Advancements in Diagnosis and Multimodal Treatment Strategies for Retroperitoneal Tumors

A Comprehensive Review

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Abstract: Retroperitoneal tumors (RPTs) encompass both benign and malignant entities, constituting ~0.1% to 0.2% of all malignant tumors, of which 70% to 80% manifest malignancy. Predominantly, retroperitoneal sarcomas (RPS) represent the most prevalent subtype among RPT. With over 70 histologic forms identified, liposarcomas and leiomyosarcomas emerge as the primary constituents of RPS. Accurate diagnosis of RPTs necessitates preoperative core-needle biopsy and comprehensive imaging assessment. The current staging protocol for RPS relies on the eighth edition of the American Joint Committee on Cancer/TNM classification. Surgical excision remains the established gold standard for treating RPS. Therapeutic approaches vary according to the underlying pathophysiology. Although chemotherapy and radiotherapy exhibit efficacy in managing metastatic and recurrent unresectable RPS, their role in primary RPS remains unresolved, necessitating further clinical trials for validation. Concurrently, ongoing research explores the potential of targeted therapies and immunotherapy. This literature review aims to provide a comprehensive overview of existing research, delineating diagnostic pathways and optimal therapeutic strategies for RPT.

Key Words: retroperitoneal tumors, retroperitoneal sarcomas, surgery, radiotherapy, chemotherapy

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The transverse peritoneal fascia and posterior parietal peritoneum envelop the retroperitoneal compartment anteriorly and posteriorly, respectively, with the anterior and posterior renal fascia demarcating it into 3 distinct parts. These include the anterior pararenal, perirenal, and posterior pararenal spaces.[1] Retroperitoneal tumors (RPTs) manifest in the soft tissues of the retroperitoneum, encompassing fat, muscle, nerves, lymph nodes, blood, or lymph vessels. Differentiating them from retroperitoneal organs and tumors associated with the pancreas, kidneys, adrenal glands, etc, is crucial, as RPT excludes metastatic tumors.[2] RPT comprises both benign and malignant tumors, with 70% to 80% being malignant, accounting for ~0.1% to 0.2% of all cancers.[3] Among these, retroperitoneal sarcomas (RPS) emerge as the most prevalent subtype. With over 70 distinct histologic sarcoma types identified, liposarcoma and leiomyosarcoma overwhelmingly constitute the majority of RPS.[4] Clinical diagnosis of RPT is challenging due to its low incidence, deep-seated location, high adaptability, limited early symptoms, substantial size, and close association with neighboring organs. Successful surgical resection faces challenges due to diverse histologic subtypes and the frequent involvement of multiple adjacent organs, necessitating a multidisciplinary treatment approach. Effective treatment planning and increased surgical resection rates hinge on precise localization and identification of RPT. Before contemplating surgery, a reliable diagnosis is imperative, often requiring a percutaneous biopsy to provide a pathologic confirmation. This review comprehensively summarizes the diagnosis and management of RPT.

CLASSIFICATION OF RETROPERITONEAL TUMOR

Benign RPT encompasses a spectrum of tumors, including nerve sheath tumors, neurofibromas, ganglion neuromas, paragangliomas, fibromatosis, and lipomas.[5] Typically, these tumors are incidentally discovered during examinations conducted for unrelated symptoms. Sassa and colleagues classified 422 cases into benign or malignant categories based on age and tumor size, reporting the proportion of histologically proven benign tumors. Among these, teratomas (15%) and neurogenic tumors (30%) emerged as the 2 most prevalent benign RPT, predominantly affecting children. The prevalence of benign RPT is notably higher in younger individuals.[6,7]

Malignant RPT constitutes a mere 0.1% to 0.2% of all malignant tumors.[8] Soft tissue sarcomas (STS) account for 15% of pediatric cancers and 1% of all adult cancers, including those originating in the extremities.[9] In the United States and Europe, RPS contribute to 15% to 25% of all STS cases.[10] The predominant malignant subtype among RPT is RPS. Despite the identification of over 70 histologic types of sarcomas, liposarcomas and leiomyosarcomas overwhelmingly constitute the majority of RPS cases.[11] Specifically, liposarcoma, leiomyosarcoma, undifferentiated sarcoma, malignant peripheral nerve sheath tumor, solitary fibrous tumor, fibrosarcoma, angiosarcoma, and synovial sarcoma are the most prevalent

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RPS, with prevalence rates of 56.3%, 27.2%, 11.3%, 1.3%, 1.1%, 1.0%, 0.6%, 0.5%, and 0.5%, respectively.[12]

