Survival of a patient with five recurrences of retroperitoneal liposarcoma over a period of 13 years: A case report and review

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Abstract. Retroperitoneal liposarcoma (RPLS) is a rare tumor that occurs in the retroperitoneal region and accounts for ~0.2% of all malignant tumor incidence. The present study describes the treatment of a surviving patient with RPLS that recurred five times in 13 years. This case has a long survival time and numerous relapses, which is a rare occurrence. The 40-year-old female patient was admitted to Shaoxing Second Hospital (Shaoxing, China) with an abdominal mass. Abdominal computed tomography (CT) scan revealed multiple liposarcoma recurrences in the abdominal, pelvic and retroperitoneal areas. As the diagnosis of RPLS was the fifth recurrence, cytoreductive surgery was performed and post-operative pathology suggested mixed liposarcoma. The patient underwent six cycles of doxorubicin and ifosfamide regimen chemotherapy and targeted therapy with anlotinib following surgery; no evidence of disease progression was found on abdominal CT scan during follow-up. The present study also reviewed the literature in terms of the clinical diagnosis, treatment, pathological characteristics and similar cases of liposarcoma with the aim of improving diagnosis and treatment.

Introduction

Liposarcoma is one of the most common types of retroperitoneal primary tumors, accounting for 10-35% of all soft tissue sarcoma (1). Retroperitoneal liposarcoma (RPLS) occurs mostly between the ages of 40 and 60 years, with a slight male predominance (2). Pathologically, liposarcoma is divided into five types (3): Well-differentiated liposarcoma (WDLPS), dedifferentiated liposarcoma (DDLPS), myxoid liposarcoma (MLS), pleomorphic liposarcoma and myxoid pleomorphic liposarcoma. WDLPS is a typical indolent malignancy but can be locally aggressive, while DDLPS has a higher grade histology, faster growth and distant metastatic potential (4). MLS is the second most common subtype, accounting for ~5% of all soft tissue sarcomas in adults (5). Histological lesions show low grade forms and poorly differentiated round cells. At a molecular level, translocation (12;16) (q13;p11), resulting in fused in sarcoma and DNA damage inducible transcript 3 (FUS-DDIT3) gene fusion, has been described in the majority of these tumors (6). The treatment is generally surgical excision with or without radiation therapy. In case of high-risk disease and positive surgical margins, chemotherapy is considered (7). Pleomorphic liposarcoma is rare and represents only 5-10% of liposarcoma (8). However, it is considered to be of the highest malignancy grade, with high invasion, metastasis and recurrence. Radiotherapy only benefits patients with large tumor size (>10 cm); however, surgery, particularly radical resection, is the primary treatment option (9). Surgical resection is the first choice of treatment (10). However, as RPLS is a large tumor, the boundary is difficult to determine and relapse is common following surgery (11,12). Abdominal computed tomography (CT) scan is key for the diagnosis, staging and follow-up of the disease (13).

Case report

A 40-year-old woman was hospitalized at Shaoxing Second Hospital (Shaoxing, China) in April 2009 due to the discovery of a retroperitoneal mass 1 week prior. The patient had complained of a retroperitoneal mass and abdominal pain for 1 week. CT examination of the abdomen confirmed a mass in the retroperitoneal space (~11x15 cm). On April 15, 2009, the patient underwent the resection of the right retroperitoneal mass and right nephrectomy due to the large space occupied by the right retroperitoneal mass. The pathological findings revealed one gray-red and gray-yellow mass (30x19x10 cm) with a capsule on the surface and a clear boundary with the surrounding area and one kidney in the center of the mass (10.5x5.5x3.5 cm), which was difficult to separate from the mass. No tumor tissue invasion was found in the kidney.

