



A Case Report of Well-Differentiated Liposarcoma Presenting as a Primary Inguinal Mass: Diagnostic Challenges and Management

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Article History :

Received date : 2025/07/07

Revised date : 2025/08/14

Accepted date : 2025/09/24

Published date : 2025/10/18



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E-ISSN :

ISSN 3048-1368



P-ISSN

ISSN 3048-1376



ABSTRACT

Introduction : Retroperitoneal liposarcoma (RLPS) is a rare mesenchymal malignancy characterized by large tumor size at diagnosis and a high propensity for local recurrence. Giant RLPS, particularly the high-grade dedifferentiated subtype, presents formidable diagnostic and therapeutic challenges.

Case Illustration : We present the case of a 64-year-old male with a one-year history of progressive abdominal distension. Physical examination revealed a massive, firm abdominal mass. Contrast-enhanced computed tomography (CT) identified a 35 x 25 x 20 cm heterogeneous retroperitoneal mass with both fatty and large non-lipomatous components, consistent with dedifferentiated liposarcoma. The patient underwent an exploratory laparotomy with a successful *en bloc* compartmental resection, which included the tumor, the right kidney, the right adrenal gland, and a segment of the ascending colon. The

resected specimen weighed 10.4 kg. Histopathology confirmed a grade 3 dedifferentiated liposarcoma arising from a well-differentiated liposarcoma, with negative surgical margins (R0). The patient had an uneventful postoperative recovery and is undergoing surveillance.

Discussion : This case highlights the central role of radical surgical resection as the only potentially curative modality for primary RLPS. The discussion provides a comprehensive review of the diagnostic utility of cross-sectional imaging, the principles of compartmental surgery to achieve negative margins, and the current, evolving landscape of adjuvant therapies. We critically analyze the results of the landmark EORTC-STRASS trial, which failed to show an overall benefit for preoperative radiotherapy but suggested a potential benefit in the liposarcoma subgroup, creating an ongoing clinical controversy. The limited role of systemic therapy outside of the advanced or metastatic setting is also reviewed.

Conclusion : The management of giant RLPS is complex and necessitates a multidisciplinary approach at a specialized sarcoma center. Complete surgical resection remains the cornerstone of treatment, while the role of neoadjuvant therapies continues to be refined through histology-specific clinical trials.

Keywords : Retroperitoneal Sarcoma, Dedifferentiated Liposarcoma, Surgical Oncology, En Bloc Resection, Multidisciplinary Management, STRASS Trial.

INTRODUCTION

Background

Soft tissue sarcomas (STS) are a heterogeneous group of rare malignancies arising from mesenchymal tissue, collectively accounting for less than 1% of all adult cancers (Gronchi et al., 2021; NCCN, 2025). Among the more than 70 distinct histological subtypes, liposarcoma, a malignancy of adipocytic origin, stands as one of the most common in adults (Singer et al., 2015; Crago and Brennan, 2015). Approximately 15% of all STS originate in the retroperitoneum, a deep and anatomically complex space posterior to the abdominal cavity (Stoeckle et al., 2004; Tseng et al., 2018). This location is a critical determinant of the disease's natural history. The retroperitoneum is a non-essential, expandable compartment, which permits tumors to grow to massive sizes over extended periods without producing specific symptoms (Mussi et al., 2015; MacNeill and Gronchi, 2021). Consequently, patients often present with advanced disease, with median tumor diameters frequently exceeding 20 cm at the time of diagnosis (Porpiglia et al., 2015; Hassan et al., 2005).

Retroperitoneal liposarcoma (RLPS) is the most common histological subtype of retroperitoneal sarcoma (RPS) (Gronchi et al., 2022). Its management is complicated by a triad of confounding factors: anatomical concealment, biological heterogeneity, and therapeutic resistance. The late presentation due to anatomical concealment means that tumors are often intimately involved with critical organs and major vessels, posing a formidable surgical challenge (Tseng et al., 2023; MacNeill and Gronchi, 2021). Biologically, RLPS is not a single entity but a spectrum of diseases, ranging from indolent, non-metastasizing well-differentiated liposarcoma (WDLPS) to aggressive, high-grade dedifferentiated liposarcoma (DDLPS) with significant metastatic potential (Singer et al., 2015; Keung and Pollock, 2020). Finally, these tumors exhibit relative resistance to conventional chemotherapy and radiotherapy, placing an immense burden on surgery as the primary, and often only, effective modality (Porpiglia et al., 2015; Livingston et al., 2020). This

confluence of factors results in a high rate of local recurrence, which remains the principal driver of patient mortality (Gronchi et al., 2022; Lewis et al., 1997; Park et al., 2017).