DIAGNOSIS OF RETROPERITONEAL TUMOR

Diagnostic Imaging

Before categorizing a tumor as predominantly RPS, it is imperative to exclude the possibility that it originated in a retroperitoneal organ. Radiologic markers, including the "rostral sign," "phantom (invisible) organ sign," "embedded organ sign," and "prominent feeding artery sign," offer valuable assistance in elucidating the tumor's origin.[13] Computed tomography (CT) and magnetic resonance imaging provide clear visualization of certain tumor contents, offering crucial clues to refine the differential diagnosis. These imaging modalities effectively differentiate tumors from adipose tissue.[14] Given the frequent association of RPS with nearby blood vessels, especially those with significant vascular origins, contrast-enhanced computed tomography angiography/venography plays a crucial role in elucidating the vascular connection and blood supply of tumors, aiding in surgical planning. Positron emission tomography–CT scans are also commonly employed for the diagnosis of RPT.[15] Utilizing positron emission tomography–CT for staging in patients meeting the criteria can enhance the understanding of lesion distribution and contribute to formulating appropriate treatment strategies, particularly for high-grade and highly metastatic potential tumors, such as leiomyosarcoma.

Needle Biopsy

Numerous benign or malignant tumors can manifest within the retroperitoneum. The most reliable diagnostic tool for establishing a histologic diagnosis is the image-guided percutaneous coaxial core needle biopsy.[16] Histologic diagnosis becomes imperative to differentiate benign RPTs from other malignancies, identify chemosensitive pathology, diagnose tumors requiring neoadjuvant therapy, and discern metastatic diseases presenting as retroperitoneal masses.[17] The transabdominal method should only be employed if a retroperitoneal biopsy is unfeasible, with a clear preference for the latter. The transabdominal technique should be a last resort, contingent on consultation with a specialized multidisciplinary team. To optimize the tissue available for pathologic examination, biopsies utilized an 18-gauge needle, a coaxial method, and a retroperitoneal route, preventing contamination of the abdominal cavity.[17] The risk of needle route seeding is minimal, and the core needle biopsy results remain unaffected by it.[18] Open or laparoscopic biopsies for RPS are not recommended, as they may alter retroperitoneal anatomy and introduce tumor contamination into the abdominal cavity, complicating subsequent reoperations.[19] In cases of tumor recurrence with diagnostic ambiguity from prior surgery, consideration should be given to another biopsy.

The recommendation for imaging-guided core needle aspiration biopsy in cases of RPS is particularly strong under the following circumstances: (1) challenging-to-resect RPTs identified through imaging assessment, (2) RPS presenting with metastases, (3) situations where a definitive diagnosis is pivotal for formulating an appropriate surgical plan, (4) cases necessitating preoperative neoadjuvant therapy, and (5) instances where differentiation between lymphoma, metastatic tumors, germ cell tumors, and other diagnoses is crucial.[20] However, patients lacking a preoperative treatment plan and those exhibiting preoperative imaging characteristics indicative of various degrees of liposarcoma differentiation may be deemed ineligible for biopsy.

Pathology Diagnosis

The challenges inherent in intraoperative freezing for pathologists are considerable, owing to the diverse pathologic subtypes within RPT. In general, the utility of intraoperative pathologic section freezing for diagnosis is limited, and it seldom alters the initially planned scope of resection. Exceptions arise only in specific circumstances, such as suspected germinal tumors, lymphopoietic system tumors, or when assessing the necessity for nerve excision. The initial pathologic diagnosis of RPT relies on histology for light-microscopy observation. After this, integration with the requisite tumor immunohistochemistry package for classification and diagnosis precedes the judicious use of molecular pathology techniques (fluorescence in situ hybridization, polymerase chain reaction, or next generation sequencing) to finalize the pathologic diagnosis. Recent years have witnessed substantial progress in employing molecular assays for detecting soft tissue tumors, a trend applicable to RPT as well. However, the standalone use of molecular testing is discouraged. Selection of any specific molecular test should follow a comprehensive diagnosis that considers relevant histology, immunohistochemistry, and a specific differential diagnosis. Given that well-differentiated and dedifferentiated liposarcomas are the predominant RPT subtypes, *MDM2* gene amplification is prevalent in the majority of patients. Particularly in cases with significant heterologous dedifferentiation (where the fat component is uncommon or entirely lost), fluorescence in situ hybridization detection of *MDM2* gene amplification or other molecular tests can aid in accurate diagnosis.[5,21] Consequently, *MDM2* gene testing is recommended for every patient with RPS.

Pathologic Staging of Retroperitoneal Sarcoma

Patients newly diagnosed with STS must undergo tumor staging, a pivotal step.[22] Given the substantial variability in prognosis and treatment approaches contingent on the stage, achieving precise and comprehensive staging is essential for formulating and implementing effective treatment strategies.

