CASE REPORT

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A long-term survivor of advanced retroperitoneal dedifferentiated liposarcoma: a successful multimodal approach with extended resection and chemotherapy

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ABSTRACT

Surgical resection is the mainstay of treatment for retroperitoneal liposarcoma (RPLS). Herein, we describe a case of dedifferentiated RPLS successfully treated with an extended surgical approach with adjuvant chemotherapy. A 61-year-old male was referred to our hospital with a chief complaint of chest tightness. Abdominal computed tomography revealed a large retroperitoneal tumor, 11 cm in diameter, extensively invading the surrounding organs: the celiac axis, the splenic artery, the pancreatic body and tail, the lesser curvature of the stomach and the left adrenal gland. Endoscopic ultrasound-guided fine-needle aspiration biopsy confirmed dedifferentiated liposarcoma, suggesting aggressive tumor biology. We performed total gastrectomy combined with distal pancreatectomy with celiac axis and left adrenal gland resection with a curative intent. The postoperative course was almost uneventful. As the pathological findings indicated a positive margin with a well-differentiated liposarcoma component, we added adjuvant chemotherapy with four cycles of doxorubicin and ifosfamide (AI). Five years after primary surgery, regular follow-up CT demonstrated a pulmonary hilar lymph node enlargement and a tumor at paraesophageal locations. After downsizing chemotherapy with eribulin followed by pazopanib, he underwent partial esophagectomy with dissection of the paraesophageal tumor. The pathological findings indicated recurrence of dedifferentiated liposarcoma with a tumor-free surgical margin. He is currently alive without any evidence of recurrence almost 7 years after the first surgery and 15 months after the second surgery. The long-term survival gained in this patient indicates that extended resections and adjuvant chemotherapy could prolong survival in patients even with RPLS with dedifferentiated tumor histology.

Keywords: retroperitoneal liposarcoma, dedifferentiated, chemotherapy, extended surgery

Abbreviations:
RPLS: retroperitoneal liposarcoma
RPS: retroperitoneal sarcoma
CT: computed tomography

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INTRODUCTION

Retroperitoneal liposarcoma (RPLS) is the most common type of soft tissue sarcoma, accounting for approximately 30% of retroperitoneal sarcoma (RPS).[1] Complete surgical resection with negative microscopic margins has been proposed as an ultimate treatment for patients with RPLS.[2-6] RPLS often exhibits a large tumor mass at initial presentation because of its slow-growing and insidious nature. By the time of diagnosis, RPLS sometimes involves the kidney, pancreas, adrenal gland, and major intra-abdominal vessels.[7] Therefore, complete surgical resection for RPLS often requires extended surgical resection of these major organs, potentially ending in a positive surgical margin. Thus, a major clinical problem in RPLS is frequent tumor relapse mainly around the surgical field. We aggressively perform extended and repeated resections under a multimodal approach in patients with RPLS.[8] However, the best tactical flow for controlling RPLS with a high risk of disease relapse remains unclear.

Herein, we demonstrate a case of dedifferentiated RPLS that was successfully treated by extended surgical resection and adjuvant chemotherapy.

CASE REPORT

A 61-year-old male was referred to our hospital with a chief complaint of chest tightness. An abdominal computed tomography (CT) scan revealed a multilobed retroperitoneal tumor with a maximum diameter of 11 cm (Figure 1). The tumor involved surrounding vital organs, such as the celiac axis, the splenic artery, the body and tail of the pancreas, the lesser curvature of the stomach, and the left adrenal gland (Figure 1A and 1B). Furthermore, the tumor invaded the posterior mediastinum through the esophageal hiatus (Figure 1C). Endoscopic ultrasound-guided fine-needle aspiration biopsy confirmed dedifferentiated liposarcoma, suggesting aggressive tumor biology. We performed total gastrectomy combined with distal pancreatectomy with celiac axis and left adrenal gland resection with curative intent (Figure 2A and 2B). The postoperative course was almost uneventful.