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Abbreviations: AI, doxorubicin and ifosfamide; RPLS, retroperitoneal liposarcoma; WDLPS, well-differentiated liposarcoma; DDLPS, dedifferentiated liposarcoma; MLS, myxoid liposarcoma; FUS-DDIT3, fused in sarcoma and DNA damage inducible transcript 3; CT, computed tomography; MDM2, mouse double minute 2 homolog

Key words: retroperitoneal liposarcoma, liposarcoma, tumor, recurrence, chemotherapy, pathology, case report

The incisal margin was negative. The pathological diagnosis indicated retroperitoneal MLS with right kidney involvement. The results of immunohistochemical analysis were as follows: S-100 protein (+), p53 (-), myogenin (-), Ki67 (2%), SMA (-), CD68 (-), β-catenin (-) and CD34 (vascular +). The grade and stage of the disease was T4N0M0, G1, IB (14). No post-operative chemotherapy was performed due to complete surgical resection.

Since the pathological diagnosis of the patient was MLS, which is not sensitive to radiotherapy (15), no radiotherapy was administered. The patient did not receive any other treatment following surgery and was followed-up regularly until June 2014, when local recurrence of the tumor was found. The patient relapsed multiple times. RPLS resection was performed using open surgery on June 3, 2014, January 12, 2017, December 25, 2018 and July 21, 2020. The post-operative pathological diagnosis in all cases was MLS liposarcoma. In June 2021, abdominal enhanced CT scan revealed post-operative changes in the right kidney and recurrence of multiple liposarcoma in the abdominal, pelvic and retroperitoneal areas (Fig. 1). On June 22, 2021, endoscopic-assisted resection of retroperitoneal tumor and intestinal adhesion release were performed due to adhesion between the tumor and surrounding tissue. More than 10 tumors were surgically removed. The post-operative pathological analysis revealed spindle cell soft tissue sarcoma (pelvic and peritoneal tumors), consistent with multiple types of liposarcoma (DDLPS, MLS and WDLPS; total size, 27.0x13.5x6.0 cm; Fig. 2). The results of immunohistochemical analysis were as follows: Creatine kinase (-), succinate dehydrogenase complex iron sulfur subunit B (+), Ki67 (30%), S-100 (small amount +), desmin (+), CD34 (vascular +), SMA (-), HMB45 (-), β-Catenin (membrane +), anaplastic lymphoma kinase (ALK) (-), BCL6 co-repressor (-), mouse double minute 2 homolog(MDM2)/chromosome 12 centromere FISH (+) and MDM2 (+). In November 2021, the patient underwent re-examination by abdominal magnetic resonance imaging (MRI; Fig. 3); the mass in the abdominal and pelvic cavities had increased. Due to progression of the disease, the patient underwent six cycles of doxorubicin and ifosfamide chemotherapy (day 1, 70 mg doxorubicin; day 1-3, 2 g ifosfamide 2 g) and anlotinib (12 mg) oral targeted therapy once a day. In May 2022, the whole abdominal enhanced CT scan was performed and it was found that the mass in the abdominal and pelvic cavities had decreased (Fig. 4). In July 2022, the whole abdominal CT scan was repeated; the mass had no obvious change compared with the previous mass (Fig. 5) and there was no evidence of disease progression. The evaluation of the chemotherapeutic efficacy was stable disease, as per the Response Evaluation Criteria In Solid Tumors criteria (16). Since the fifth recurrence in June 2021 of liposarcoma, >1 year survival has been achieved. The timeline of the case is presented in Fig. 6.

Discussion

RPLS is usually discovered relatively late; as the retroperitoneal space is large, there are no obvious symptoms in the early stages of the disease. It often presents as a painless mass that grows at a slow rate. As tumor increases in size, it compresses adjacent organs and causes discomfort. Abdominal pain is the main clinical manifestation, followed by abdominal swelling (17). As symptoms do not appear until the late stage of disease progression, patients often have large tumors when they visit the hospital. The present patient had no obvious signs at the initial diagnosis, although the abdominal mass was palpable.

RPLS lacks specific clinical symptoms, thus, it is very important to detect it through imaging examination. CT scan is the first choice for the examination of liposarcoma as it can determine size and location of the tumor and it can preliminarily evaluate pathological classification and malignancy, clarify the degree of tumor compression and invasion of surrounding organs and vessels and provide a reference for the formulation of surgical plans (13). Compared with CT scan, an MRI has a higher resolution for soft tissue, more accurately diagnoses retroperitoneal tumors, clearly displays the distribution of tumor blood vessels and association between key blood vessels and can be used to evaluate the degree of tumor invasion (18), which provides guidance for formulation of surgical plans.