The staging of RPS employs the American Joint Committee on Cancer staging system, identical to that used for limb/trunk STS. The current classification utilizes the eighth edition of the staging system, revised in 2017, based on primary tumor (T), regional lymph nodes (N), metastases (M), and histologic grade (G) (Table 1). The Fédération Nationale des Centres de Lutte Contre le Cancer grade considers 3 parameters: (1) differentiation, (2) mitotic activity, and (3) extent of necrosis, each scored on a scale of 1 to 3 for differentiation and mitotic activity and 0 to 2 for necrosis. The American Joint Committee on Cancer's anatomic stage/prognostic group is outlined in Table 2.[23]

TREATMENT

Surgical Treatment

If conclusive tumor histology can be determined through puncture biopsy and/or imaging before surgery, benign RPT may not require treatment. However, surgical excision becomes necessary to differentiate between benign

TABLE 1 . The AJCC Staging System for RPS—Eighth Edition

Category	Description
Tx	Primary tumors cannot be assessed
T0	No evidence of a primary tumor
T1	Tumor ≤ 5 cm
T2	Tumor > 5 cm and ≤ 10 cm
T3	Tumor > 10 cm and ≤ 15 cm
T4	Tumor > 5 cm
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
M0	No distant metastasis
M1	Distant metastasis
Gx	Grade cannot be assessed
G1	Total differentiation, mitotic count, and necrosis score of 2 or 3
G2	Total differentiation, mitotic count, and necrosis score of 4 or 5
G3	Total differentiation, mitotic count, and necrosis score of 6, 7, or 8

AJCC indicates American Joint Committee on Cancer; RPS, retroperitoneal sarcoma.

and malignant tumors in patients experiencing symptoms like discomfort or a rapidly growing tumor size. According to the study's findings, 91.6% of R0/R1 tumors were successfully removed during surgery for benign RPT.[24]

Surgery remains the primary approach for RPS. Due to their larger size, anatomically challenging locations, which are difficult to access postsurgery, and wide margins constrained by nearby vital tissues, RPS prognosis is significantly worse than that of limb sarcomas. Complete resection, potentially involving the removal of nearby organs when necessary, enhances tumor prognosis. Most studies indicate that predominantly positive margins (R2) strongly correlate with poor clinical outcomes compared with macroscopic resection margin clearance (R0/R1), though the benefit of R0 over R1 in terms of tumor outcomes remains uncertain.[25,26] Complete resection reduces the risk of local recurrence and distant metastases while improving patient prognosis. Favorable tumor histology or biology, enhanced multimodality therapy, perioperative management, surgical technique, and patient biology collectively contribute to improved RPS prognosis.[27] The 5-year postoperative RPS survival rate increased from 47% in 1998 to 2005 to 58.4% in 2002 to 2012, whereas the 10-year postoperative RPS survival rate increased from 27% to 45.3%.[28,29]

TABLE 2 . AJCC Anatomic Stage/Prognostic Groups

	T	N	M	G
Stage IA	T1	N0	M0	G1, Gx
Stage IB	T2	N0	M0	G1, Gx
	T3	N0	M0	G1, Gx
	T4	N0	M0	G1, Gx
Stage II	T1	N0	M0	G2, G3
Stage IIIA	T2	N0	M0	G2, G3
Stage IIIB	T3	N0	M0	G2, G3
	T4	N0	M0	G2, G3
Stage IV	Any T	N1	M0	Any G
	Any T	Any N	M1	Any G

AJCC indicates American Joint Committee on Cancer.

Determining the extent of surgical resection, covering the entire tumor and any nearby implicated organs requires a carefully designed surgical plan based on imaging findings and intraoperative investigation.[30,31] The surgical strategy must consider the various pathologic types of the tumor. As leiomyosarcomas often exhibit distant metastases and liposarcomas frequently recurs locally, treatment approaches for these two conditions need to be tailored accordingly.[32] The likelihood of local recurrence in retroperitoneal liposarcoma is substantial, and local recurrence is a significant factor in disease-related mortality. Total retroperitoneal fat removal on the affected side may help lower the risk of tumor residual, as highly differentiated retroperitoneal liposarcoma closely resembles normal adipose tissue. Consequently, retroperitoneal liposarcoma resection should cover at least the asymmetrical area observed in imaging.[19] Organs close to the tumor that are not immediately adherent or invaded should be preserved as much as possible while ensuring negative margins in leiomyosarcoma with well-defined borders.

For leiomyosarcoma originating from large vessels, attention to microscopically negative venous incision margins is crucial. Isolated fibrous tumors pose minimal risk of local recurrence, typically requiring limited resection. In contrast, malignant peripheral nerve sheath tumors, frequently arising from the retroperitoneal plexus, pose significant challenges for R0 resection, carrying a dismal prognosis. A thorough evaluation of potential injury to adjacent vital vascular nerve structures is necessary before surgery. Due to the tumor's substantial size, often pressing against or invading nearby blood arteries and organs, surgery is challenging and frequently involves the simultaneous removal of other organs such as the kidney, adrenal gland, spleen, small intestine, or colon. Successfully removing RPTs demands a surgical team proficient in various specialties, spanning from the abdomen to the pelvis, and encompassing the handling of large blood vessels, complete thoracoabdominal wall resection and reconstruction, diaphragmatic resection and reconstruction, resection and reconstruction of large blood vessels, and bone reconstruction.