Macroscopically, the resected specimen revealed a whitish ~ yellowish multilobular solid tumor involving the pancreas and stomach (Figure 2C and 2D). Microscopically, a dedifferentiated liposarcoma considered Fédération Nationale des Centres de Lutte Contre le Cancer grade 2 was seen (Figure 3). The surgical margin of the dedifferentiated component was negative, but that of the well-differentiated component was positive at near the exfoliated surface of the celiac axis and the pancreas (Figure 3D). Considering the residual foci, we performed adjuvant chemotherapy with doxorubicin (25 mg/m^2 per day on days 1–2) and ifosfamide (1.5 g/m^2 per day on days 1–5) (AI) every three weeks. After completing four courses of AI, the patient survived with no evidence of recurrence for five years.

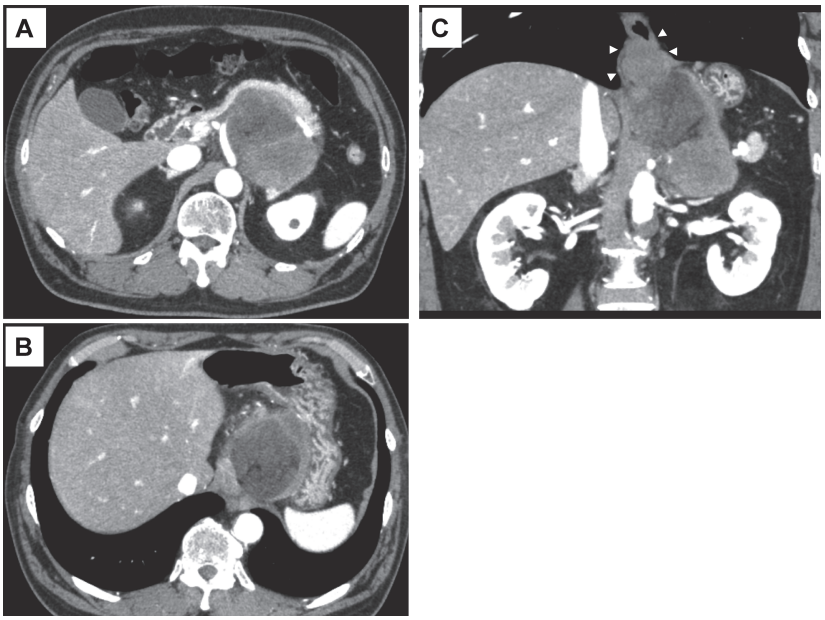

Fig. 1 CT scan images
Fig. 1A: The tumor involved the celiac axis, the splenic artery, the body and tail of the pancreas.
Fig. 1B: The tumor involved the lesser curvature of the stomach and the left adrenal gland.
Fig. 1C: The tumor invaded the posterior mediastinum through the esophageal hiatus (arrowhead).

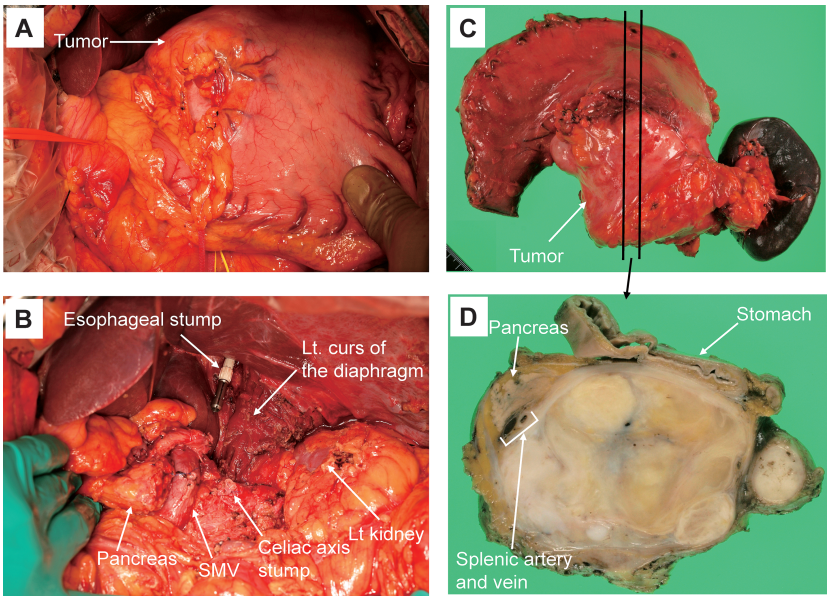

Fig. 2 Intraoperative photos and macroscopic findings of the resected specimen at the first surgery
Fig. 2A: A giant whitish tumor was located on the dorsal side of the stomach.
Fig. 2B: After tumor resection. SMV, superior mesenteric vein.
Fig. 2C: The tumor involved the pancreas and stomach.
Fig. 2D: The sliced specimen showed a whitish ~ yellowish multilobulated solid tumor involving the pancreas and stomach.