According to the World Health Organization classification of soft tissue tumors, liposarcoma is divided into five types (3): WDLPS, DDLPS, MLS, pleomorphic liposarcoma and myxoid pleomorphic liposarcoma. Different pathological types have different levels of invasiveness and prognoses. WDLPS is a low-grade malignancy with the best prognosis (19). Pleomorphic and round cell types are highly malignant, prone to local recurrence and metastasis and have the worst prognosis. The myxoid type is in between. The present case recurred multiple times but had no distant metastasis (apart from the fifth recurrence), which may be due to the higher degree of differentiation. Liposarcoma easily relapses following surgery due to its unique growth site and diverse pathological morphology (11,12). Moreover, with an increased number of recurrences and operations following the initial surgery, malignancy increases and the recurrence interval shortens. These two previous research findings are highly consistent with the disease development characteristics of our case. The patient experienced five relapses, which is rare, and the fifth relapse exhibited a transformation of the pathological type, indicating higher invasion and a poor prognosis.

For the treatment of RPLS, radical surgical resection is the first choice and is the only possible cure at present. In order to achieve therapeutic effects, while ensuring safety, as much of the tumor should be removed as possible (20). In cases of malignant invasion of RPLS, complete resection is often combined with removal of the adjacent organs that may be affected, such as the kidney, spleen and gastrointestinal tract. In particular, it is recommended to perform radical resection of the affected kidney (21). In the present case, at the time of initial treatment, the right kidney was invaded by the tumor and it was difficult to separate the tumor tissue. If the right kidney was not removed, tumor tissue would remain, which would increase the post-operative recurrence rate. Based on the general condition of the patient and the function of left kidney being acceptable, the patient opted to undergo right kidney resection. Even if the tumor is completely resected, ~50% of patients exhibit tumor recurrence within 5 years (22). However, the difficulty and risk of operation following recurrence are significantly increased and the post-operative efficacy is poor. The 5-year overall survival rate is ~30%. During the

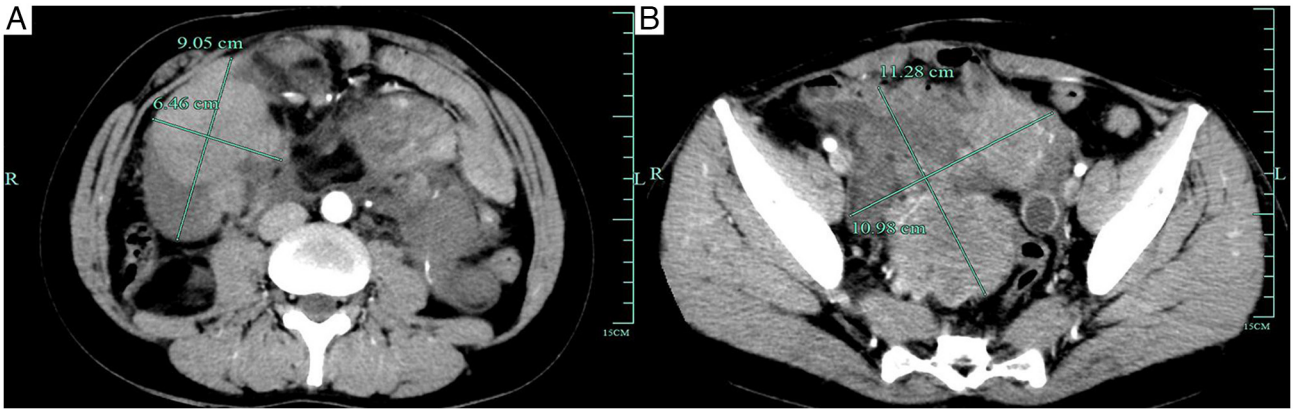

Figure 1. Abdominal computed tomography scan illustrating multiple masses in the abdominal cavity and pelvic cavity. Some masses were fused and viscera were compressed (June 3, 2021). (A) Abdominal mass (9.05x6.46 cm). (B) Pelvic mass (11.28x10.98 cm).