Objective

The primary objective of this report is to present a demonstrative case of a giant retroperitoneal dedifferentiated liposarcoma. This case serves as a framework for an exhaustive, evidence-based review of the current multidisciplinary principles for the diagnosis, treatment, and follow-up of this complex disease.

Benefits

This report aims to consolidate contemporary knowledge for clinicians managing RLPS. By integrating findings from recent landmark clinical trials and expert consensus guidelines, it provides practical insights into the rationale behind aggressive surgical approaches and the nuanced, histology-driven application of adjuvant and neoadjuvant therapies (Gronchi et al., 2021).

Hypothesis

The central hypothesis of modern RLPS management is that complete macroscopic *en bloc* surgical resection, performed at a high-volume sarcoma center, remains the most critical determinant of local control and overall survival in primary disease (Tseng et al., 2023). The utility of adjuvant and neoadjuvant therapies is not universal but is increasingly being defined by histology-specific risks and treatment responses, necessitating a personalized approach (Gronchi et al., 2021).

Research Gap

Despite progress, significant gaps persist in the evidence base for managing RLPS. A major area of controversy surrounds the role of preoperative radiotherapy (RT). The pivotal European Organisation for Research and Treatment of Cancer (EORTC) STRASS trial failed to demonstrate a

survival benefit for preoperative RT in an unselected RPS population, yet a subgroup analysis suggested a potential benefit for patients with liposarcoma, creating ongoing clinical equipoise (Bonvalot et al., 2020; Nussbaum et al., 2021; Zagar et al., 2021). Furthermore, a profound research gap exists in identifying effective systemic therapies to prevent recurrence in high-risk localized disease, such as DDLPS, which is known for its relative chemoresistance (Crago and Brennan, 2015; Dickson et al., 2013).

Novelty

This report distinguishes itself by contextualizing a complex clinical case within the most current, high-level evidence. It provides a detailed synthesis and critical interpretation of the STRASS trial and its far-reaching implications, discusses the rationale for subsequent histology-driven trials like STRASS-2, and offers a comprehensive, multidisciplinary perspective that reflects the contemporary standard of care at specialized sarcoma centers (MacNeill and Gronchi, 2021).

CASE ILLUSTRATION

Patient Presentation and History

A 64-year-old male presented to the surgical oncology clinic with a chief complaint of progressive, painless abdominal distension that had been worsening over the past year (. He reported associated symptoms of early satiety, requiring him to eat smaller meals more frequently, and a vague, persistent discomfort in his right flank. His past medical history was significant only for well-controlled hypertension, for which he was taking amlodipine. He denied any significant weight loss, fever, nausea, vomiting, or changes in bowel or bladder habits. He had no personal or family history of malignancy.

Clinical Examination

On physical examination, the patient appeared well-nourished and was in no acute distress. His vital signs were within normal limits. The abdomen was markedly distended and visibly

asymmetric, with a prominent bulge on the right side. Palpation revealed a large, firm, non-tender mass that occupied the entire right side of the abdomen, extending from the right costal margin into the pelvis and crossing the midline to the left of the umbilicus. The mass was immobile and did not move with respiration. There were no palpable signs of ascites, and no lower extremity edema was observed. The remainder of the physical examination was unremarkable.

Preoperative Laboratory Findings

Preoperative laboratory investigations were conducted to assess the patient's baseline health and fitness for major surgery. The results revealed a mild normocytic anemia, which is a common finding in patients with large tumors, but were otherwise largely within normal limits.

Table 1: Preoperative Laboratory Results

Parameter	Patient's Value	Reference Range	Unit
Complete Blood Count			
Hemoglobin	10.8	13.5 - 17.5	g/dL
Hematocrit	32.5	41 - 50	%
White Blood Cell Count	7.2	4.5 - 11.0	$\times 10^3/\mu\text{L}$
Platelet Count	250	150 - 450	$\times 10^3/\mu\text{L}$