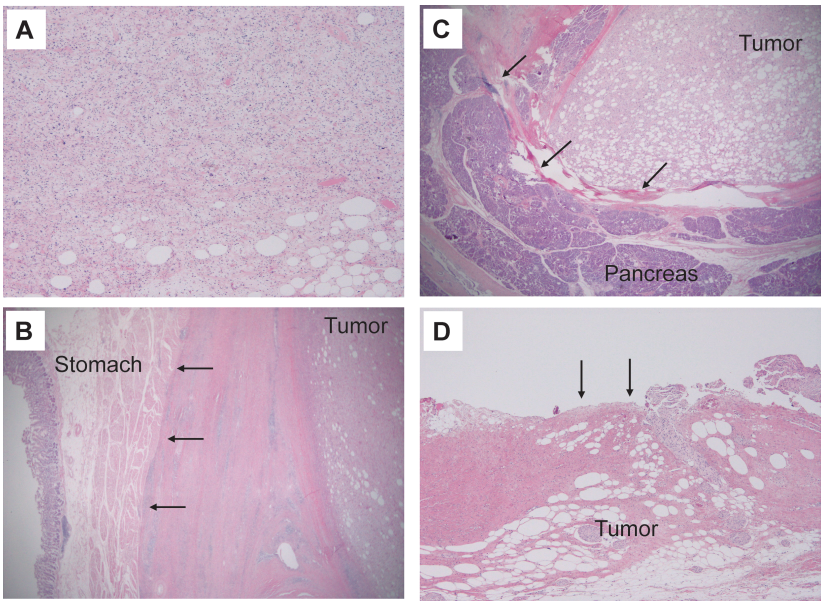

Fig. 3 Pathological findings of the resected specimen at the first surgery
Fig. 3A: Hematoxylin and eosin staining of the tumor (H&E stain, ×40).
Fig. 3B: The tumor invaded the proper muscular layer of the stomach (arrows) (H&E stain, ×12.5).
Fig. 3C: The tumor invaded the pancreas (arrows) (H&E stain, ×12.5).
Fig. 3D: A positive margin with a well-differentiated component at near the exfoliated surface of the celiac axis and the pancreas (arrows) (H&E stain, ×40).

Regular follow-up CT, unfortunately, demonstrated a pulmonary hilar lymph node enlargement and a tumor at paraesophageal locations (Figure 4A and 4B). After two courses of chemotherapy with eribulin (1.0 mg/m^2 per day on days 1 and 8 every 4 weeks), the left hilar lymph node shrinked whereas the paraesophageal tumor enlarged. So, we switched eribulin to pazopanib (400 mg per day). After performing pazopanib for four months, the left hilar lymph node metastasis almost normalized in size, whereas the paraoesophageal tumor kept enlargement (Figure 4C and 4D). No other recurrences were detected by positron emission tomography-CT. He underwent partial esophagectomy with dissection of the paraesophageal tumor as the second surgery. Esophagojejunal anastomosis leakage occurred after surgery but was alleviated by drainage therapy.

The pathological findings showed disease relapse of dedifferentiated liposarcoma, in which low cellular intensity and nuclear atypia suggested low-grade malignancy (Figure 5). The surgical margin was negative. The patient is healthy without any complaints for four months after the second surgery.