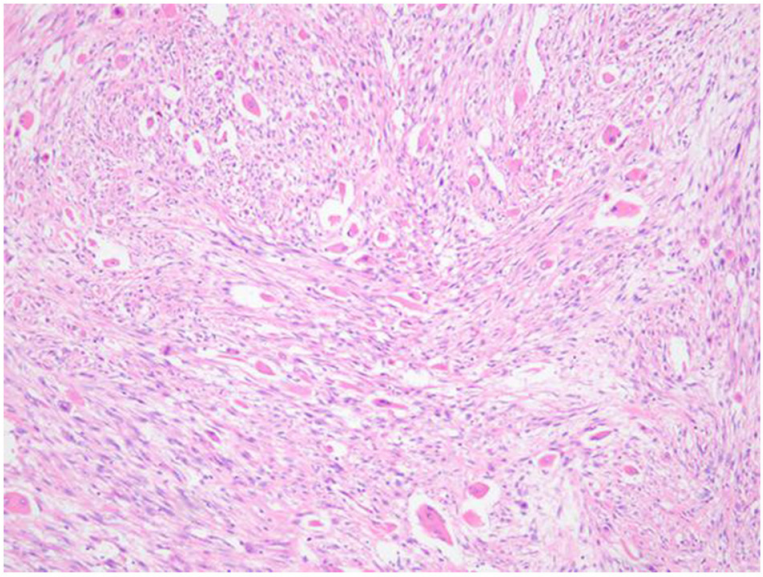

Figure 2. Pathological analysis (hematoxylin and eosin staining, x100 magnification) showed dedifferentiated, myxoid and well-differentiated liposarcoma.

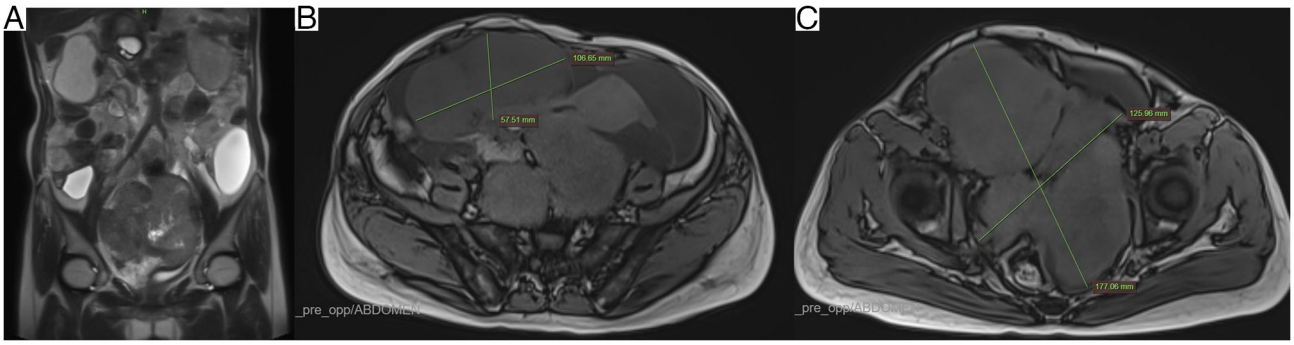

Figure 3. Abdominal magnetic resonance imaging. (A) Multiple abdominal and pelvic masses (November 10, 2021). (B) Abdominal mass (10.67x5.71 cm). (C) Pelvic mass (17.7x12.6 cm).

course of disease, the present patient had five recurrences, five complete resections and one cytoreductive surgery. At present, the patient survival period is 13 years, which is rare. Telephone follow-up is performed every three months for this patient. The patient has good compliance and often visits the hospital for follow-up.; thus, each relapse can be identified and treated in a timely manner.