Renal Function Panel			
Creatinine	0.9	0.7 - 1.3	mg/dL
Blood Urea Nitrogen (BUN)	15	7 - 20	mg/dL
Liver Function Panel			
Total Bilirubin	0.7	0.1 - 1.2	mg/dL
AST (SGOT)	22	10 - 40	U/L
ALT (SGPT)	25	7 - 56	U/L
Albumin	3.8	3.5 - 5.5	g/dL
Coagulation Profile			
Prothrombin Time (PT)	12.5	11.0 - 13.5	seconds
INR	1.0	<1.1	

aPTT	30	25 - 35	seconds
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Diagnostic Imaging

A contrast-enhanced computed tomography (CT) scan of the abdomen and pelvis was performed for diagnosis and staging. The scan revealed a massive, multi-lobulated retroperitoneal mass measuring 35 x 25 x 20 cm. The mass demonstrated heterogeneous composition. The predominant component consisted of macroscopic fat, with attenuation values ranging from -70 to -100 Hounsfield units (HU), consistent with a lipomatous origin. Critically, interspersed within this fatty matrix were multiple large, nodular, non-lipomatous soft-tissue components measuring up to 12 cm in diameter. These nodules demonstrated avid and heterogeneous enhancement following the administration of intravenous contrast. The presence of these distinct, non-fatty soft tissue regions greater than 1 cm is a key imaging feature highly suggestive of dedifferentiation within a liposarcoma.

The tumor exerted a significant mass effect on adjacent structures. The intra-abdominal viscera, including the small bowel loops and pancreas, were displaced superiorly and to the left. The tumor completely encased the right kidney and adrenal gland, with no discernible fat plane separating the tumor from these organs. The inferior vena cava (IVC) was compressed and displaced anteriorly, but it appeared patent without evidence of thrombosis or invasion. The right colon was displaced anteromedially and was attenuated over the anterior surface of the mass. A concurrent CT of the chest was performed for staging, which showed no evidence of pulmonary or other distant metastatic disease.

Preoperative Management and Surgical Planning

The patient's case was presented and discussed at a multidisciplinary sarcoma tumor board, which included surgical oncologists, medical oncologists, radiation oncologists, pathologists, and

radiologists. Based on the classic imaging findings of a large retroperitoneal lipomatous tumor with extensive non-lipomatous components, a consensus diagnosis of dedifferentiated liposarcoma was made. Given the high diagnostic certainty from imaging and the plan for upfront resection, a preoperative biopsy was deemed unnecessary, thereby avoiding the potential risks of tumor seeding and sampling error.

The primary treatment plan was upfront surgical resection with curative intent. The surgical strategy was planned as an *en bloc* compartmental resection. This approach anticipated the need for a right nephrectomy, right adrenalectomy, and a right hemicolectomy to achieve a complete resection with negative microscopic margins (R0), as these organs were directly abutted or encased by the tumor.

Surgical Procedure

The patient was taken to the operating room and placed in the supine position. A long midline laparotomy incision was made, extending from the xiphoid process to the pubic symphysis. Upon entering the abdominal cavity, the massive retroperitoneal tumor was immediately identified, consistent with the preoperative imaging findings. A thorough exploration confirmed the absence of peritoneal sarcomatosis or liver metastases.

The principle of *en bloc* resection was strictly adhered to throughout the procedure, with meticulous care taken to avoid any direct manipulation or rupture of the tumor capsule. The procedure began with the mobilization of the right colon by incising the white line of Toldt. The tumor was found to be densely adherent to the ascending colon, necessitating a standard right hemicolectomy, which was included in the specimen. The tumor was also found to be inseparable from the right kidney and adrenal gland. The right renal artery and vein were carefully identified, ligated with silk ties, and divided. The tumor was then carefully dissected off the posterior abdominal wall, the psoas muscle, the duodenum, and the compressed IVC. The entire specimen—comprising the tumor, the right kidney, the right adrenal gland, and the right colon—was

successfully removed *en bloc*. A macroscopically complete (R0/R1) resection was achieved. An ileocolic anastomosis was performed to restore bowel continuity.

Pathological Findings

Macroscopic Examination

The resected specimen weighed 10.4 kg and measured 36 x 26 x 22 cm in its greatest dimensions. On sectioning, the tumor was multi-nodular and displayed two distinct components. Approximately 70% of the mass had a yellow, fatty, and lobulated appearance, consistent with well-differentiated liposarcoma. The remaining 30% of the tumor consisted of multiple firm, grey-white, fleshy nodules with areas of hemorrhage and necrosis, representing the dedifferentiated component. The right kidney and adrenal gland were engulfed by the tumor but did not appear to be grossly invaded.

