with curative-intent gastrectomy and cytoreductive surgery (CRS) for localized peritoneal metastasis. The presentation of the LTH metastasis was extremely uncommon, but the combination of intensive follow-up of contrast CT with additional FDG-PET CT was helpful in detecting and confirming this metastasis during surveillance. Although the patient had peritoneal metastases, which generally confer a dismal prognosis, curative-intent radical surgery followed by adjuvant chemotherapy and repeated salvage surgeries for abdominal wall and LTH cancer recurrences have allowed an unexpectedly long survival of at least 5 years from treatment initiation.

This is the first case report of metastasis to the LTH from GC. To our knowledge, only four cases of metastasis to the LTH and falciform ligament have been reported [5-8]; these originated from thyroid cancer, prostate cancer, breast cancer and intrahepatic cholangiocarcinoma, respectively (Table 1). The thyroid cancer and prostate cancer patients experienced the metastasis more than 10 years after the initial resection. The metastasis from prostate cancer was speculated to have derived from occult peritoneal metastasis, whereas the other 3 cases were explained by hematogenous metastatic pathways. The breast cancer patient's recurrence at the LTH appeared 2 years after radical mastectomy and adjuvant chemotherapy. During that period, the patient had undergone breast reconstructive surgery using the rectus abdominis flap. The authors speculated that this vascular pedicle flap might have been the anatomical pathway (via superior epigastric vessels and the remnant umbilical vein) from the primary site to the LTH, or that this metastasis was caused by avascular foci stimulated by the surgical procedure. Nomura et al. also reported a case of resected intrahepatic cholangiocarcinoma in segment IV with simultaneous metastasis in the falciform ligament. They speculated that anastomosis of falciform ligament and supraepigastric vessels might have been the metastatic pathway. In our patient, the metastasis to the LTH, which was already separated at the primary surgery, was a solitary lesion. Based on the clinical course and pathological findings, it is possible that a cancer cell might have exfoliated from the previous abdominal wall metastasis and invaded the LTH via lymphatic vessels at the stump of the LTH. The patient's metastasis to the abdominal wall itself could be considered a rare occurrence, and it was difficult to determine whether its implantation occurred at the time of the primary gastrectomy or constituted a PM recurrence. Nevertheless, the timing was 16 months after cessation of adjuvant chemotherapy, which might suggest that the adjuvant chemotherapy had some anti-tumor effect. These metastases were clinically judged as oligometastases, so we decided to perform local resection.

Although FDG-PET CT for GC recurrence surveillance is still controversial in terms of size and type of recurrence sites, avidity with different histologies, and cost-benefit at outpatient clinics [9-11], additional FDG-PET CT offers detailed information on metastasis, especially when recurrence is suspected in the clinical setting [12]. In our patient, FDG-PET CT was helpful in identifying successive oligometastatic lesions and planning local therapy.

Multidisciplinary treatment and therapeutic strategies for metastatic GC have been attempted previously [13]. Advanced GC with PM still has a relatively poor prognosis despite the use of systemic chemotherapy. Optimal treatment strategies have differed widely in the eastern and western settings and remain controversial [14, 15]. The phase 3 randomized controlled REGATTA study did not favor palliative gastrectomy with adjuvant chemotherapy for incurable advanced GC with a single non-curable factor, but the cohort did not include patients with P1 status in JCGC 15th [16]. Slight PM is often difficult to diagnose radiologically in preoperative settings. When PM is diagnosed intraoperatively, if the metastasis is focal, i.e., judged as P1 or P2, palliative or radical gastrectomy followed by systemic chemotherapy could be acceptable and might have survival benefit from retrospective studies [17-19], but patients with type 4 GC were not considered appropriate candidates for such treatment [18]. According to a large retrospective study with 506 patients conducted by Yamaguchi et is)