As liposarcoma is not sensitive to radiotherapy, chemotherapy or immunotherapy, patients generally do not receive routine adjuvant treatment following surgery (23). With

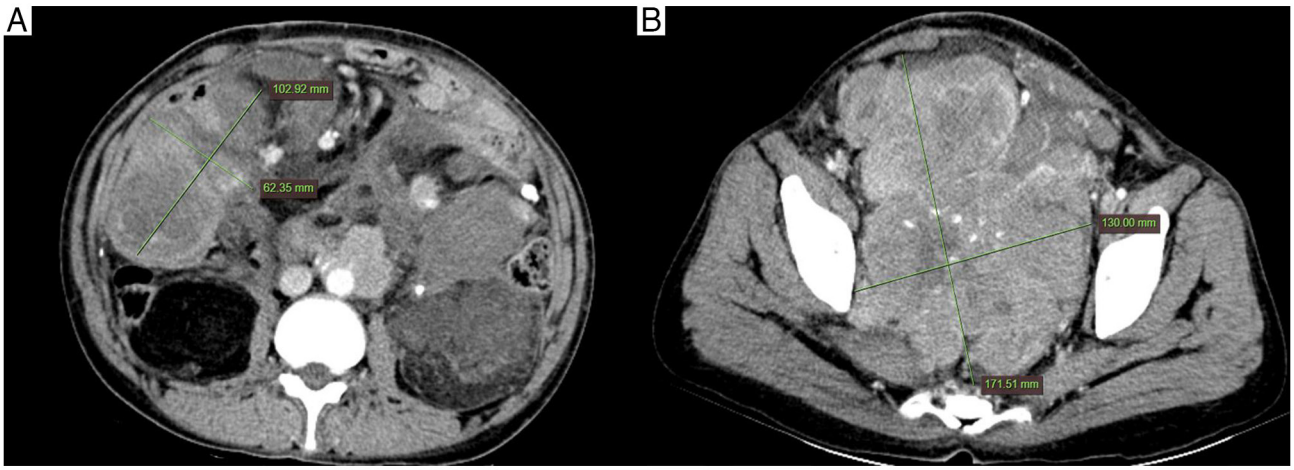

Figure 4. Abdominal enhanced computed tomography scan illustrating multiple masses, such as fat and soft tissue foci, in abdominal and pelvic cavities. The head of the pancreas was partly involved (May 27, 2022). (A) Abdominal mass (10.29x6.24 cm). (B) Pelvic mass (17.15x13.00 cm).