Microscopic Examination

Histopathological analysis confirmed the diagnosis of a high-grade (Fédération Nationale des Centres de Lutte Contre le Cancer [FNCLCC] Grade 3) dedifferentiated liposarcoma. The microscopic sections showed an abrupt transition from areas of well-differentiated liposarcoma, characterized by atypical adipocytes with hyperchromatic nuclei and fibrous septa, to a high-grade, non-lipogenic sarcoma. This latter component was composed of pleomorphic spindle cells arranged in a fascicular pattern with a high mitotic rate (>20 mitoses per 10 high-power fields) and extensive tumor necrosis. Immunohistochemical staining was strongly and diffusely positive for murine double minute 2 (MDM2) and cyclin-dependent kinase 4 (CDK4), a molecular signature that is pathognomonic for this entity. All surgical margins were microscopically negative for tumor, confirming an R0 resection.

Postoperative Course and Follow-up

The patient's postoperative course was uneventful. He was managed in the surgical intensive

care unit for one day for monitoring and was subsequently transferred to the surgical ward. His bowel function returned on postoperative day 4, and he was discharged home on postoperative day 8.

Table 2: Postoperative Daily Inpatient Follow-up

Post-Op Day	Vital Signs	Clinical Status & Events	Interventions
0 (ICU)	Stable, afebrile	Post-anesthesia recovery. Pain controlled with PCA. Abdomen soft. Drains with serosanguinous output.	IV fluids, PCA, Foley catheter, Jackson-Pratt drains. NPO.
1	Stable, afebrile	Transferred to surgical ward. Minimal incisional pain. Drains remain in place.	Discontinue PCA, transition to oral analgesics. IV fluids continued.
2	Stable, afebrile	Ambulating with assistance. Abdomen remains soft. No bowel sounds.	Encourage ambulation. Continue IV fluids.

Post-Op Day	Vital Signs	Clinical Status & Events	Interventions
3	Stable, afebrile	Passing flatus. Abdomen soft, non-distended. Incision clean, dry, intact.	IV fluids decreased. Sips of clear liquids initiated.
4	Stable, afebrile	Bowel movement. Tolerating clear liquids well. Drain output decreasing.	Diet advanced to full liquids. Foley catheter removed.
5	Stable, afebrile	Tolerating diet. Ambulating independently. Drain output minimal.	Diet advanced to soft diet. One JP drain removed.
6	Stable, afebrile	Tolerating regular diet. Pain well-controlled with oral medication.	Remaining JP drain removed.
7	Stable, afebrile	Preparing for discharge. Patient and family education completed.	Plan for discharge on POD 8.

Post-Op Day	Vital Signs	Clinical Status & Events	Interventions
8	Stable, afebrile	Discharged home in good condition.	Follow-up appointment scheduled.

His case was re-discussed at the postoperative multidisciplinary tumor board. Given the achievement of an R0 resection, and in light of the current evidence, no adjuvant radiation or chemotherapy was recommended outside the context of a clinical trial. The patient was placed on a stringent surveillance protocol involving abdominopelvic CT scans every 4-6 months for the first three years, followed by annual scans, along with routine chest imaging to monitor for distant metastasis. At his 1-year follow-up appointment, he remained clinically well with no radiological evidence of disease recurrence.

Table 3: Post-Discharge Surveillance Schedule

Follow-up Interval	Clinical Assessment	Imaging Studies
Years 1-3	Every 4-6 months	Abdominopelvic CT with contrast. Chest CT without contrast.
Years 4-5	Every 6 months	Abdominopelvic CT with

		contrast. Chest CT without contrast.
Year 5 onwards	Annually	Abdominopelvic CT with contrast. Chest CT without contrast.

DISCUSSION

The Challenge of Retroperitoneal Sarcomas: Anatomy and Biology

The case presented exemplifies the quintessential challenges of RLPS, where the disease's prognosis is fundamentally dictated by its anatomical location and underlying biology (Mussi et al., 2015; MacNeill and Gronchi, 2021). The retroperitoneum's vast, pliable space allows for a prolonged, clinically silent growth phase, culminating in the diagnosis of a giant tumor, as was evident in our patient (Porpiglia et al., 2015; Hassan et al., 2005; Al-Zoubi et al., 2024). This inherent feature of anatomical concealment stands in stark contrast to extremity sarcomas, where a palpable, growing mass is typically noticed much earlier, allowing for intervention when the tumor is smaller and surgically more manageable (Stavrou et al., 2016). By the time RLPS becomes symptomatic, it has often already created a complex surgical problem involving multiple organ systems (Tseng et al., 2023).