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Prognosis after Dx	No recurrence, 6 months	Not reported	Died, 6 months (Brain metastasis	No recurrence, 6 months	
Adjuvant treatment	131-I	None	Cx (Epirubicin + Docetaxel)	None	
Metastatic pathway	Hematogenous (high vascularity in the specimen)	Occult peritoneal dissemination	Hematogenous (superior epigastric vessels, remnant umbilical vein)	Hematogenous (Intramembrane falciform ligament vein)	
Diagnostic method	Resection	Surgical biopsy	Resection	Combined resection with primary tumor (Left hepatectomy)	
Preope Cx	None	None	None	None	
Size (cm) at the detection	Not reported	$1.5 \times 2.7$	ω	2.9	
Imaging modality	18F-FDG PET/CT, 123I whole- body scan	68GaPSMA- PET/MRI	CT	CT, MRI	
Timing of metastasis from primary surgery	20 years	11 years	2 years	Simultaneous	
Primary tumor	Thyroid cancer	Prostate cancer	Breast	Intrahepatic cholangio- carcinoma	
Patient (Age/sex)	69/F	28/M	4/69	85/F	
Author	Garcia- Burillo et al [6]	Kranzbuhler et al [7]	Prete et al [8]	Nomura et al [9]	
	Timing of Size (cm) Preope Diagnostic method Metastatic pathway Adjuvant (Age/sex) tumor from primary modality detection Cx	Patient Primary metastasis modality (Age/Sex) tumor from primary modality surgery  Adjuvant primary modality at the Cx belonge at the Cx beneficial at the cancer at the Cx beneficial at the Cx beneficial at the cancer at the Cx beneficial at the cancer at the Cx beneficial at the cancer at the Cx beneficial at the C	Patient Primary from primary from primary at the surgery tumor surgery to solar from primary fro	Patient (Age/sex)Primary tumorTiming of metastasis surgeryImaging at the surgerySize (cm) at the CXPreope CXPreope CXDiagnostic method (Age) (Age)Metastatic pathway at the Agiuvant Hematogenous (Aigh vascularity in the specimen)Adjuvant treatment69/FThyroid cancer20 years131 whole-body scan PET/MRINoneNoneSurgical biopsyOccult peritoneal disseminationNone58/MProstate cancer11 yearsPET/MRI PET/MRI1.5 x 2.7NoneNoneHematogenous (Superior epigastric vessels, remnant umbilical vein)Cx	Patient (Age/Sex)Primary tumor surgeryTiming of from primary surgeryImaging at the surgeryPreope detectionDiagnostic method CxDiagnostic methodMetastatic pathwayAdjuvant treatment69/FThyroid cancer20 years18F-FDG PET/CT, reportedNoneResectionHematogenous (high vascularity in the specimen)131-I58/MProstate 

Male; F, Female; CT, Computed tomography; Cx, Chemotherapy; Dx, diagnosis; Preope, preoperative.

al., adjuvant chemotherapy after radical gastrectomy with macroscopic complete resection of PM had some survival benefits for GC patients with CY1 and/or P1a, but its 5-year survival was only 22-27% and the median survival time was 24.7-29.5 months [4]. Upfront radical gastrectomy with macroscopic complete resection of limited PM in combination with adjuvant chemotherapy could be indicated in selected patients with symptoms like obstruction or bleeding. In preoperatively high-risk-of-PM cases such as T3/4 and type4 GC, staging laparoscopy/exploratory laparotomy followed by neoadjuvant systemic chemotherapy with the goal of eventual conversion surgery has become somewhat of a standardized strategy [20]. Recently, Yoshida et al. reported a large international multicenter retrospective study (CONVO-GC-1) in which patients with limited PM (P1 and/or CY1 status) had better survival after R0 resection, with a median survival time of 44.8 months (p < 0.001) [21]. Several prospective randomized trials, such as "RENAISSANCE" (NCT02578368), are underway to address issues related to conversion surgery for metastatic GC [20].

Our patient experienced two recurrences at unusual sites in the abdomen, mimicking PM; however, these were solitary occurrences, and ascites was never seen throughout the period. The behavior of these metastases was thought to be different from that of devastating PM. The indication for surgical resection of these lesions was based on the concept of oligometastasis, resulting in prolonged patient survival [3]. Further research is needed to clarify the definition of oligometastasis in metachronous PM and cases of miscellaneous metastasis and to establish a treatment strategy.

In summary, we described the first rare case of LTH and abdominal wall metastasis from GC. At the time of the initial diagnosis, the GC had already developed peritoneal disease; however, the combination of curative-intent gastrectomy with adjuvant chemotherapy might have had a survival benefit. Subsequent salvage surgeries for oligometastatic lesions in the abdominal wall and LTH have led to a favorable overall survival of almost 5 years to date.

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