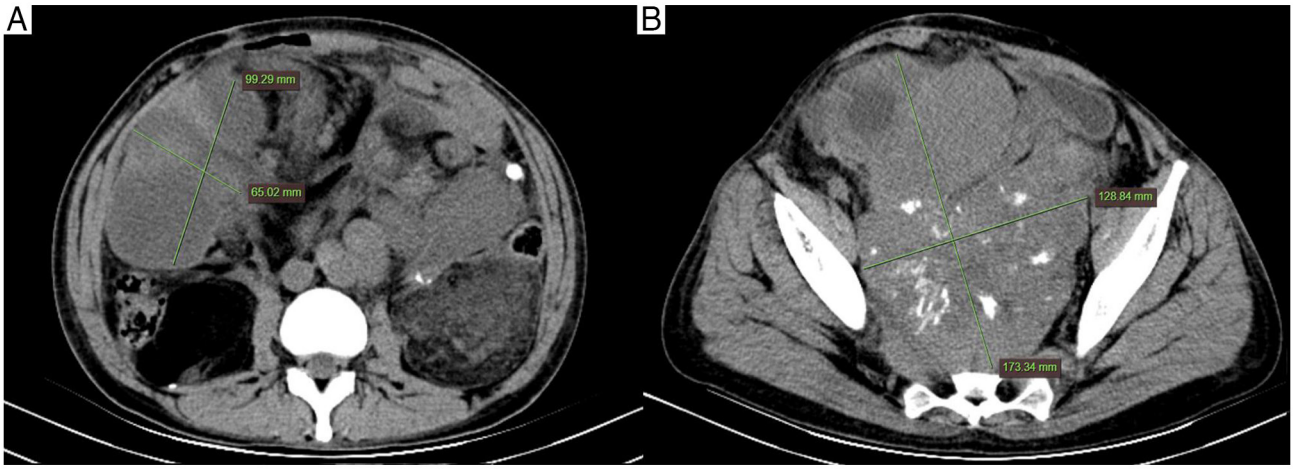

Figure 5. Abdominal computed tomography scan illustrating multiple liposarcomas recurring in the abdominal pelvic cavity and retroperitoneum, involving the pancreatic head, similar to abdominal computed tomography scan in May 2022 (July 8, 2022). (A) Abdominal mass (9.93x6.50 cm). (B) Pelvic mass (17.33x12.88 cm).

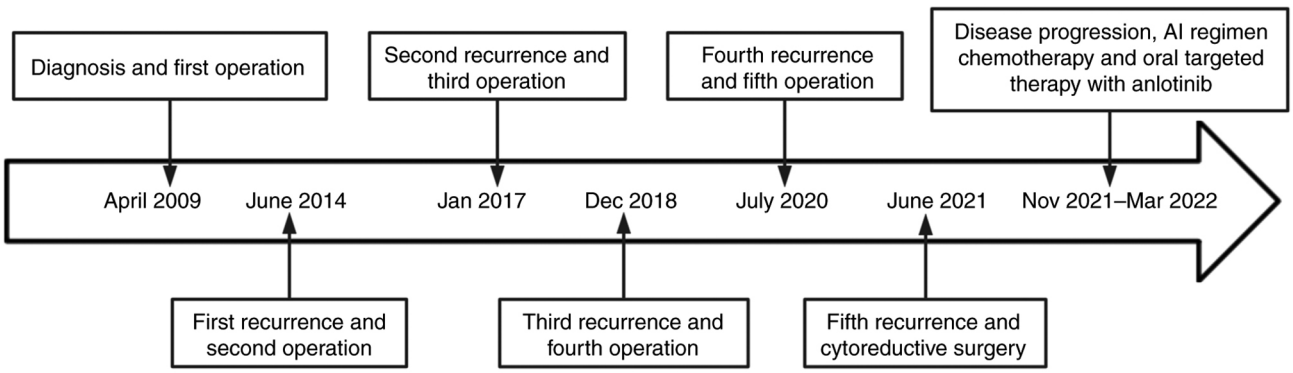

Figure 6. Timeline illustrating the recurrence of liposarcoma in the patient. The patient received five surgical treatments, one cytoreductive surgery, chemotherapy and targeted treatment and was followed-up for 13 years. AI, doxorubicin and ifosfamide.

basic and clinical research, some promising research results and treatment models have emerged. Systemic treatment methods, such as chemotherapy, molecular targeted therapy and immunotherapy (24) and radiotherapy (25) have been applied in clinical practice. Radiotherapy exerts significantly different effects on various pathological types of RPLS and may improve local control of patients with WDLPS and G1-2 DDLPS (4). There are reports that chemotherapeutic drugs

Table I. Clinical and histopathological features, follow-up and clinical outcomes of 16 patients with recurrent retroperitoneal liposarcoma in the past 10 years.