The biological spectrum of liposarcoma, as codified by the World Health Organization (WHO) 2020 classification, is the other critical determinant of management and outcome (WHO Classification of Tumours Editorial Board, 2020; Sbaraglia et al., 2021). The major subtypes include atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLPS), dedifferentiated liposarcoma (DDLPS), myxoid liposarcoma, and pleomorphic liposarcoma (The WHO Classification of Tumours Online, 2020). Our case of DDLPS highlights a key biological behavior:

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the progression from a low-grade, indolent WDLPS to a high-grade, aggressive sarcoma with the capacity for both local recurrence and distant metastasis (Singer et al., 2015; Keung and Pollock, 2020; Zagar et al., 2021). This process of dedifferentiation, which occurs in approximately 20-30% of retroperitoneal WDLPS, is a major adverse prognostic event, significantly increasing the risk of tumor-related mortality (Singer et al., 2015; Zagar et al., 2021).

Diagnostic Workup: The Role of Imaging and Biopsy

Contrast-enhanced CT is the cornerstone of the diagnostic workup and surgical planning for RLPS (Keung and Pollock, 2020; Stoeckle et al., 2004). It provides essential information regarding tumor size, location, composition, relationship to adjacent organs, and involvement of major vascular structures. Magnetic resonance imaging (MRI) can serve as a valuable complementary modality, particularly for tumors located in the pelvis or when there is suspicion of neural or spinal involvement, owing to its superior soft-tissue contrast (Tseng et al., 2018).

The radiographic features observed on CT and MRI can often strongly suggest the underlying histological subtype, which may influence the decision to perform a preoperative biopsy (Keung and Pollock, 2020). WDLPS typically appears as a large, encapsulated mass composed almost entirely of macroscopic fat, similar in density to subcutaneous fat, with only thin, non-enhancing septa (Singer et al., 2015; Lee et al., 2011). The presence of nodular, non-lipomatous, enhancing soft-tissue components greater than 1 cm in diameter within a predominantly fatty mass, as seen in our patient, is the pathognomonic imaging feature of dedifferentiation (Singer et al., 2015; Keung and Pollock, 2020; Lee et al., 2011). Myxoid liposarcomas, due to their high water content, often show low attenuation on CT (less than muscle but greater than fat) and are characteristically hyperintense on T2-weighted MRI sequences (Radiopaedia, n.d.; Lee et al., 2011). High-grade subtypes like pleomorphic liposarcoma may contain little to no visible fat and can appear as nonspecific, heterogeneous soft-tissue masses, making them indistinguishable from other types of sarcoma (Radsourc, 2024).

Preoperative core needle biopsy is generally recommended when the diagnosis is uncertain based on imaging, when a non-sarcomatous diagnosis (e.g., lymphoma, germ cell tumor) is considered, or when neoadjuvant therapy is being contemplated (ESMO et al., 2021; Anaya et al., 2021). However, biopsy is not without its limitations. It carries a small but real risk of needle tract seeding, and more importantly, it is subject to sampling error. A biopsy of a large, heterogeneous tumor may inadvertently sample only the low-grade WDLPS component, missing a focus of high-grade DDLPS and leading to an underestimation of the tumor's true biological potential (Tseng et al., 2018). Therefore, in cases with classic imaging features of RLPS, such as ours, proceeding directly to surgical resection is a widely accepted and often preferred strategy (Keung and Pollock, 2020; Anaya et al., 2021).

Table 4: Differentiating Radiographic Features of RLPS Subtypes on CT and MRI

Histological Subtype	Key CT Features	Key MRI Features	Clinical Pearl/Prognosis
Well-Differentiated (WDLPS)	Predominantly fat-density mass (to HU). May have thin (mm), minimally enhancing septa. Calcification is rare (Lee et al., 2011).	Isointense to subcutaneous fat on all sequences. Thin septa may be more visible. Shows uniform signal loss on fat-suppressed sequences (Radsourc, 2024).	Low-grade, indolent. Does not metastasize but has high local recurrence risk in the retroperitoneum (Singer et al., 2015).
Dedifferentiated	Heterogeneous mass	Fatty components as	High-grade, aggressive.