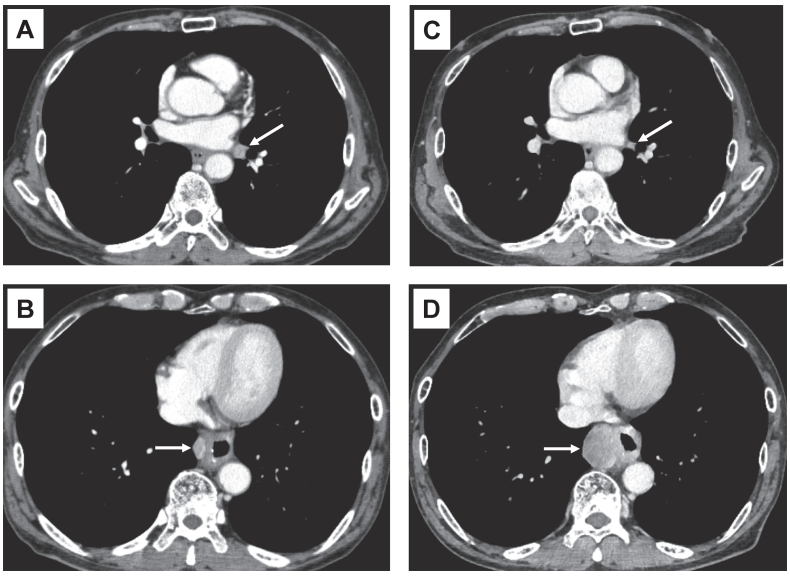

Fig. 4 CT scan images of recurrent lesions
Fig. 4A: Left hilar lymph node metastasis (arrow).
Fig. 4B: Paraesophageal tumor (arrow).
Fig. 4C: Left hilar lymph node metastasis after four months of chemotherapy (arrow).
Fig. 4D: Paraesophageal tumor after four months of chemotherapy (arrow).

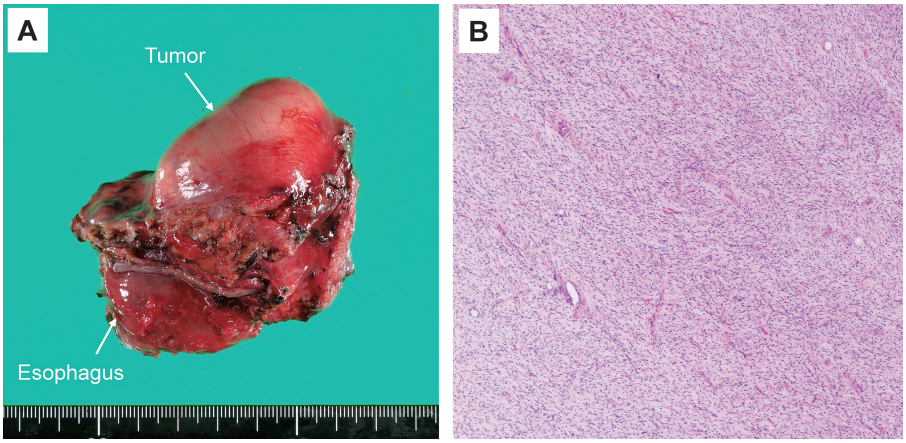

Fig 5 Macroscopic and pathological findings of the resected specimen at the second surgery
Fig. 5A: Macroscopic findings of the resected specimen.
Fig. 5B: Pathological findings indicated recurrence of dedifferentiated liposarcoma. The malignancy of the tumor was low grade because cellular intensity and nuclear variation were low (H&E stain, ×40).

DISCUSSION

Soft tissue sarcoma is a relatively rare tumor representing approximately 1% of all malignant tumors.[9] RPLS is the most common type of soft tissue sarcoma arising from the retroperitoneal space.[1] Because of its anatomical location, RPLS seems asymptomatic in the early stage. Therefore, RPLS has usually formed a large mass at initial presentation, as in the patient presented. RPLS is broadly divided into well-differentiated, dedifferentiated, myxoid/round, and pleomorphic types according to histological tumor features. This histologic subtype is closely associated with surgical strategy and survival probability. Patients with well-differentiated liposarcoma have relatively favorable survival; in contrast, those with dedifferentiated liposarcoma have poor survival.[10]

Complete surgical resection with tumor-free margins is the only curative therapy for patients with RPLS.[2-6] However, this approach often needs extended surgical resection due to extensive involvement of surrounding vital organs. Pasquali et al reviewed 55 patients with RPLS who underwent en bloc tumor resection and reported that the incidence of tumor-free surgical margins reached as high as 90% in a specialized team.[11] In the initial surgery of our case, unfortunately, a positive margin with a well-differentiated component was observed, but a negative margin with a dedifferentiated component was gained. Interestingly, dedifferentiated RPLS requires a negative margin to minimize the chance of local recurrence, whereas well-differentiated RPLS does not.[12-14] Thus, the surgical strategy regarding margin status depends on tumor histopathology.