First author, year	Sex	Age, years	Diameter, cm[a]	Wide excision[a]	Pathological type[a]	Complete resection[a]	Adjuvant therapy	Number of relapses/ metastases	Pathological type after recurrence	Follow-up, months	(Refs.)
Joel *et al*, 2020	M	73	16	Yes	D	Yes	C, T	1	D	NA	(29)
Tomoyuki *et al*, 2018	M	34	22	Yes	D	Yes	C	2	D	42	(30)
Francesk *et al*, 2021	M	62	25	No	W	No	C	1	D	32	(31)
Niemetz *et al*, 2020	M	66	20	Yes	Mix	Yes	C, R	8	D	205	(32)
Nagy *et al*, 2013	M	60	17	Yes	D	Yes	C	7	NA	42 (death)	(33)
Kanthala *et al*, 2021	F	40	NA	No	NA	Yes	C	2	D	72	(34)
Ramu *et al*, 2018	M	61	30	No	NA	Yes	R	5	Myx	89	(35)
El-Helou *et al*, 2020	M	70	50	No	W	Yes	No	3	W	60	(36)
Nukada *et al*, 2018	F	60	NA	No	W	Yes	No	6	W	288	(37)
Li *et al*, 2021	F	24	36	Yes	NA	Yes	No	1	D	24	(38)
Guo *et al*, 2019	F	70	NA	No	NA	Yes	No	4	Myx	60	(39)
Ono *et al*, 2018	M	62	NA	Yes	W	Yes	No	5	W	192	(40)
Kuribayashi *et al*, 2018	F	47	4.5	Yes	D	Yes	No	1	D	53	(41)
Alsalameh *et al*, 2019	F	63	35	No	W	Yes	No	1	W	34	(42)
Li *et al*, 2019	F	63	20	No	Mix	Yes	C	1	NA	19	(43)
Guo *et al*, 2022	F	60	26	Yes	D	Yes	No	5	D	63	(44)

[a]At first treatment. F, female; M, male; D, dedifferentiated liposarcoma; W, well-differentiated liposarcoma; Mix, mixed liposarcoma; Myx, myxoid liposarcoma; C, chemotherapy; R, radiotherapy; T, targeted therapy; NA, not available.

have a certain effect on RPLS and anthracycline (26) drugs alone or in combination with ifosfamide and/or imipramine can be used as the first-line regimen for the treatment of liposarcoma (27,28). In the present study, following the fifth relapse, the tumor could not be completely removed by surgery; thus, the patient was treated with doxorubicin combined with ifosfamide chemotherapy and oral targeted therapy with anlotinib.

The present study reviewed cases of recurrent RPLS reported in the literature published in PubMed (https://pubmed.ncbi.nlm.nih.gov/) over the past 10 years. A total of 16 original studies with complete and representative data were selected. The clinical data are summarized in Table I (29-44). There were eight males (50%) and eight females (50%), with a median age of 61.5 years (range, 24-73 years). Of these 16 cases, three (18.75%) had >5 relapses. Two cases (12.5%) exhibited a change in pathological type following recurrence. Only one case (6.25%) did not achieve R0 surgical resection. In total, eight patients (50%) received adjuvant treatment, such as chemotherapy, after onset or first recurrence. Only one patient (6.25%) succumbed; this patient experienced recurrence seven times in >3 years and had undergone eight surgeries. The longest survival time was 24 years. Surgical resection is still the optimal choice for treatment of liposarcoma and adjuvant treatment (10), such as chemotherapy, radiotherapy and targeted therapy, can be administered.

In conclusion, RPLS is rarely observed in clinical practice. CT scan is the first choice of examination and surgery is the only curative treatment for this disease. A close follow-up

should be performed to identify recurrence at an early stage. If recurrence occurs following surgery, operation should be attempted. If the operation fails to completely remove the tumor, it can be supplemented with chemotherapy, radiotherapy, targeted therapy and other auxiliary treatment after the surgery and a positive effect can still be achieved. In the present case, combination of tumor reduction surgery, targeted therapy and chemotherapy provided guidance for the treatment of recurrent RPLS. Considering the existence of FUS/DDIT3 gene fusion in MLS, FISH assay can better guide diagnosis and treatment. Periodic review and early diagnosis and treatment are key to improving the quality of life and survival time of patients with liposarcoma.

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Availability of data and materials

The datasets used and/or analyzed during the current are available from the corresponding author on reasonable request.

Authors' contributions

MQ, DL and ZX contributed to the conception and design of the study. Data collection and analysis were performed by MQ and DL. The manuscript was written by MQ. MQ and ZX confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The requirement for ethics approval was waived by the Ethics Committee of Shaoxing Second Hospital (Shaoxing, China) due to the retrospective nature of the study.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of potentially identifying images or data included in this article.

Competing interests

The authors declare that they have no competing interests.

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