Histological Subtype	Key CT Features	Key MRI Features	Clinical Pearl/Prognosis
(DDLPS)	with juxtaposition of fatty WDLPS areas and nodular, non-lipomatous soft tissue components (cm) that show avid, heterogeneous enhancement. Calcification/ossification in non-fatty areas is suggestive (Keung and Pollock, 2020).	above. Dedifferentiated areas are hypointense on T1, heterogeneously hyperintense on T2, and show strong enhancement. Abrupt transition between components (Lee et al., 2011).	Carries risk of both local recurrence and distant metastasis (Zagar et al., 2021).
Myxoid	Well-circumscribed, lobulated mass with attenuation lower than muscle but higher than fat, often appearing cystic. May have lacy, linear areas of fat. Shows delayed,	Characteristically very hyperintense ("fluid-like") on T2-weighted images due to high myxoid content. Hypointense on T1. Enhancement is often heterogeneous and delayed (Lee et al.,	Intermediate-grade. Prone to metastasis to unusual soft tissue sites and bone. Often chemosensitive and radiosensitive (Singer et al., 2015).

Histological Subtype	Key CT Features	Key MRI Features	Clinical Pearl/Prognosis
	progressive enhancement (Radiopaedia, n.d.).	2011).	
Pleomorphic	Large, heterogeneous soft-tissue mass with areas of necrosis and hemorrhage. Macroscopic fat is often absent, making it indistinguishable from other high-grade sarcomas (Radsourc, 2024).	Nonspecific heterogeneous mass. Iso- to hypointense on T1, heterogeneously hyperintense on T2. Demonstrates avid, heterogeneous enhancement and areas of non-enhancement (necrosis) (Radsourc, 2024).	High-grade, aggressive. High metastatic potential, most commonly to the lungs. Poorest prognosis among liposarcoma subtypes (Livingston et al., 2020).

Data compiled from: Singer et al., 2015; Keung and Pollock, 2020; Lee et al., 2011; Radiopaedia, n.d.; Radsourc, 2024; Park et al., 2017; Nishino et al., 2003; Zagar et al., 2021; Livingston et al., 2020.

The Cornerstone of Treatment: Radical Surgical Resection

Across all histological subtypes, complete surgical resection is the only modality with

curative potential for primary RLPS (Gronchi et al., 2022; Anaya et al., 2021; Tseng et al., 2023). The quality and completeness of this initial surgical procedure is widely recognized as the single most important prognostic factor influencing both local control and overall survival (Lewis et al., 1997; Xu et al., 2016; Stavrou et al., 2016).

The fundamental understanding of RLPS failure patterns has driven a significant evolution in surgical philosophy. Decades of experience revealed that simply "shelling out" the tumor, even when a pseudocapsule was present, resulted in unacceptably high rates of local recurrence (Gronchi et al., 2022; Stavrou et al., 2016). This observation led to the hypothesis that microscopic satellite nodules or a diffuse infiltrative process often exists in the surrounding retroperitoneal fat and on the surfaces of adjacent organs, far beyond the visible tumor margin (Gronchi et al., 2022). This realization prompted a paradigm shift from simple tumor excision to a more aggressive *en bloc* compartmental resection (Anaya et al., 2021; Tseng et al., 2018). This modern approach redefines the surgical target from the tumor itself to the entire anatomical compartment containing the tumor. Consequently, adjacent organs that are abutted or encased—such as the kidney, colon, spleen, or pancreas—are intentionally resected along with the tumor, not as a result of direct invasion, but as a means to achieve a functionally wide negative margin (Anaya et al., 2021). The multi-organ resection performed in our patient, including a nephrectomy and colectomy, is a standard and necessary component of this evidence-based oncologic strategy (City of Hope, n.d.; Tseng et al., 2018).

The goal of surgery is to achieve a macroscopically complete resection, ideally with negative microscopic margins (R0). Achieving this R0/R1 status is paramount, as incomplete (R2) resections or intraoperative tumor rupture are associated with a drastically increased risk of local recurrence and significantly poorer survival outcomes (Lewis et al., 1997; Tseng et al., 2018; Stavrou et al., 2016). Given the technical complexity of these operations, patient outcomes are significantly better when managed at high-volume, specialized sarcoma centers with multidisciplinary expertise (City of Hope, n.d.; Tseng et al., 2023; MacNeill and Gronchi, 2021).