At present, supporting evidence of adjuvant chemotherapy is lacking in RPLS.[15,16] Nevertheless, there are some case reports that show the significant effectiveness of chemotherapy or neoadjuvant chemotherapy in RPLS.[17,18] In our case, we administered four courses of AI as adjuvant chemotherapy after aggressive surgery. However, weather this adjuvant chemotherapy contributed to the long-term recurrence-free survival (five years) after the first surgery is uncertain.

Making a surgical decision for recurrent RPLS remains challenging. Although some reports recommend reresection for relapse,[19-21] repeat surgery requires technical demand with a considerable risk of morbidity and mortality even in high-volume centers. Hamilton et al reported that durable disease control with prolonged survival may be achieved only in select patients who received reresection for this complicated disease.[19] Therefore, the indication of reresection should be carefully but proactively considered, balancing the survival benefit with the surgery-associated risk. We performed reresection for disease recurrence on the basis of the following factors. First, the recurrence was limited and well controlled by chemotherapy. Second, the time interval to recurrence was longer than five years. Third, complete resection seemed possible by partial esophagectomy with resection of the paraesophageal tumor. To our best knowledge, this is the first case report that successfully achieved a long-term survival after an extended surgery such as total gastrectomy with distal pancreatectomy and celiac axis resection for advanced retroperitoneal dedifferentiated liposarcoma. An adjuvant chemotherapy and an aggressive surgery for the recurrent disease may also contributed to the long-term survival. Consequently, the patient is healthy without any evidence of recurrence 7 years after the first surgery and 15 months after the second surgery, which indicates that a resection-based multimodal approach may provide a survival benefit in select patients with RPLS.

CONCLUSIONS

We present a long-term survivor with dedifferentiated RPLS successfully treated by extended resections and adjuvant/neoadjuvant chemotherapy. Such a multidisciplinary approach may provide a favorable long-term outcome in select patients even with advanced or recurrent dedifferentiated

RPLS.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1 Sassa N, Yokoyama Y, Nishida Y, et al. Clinical characteristics and surgical outcomes of retroperitoneal tumors: a comprehensive data collection from multiple departments. *Int J Clin Oncol*. 2020;25(5):929–936. doi:10.1007/s10147-020-01620-1.

2 Keung EZ, Chiang YJ, Cormier JN, et al. Treatment at low-volume hospitals is associated with reduced short-term and long-term outcomes for patients with retroperitoneal sarcoma. *Cancer*. 2018;124(23):4495–4503. doi:10.1002/cncr.31699.

3 Bonvalot S, Miceli R, Berselli M, et al. Aggressive surgery in retroperitoneal soft tissue sarcoma carried out at high-volume centers is safe and is associated with improved local control. *Ann Surg Oncol*. 2010;17(6):1507–1514. doi:10.1245/s10434-010-1057-5.

4 Bonvalot S, Raut CP, Pollock RE, et al. Technical considerations in surgery for retroperitoneal sarcomas: position paper from E-Surge, a master class in sarcoma surgery, and EORTC-STBSG. *Ann Surg Oncol*. 2012;19(9):2981–2991. doi:10.1245/s10434-012-2342-2.

5 Gronchi A, Miceli R, Colombo C, et al. Frontline extended surgery is associated with improved survival in retroperitoneal low- to intermediate-grade soft tissue sarcomas. *Ann Oncol*. 2012;23(4):1067–1073. doi:10.1093/annonc/mdr323.

6 Moyon FX, Moyon MA, Tufino JF, Yu A, Mafla OL, Molina GA. Massive retroperitoneal dedifferentiated liposarcoma in a young patient. *J Surg Case Rep*. 2018;2018(10):rjy272. doi:10.1093/jscr/rjy272.