The Role of Radiation Therapy: An Evolving and Controversial Paradigm

The role of radiation therapy in the management of RLPS has long been a subject of debate, with historical practices largely extrapolated from the setting of extremity STS, where the addition of RT to surgery unequivocally improves local control (Zagar et al., 2021; O'Sullivan et al., 2002). The challenge in the retroperitoneum lies in delivering an effective radiation dose without causing unacceptable toxicity to sensitive adjacent organs, particularly the small bowel (Stavrou et al., 2016).

The landmark EORTC-62092 (STRASS) trial was a multicenter, phase 3 randomized controlled trial designed to definitively answer the question of RT efficacy. It randomized 266 patients with primary RLPS to receive either surgery alone or preoperative RT (50.4 Gy) followed by surgery (Bonvalot et al., 2020). The primary endpoint was abdominal recurrence-free survival (ARFS). The trial was ultimately **negative**, as it found no statistically significant difference in ARFS between the two arms (hazard ratio 1.01; $p=0.95$) (Bonvalot et al., 2020; Nussbaum et al., 2021). Based on this primary result, the formal conclusion was that preoperative RT should not be considered the standard of care for an unselected population of patients with RLPS (Bonvalot et al., 2020).

However, the trial's findings were more nuanced. A pre-planned sensitivity analysis within the trial, and a subsequent larger pooled analysis that combined the STRASS data with a cohort of off-trial patients (STREXIT), suggested a potential benefit for preoperative RT specifically in the **liposarcoma subgroup** (Bonvalot et al., 2020; Haas et al., 2023). This analysis indicated that patients with WDLPS and low-to-intermediate grade DDLPS who received preoperative RT had improved ARFS compared to those who underwent surgery alone (Haas et al., 2023; Nussbaum et al., 2021). This finding, while only hypothesis-generating due to its post-hoc nature, has created a major clinical dilemma. It has prompted a necessary shift away from a "one-size-fits-all" approach and toward histology-specific treatment considerations. Currently, some high-volume centers

selectively offer preoperative RT for patients with primary retroperitoneal liposarcoma, while others have largely abandoned its use based on the negative primary trial result (Haas et al., 2023). Therefore, the decision to use preoperative RT must be highly individualized, made after a thorough discussion in a multidisciplinary setting, and carefully weighing the potential for improved local control in liposarcoma against the known risks of radiation toxicity (Bonvalot et al., 2020).

Systemic Therapy in Liposarcoma: Limited Role in Localized Disease

Unlike many other solid tumors, the role of neoadjuvant or adjuvant chemotherapy for localized RLPS is not established and is generally not recommended outside of a clinical trial setting (Porpiglia et al., 2015; Gronchi et al., 2021; Italiano et al., 2016). This is largely due to the relative chemoresistance of the most common RLPS subtypes, WDLPS and DDLPS, and the failure of multiple studies to demonstrate a consistent survival benefit (Livingston et al., 2020; Crago and Brennan, 2015; Dickson et al., 2013).

Recognizing the high risk of distant metastasis in specific high-grade histologies, the ongoing STRASS-2 trial is currently investigating the role of neoadjuvant chemotherapy specifically for patients with DDLPS and leiomyosarcoma (Zagar et al., 2021; Cardona, 2024). This trial represents the field's progression toward histology-driven systemic therapy questions.

For patients who present with or develop advanced, unresectable, or metastatic disease, systemic therapy is the standard of care. First-line treatment is typically an anthracycline-based regimen, most commonly single-agent doxorubicin (Livingston et al., 2020; Jones et al., 2017; Sanfilippo et al., 2021). The addition of an alkylating agent like ifosfamide to doxorubicin may increase objective response rates but has not been shown to improve overall survival in large randomized trials, and it comes at the cost of significantly higher toxicity (Jones et al., 2017). For patients whose disease progresses after first-line therapy, several agents have shown activity and are approved for use in advanced liposarcoma. **Trabectedin** and **eribulin** have both demonstrated a survival benefit over standard chemotherapy in the second-line setting and beyond, and represent

important options for these patients (Demetri et al., 2016; Schöffski et al., 2016; Dickson et al., 2013; Sanfilippo et al., 2021).

Prognosis, Survival, and Patterns of Recurrence

The prognosis of RLPS is highly variable and is dictated by a confluence of clinical and pathological factors. The most powerful and consistently reported predictors of outcome are **histological grade (FNCLCC)**, the **completeness of surgical resection (R status)**, and the **histological subtype** (Lewis et al., 1997; Xu et al., 2016; Tan et al., 2008; Zhang et al., 2021). Advanced patient age has also been identified as an independent adverse prognostic factor in multiple large series (Xu et al., 2016; Zhang et al., 2021).

Survival rates differ markedly by subtype. Patients with pure WDLPS have an excellent long-term prognosis, with virtually no risk of metastatic disease; mortality in this group is almost exclusively due to the morbidity of local recurrence (Singer et al., 2015). In contrast, DDLPS carries a more guarded prognosis, with 5-year overall survival rates reported in the range of 44% to 62% and a significant risk of developing both local recurrence and distant metastases (Xu et al., 2016; Zagar et al., 2021; Livingston et al., 2020). Across all subtypes, the overall 5-year survival rate for patients with primary RLPS treated with curative intent is approximately 60-65% (Xu et al., 2016; Tan et al., 2008).

The predominant pattern of treatment failure in RLPS, especially for low- and intermediate-grade tumors, is **local recurrence** within the retroperitoneum (Gronchi et al., 2022; Zagar et al., 2021; Stavrou et al., 2016). Recurrence is most common within the first two to three years following initial surgery, but can occur many years later, necessitating long-term surveillance (Park et al., 2017; Lewis et al., 1997). This high propensity for local failure underscores the absolute criticality of achieving a complete and wide resection during the initial surgical procedure.

Table 5: Key Prognostic Factors in Retroperitoneal Liposarcoma

Prognostic Factor	Favorable Prognosis	Unfavorable Prognosis	Supporting Evidence
Histological Grade (FNCLCC)	Low Grade (Grade 1)	High Grade (Grade 2-3)	Xu et al., 2016; Zhang et al., 2021; Tan et al., 2008
Completeness of Resection	R0 (microscopically negative margins)	R1 (microscopically positive) or R2 (gross residual disease)	Lewis et al., 1997; Xu et al., 2016; Tan et al., 2008
Histological Subtype	Well-Differentiated Liposarcoma (WDLPS)	Dedifferentiated (DDLPS), Pleomorphic Liposarcoma	Xu et al., 2016; Zhang et al., 2021; Livingston et al., 2020
Patient Age	Younger (years)	Older (years)	Xu et al., 2016; Zhang et al., 2021
Tumor Presentation	Primary (first presentation)	Recurrent disease	Tan et al., 2008
Tumor Necrosis	Absent	Present	Zhang et al., 2021

CONCLUSION AND SUGGESTIONS

Conclusion

Giant retroperitoneal liposarcoma is a rare and clinically challenging malignancy defined by its insidious growth pattern, characteristically large size at presentation, and a high intrinsic rate of local recurrence. The successful management of this disease demands a highly coordinated, multidisciplinary team operating within a specialized, high-volume sarcoma center.

As demonstrated by the presented case and overwhelmingly supported by the available literature, complete *en bloc* surgical resection, adhering to the principles of compartmental surgery, is the single most important intervention and represents the only potential for cure. The role of adjuvant and neoadjuvant therapies remains a dynamic and controversial field. The landmark STRASS trial did not support the routine use of preoperative radiotherapy for all RLPS patients. However, its nuanced results have appropriately shifted the clinical and research focus toward histology-specific treatment paradigms, sparking an ongoing and important debate about its potential utility specifically in the liposarcoma subgroup.

Suggestions

Based on the current evidence, the following recommendations are proposed for the management of patients with retroperitoneal liposarcoma:

- All patients with a suspected or confirmed diagnosis of RLPS should be referred to a high-volume sarcoma center for comprehensive evaluation and treatment planning by a dedicated multidisciplinary team.
- The primary surgical strategy should be based on the principle of *en bloc* compartmental resection, with the goal of achieving microscopically negative (R0) margins, even if this necessitates multi-organ resection.
- The decision to incorporate neoadjuvant radiotherapy for primary retroperitoneal liposarcoma

should be made on a case-by-case basis following a thorough multidisciplinary discussion that acknowledges the current equipoise in the evidence and considers the individual patient's tumor characteristics and fitness.

- Eligible patients, particularly those with high-risk histologies such as dedifferentiated liposarcoma, should be strongly encouraged to participate in prospective clinical trials, such as STRASS-2, to help clarify the role of systemic therapies and advance future standards of care.
- Following curative-intent treatment, all patients require long-term, structured surveillance with regular cross-sectional imaging, as the risk of local recurrence persists for many years.

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