7 Messiou C, Moskovic E, Vanel D, et al. Primary retroperitoneal soft tissue sarcoma: Imaging appearances, pitfalls and diagnostic algorithm. *Eur J Surg Oncol*. 2017;43(7):1191–1198. doi:10.1016/j.ejso.2016.10.032.

8 Chouliaras K, Senehi R, Ethun CG, et al. Recurrence patterns after resection of retroperitoneal sarcomas: An eight-institution study from the US Sarcoma Collaborative. *J Surg Oncol*. 2019;120(3):340–347. doi:10.1002/jso.25606.

9 Thway K, Jones RL, Noujaim J, Zaidi S, Miah AB, Fisher C. Dedifferentiated Liposarcoma: Updates on Morphology, Genetics, and Therapeutic Strategies. *Adv Anat Pathol*. 2016;23(1):30–40. doi:10.1097/PAP.0000000000000101.

10 Zaidi MY, Canter R, Cardona K. Post-operative surveillance in retroperitoneal soft tissue sarcoma: The importance of tumor histology in guiding strategy. *J Surg Oncol*. 2018;117(1):99–104. doi:10.1002/jso.24927.

11 Pasquali S, Vohra R, Tsimopoulou I, Vijayan D, Gourevitch D, Desai A. Outcomes Following Extended Surgery for Retroperitoneal Sarcomas: Results From a UK Referral Centre. *Ann Surg Oncol*. 2015;22(11):3550–3556. doi:10.1245/s10434-015-4380-z.

12 Singer S, Antonescu CR, Riedel E, Brennan MF. Histologic subtype and margin of resection predict pattern of recurrence and survival for retroperitoneal liposarcoma. *Ann Surg*. 2003;238(3):358–370; discussion 70–1. doi:10.1097/01.sla.0000086542.11899.38.

13 Lahat G, Anaya DA, Wang X, Tuvin D, Lev D, Pollock RE. Resectable well-differentiated versus dedifferentiated liposarcomas: two different diseases possibly requiring different treatment approaches. *Ann Surg Oncol*. 2008;15(6):1585–1593. doi:10.1245/s10434-007-9805-x.

14 Ikoma N, Roland CL, Torres KE, et al. Concomitant organ resection does not improve outcomes in primary retroperitoneal well-differentiated liposarcoma: A retrospective cohort study at a major sarcoma center. *J Surg Oncol*. 2018;117(6):1188–1194. doi:10.1002/jso.24951.

15 Adjuvant chemotherapy for localised resectable soft-tissue sarcoma of adults: meta-analysis of individual data. Sarcoma Meta-analysis Collaboration. *Lancet*. 1997;350(9092):1647–1654.

16 ESMO/European Sarcoma Network Working Group. Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2014;25(Suppl 3):iii102–112. doi:10.1093/annonc/mdu254.

17 Kus T, Aktas G, Kalender ME, Tutar E, Ulker E, Camci C. Complete response of a recurrent-metastatic liposarcoma with dedifferentiated histological features following the administration of trabectedin and review

of literature. *J Cancer Res Ther*. 2015;11(4):974–976. doi:10.4103/0973-1482.158032.

18 Yokoyama Y, Nishida Y, Ikuta K, Nagino M. A case of retroperitoneal dedifferentiated liposarcoma successfully treated by neoadjuvant chemotherapy and subsequent surgery. *Surg Case Rep*. 2020;6(1):105. doi:10.1186/s40792-020-00865-2.

19 Hamilton TD, Cannell AJ, Kim M, et al. Results of Resection for Recurrent or Residual Retroperitoneal Sarcoma After Failed Primary Treatment. *Ann Surg Oncol*. 2017;24(1):211–218. doi:10.1245/s10434-016-5523-6.

20 Grobmyer SR, Wilson JP, Apel B, et al. Recurrent retroperitoneal sarcoma: impact of biology and therapy on outcomes. *J Am Coll Surg*. 2010;210(5):602–608, 608–610. doi:10.1016/j.jamcollsurg.2009.12.024.

21 van Dalen T, Hoekstra HJ, van Geel AN, et al. Locoregional recurrence of retroperitoneal soft tissue sarcoma: second chance of cure for selected patients. *Eur J Surg Oncol*. 2001;27(6):564–568. doi:10.1053/ejso.2001.1166.