An experienced surgeon managing RPS must decide whether certain vital organs, such as the kidney, duodenum, head of the pancreas, and bladder, should be preserved during RPS surgery, meticulously analyzing the biological behavior of the tumor and the degree of its invasion. The potential perioperative problems and long-term functional impairment after resection need to be completely taken into account for which vascular and neuronal structures can be removed. A repeat radical resection should be considered if the initial surgery for RPS is a simple resection and the residual tumor is discovered on imaging within a short time after surgery. Close monitoring can also rule out any potential multifocal distribution. Reexcision should be used to describe the degree of surgical resection performed when the primary tumor was still present to fulfill the goal of radical resection. Patients may frequently have repeated postoperative recurrences, which is a prevalent pattern of therapy failure in RPS. Although there is some uncertainty regarding the efficacy of surgery for locally recurrent RPS,[33] there is evidence that surgery is beneficial for some patients, even after multiple recurrences.[34,35] In everyday practice, a multidisciplinary team of RPS specialists should review and weigh all available treatment options before deciding whether to conduct surgery for recurring diseases. Important prognostic markers that influence the patient's disease-free survival (DFS) and overall survival (OS)

after reoperation include the interval between recurrences, histologic subtype, and grade, and the availability of another complete tumor resection.[33,36] Reoperation can be delayed until the tumor grows rapidly or appears to have a dedifferentiated component on imaging, particularly if the residual tumor under the sarcoid is a highly differentiated liposarcoma.[37] If the tumor involves the superior mesenteric artery, abdominal aorta, celiac trunk, portal vein, bone, grows into the spinal canal, and invades numerous vital organs such as the liver, pancreas, and/or large vasculature, RPS is considered unresectable. Palliative resection of RPS, where most or part of the tumor is removed, generally offers no clinical benefit.[38] Patients with RPS who have distant metastases, such as the liver and lung, should be considered for surgical resection based on their clinical subtype, biological traits, whether the primary foci can be entirely removed, and the intended use of surgery. Resection of the main site may be an option if the tumor is less aggressive or the metastases can be managed surgically or through other techniques. The preferred course of treatment for oligometastases is typically surgical resection.

Radiation Therapy for Retroperitoneal Sarcoma

In contrast to individuals acquiring STS at other sites, patients with recurrent or metastatic RPS generally exhibit poorer survival outcomes and prognoses.[39] The disease-specific survival rates for RPS are 50% after 5 years and 35% after 10 years.[11] RPS tumors are typically situated proximal to vital organs or structures within the abdominal cavity, posing challenges for achieving radical surgery with extensive tumor removal. This predicament often leads to local recurrence and metastases in distant body regions, necessitating a combination of treatments, such as radiation therapy and chemotherapy.[40]

The efficacy of perioperative radiation has garnered increasing interest in recent years. A substantial case-control, propensity score-matched study involving 9068 patients comprised 563 individuals who underwent preoperative radiotherapy, 2215 who received postoperative radiotherapy, and 6290 who underwent only surgery. According to the study's findings, preoperative radiotherapy significantly increased OS compared with surgery alone (hazard ratio [HR]: 0.70, 95% CI: 0.59-0.82; $P < 0.0001$), as did postoperative radiotherapy (HR: 0.78, 95% CI: 0.71-0.85; $P < 0.0001$).[41] A meta-analysis yielded similar results, indicating that the combination of radiation and surgery significantly increased median OS ($P < 0.00001$) and 5-year OS ($P < 0.001$) compared with surgery alone. Both preoperative radiotherapy ($P < 0.001$) and postoperative radiotherapy ($P = 0.001$) significantly enhanced median recurrence-free survival compared with surgery alone.[42]

However, a phase 3 randomized study (EORTC62092) found that surgery combined with preoperative radiotherapy did not improve local control rates or demonstrate a survival advantage over surgery alone.[43] In an investigation into radiotherapy's impact on liposarcoma, a recent study compared the effect of radiotherapy on abdominal recurrence-free survival in patients with RPS treated in the EORTC-STBSG-62092 (STRASS) phase 3 randomized controlled trial (STRASS cohort) and nontrial (STREXIT cohort) through propensity matching. The study revealed that preoperative radiotherapy significantly increased abdominal recurrence-free survival in patients with grade 1 and grade 1 to 2 dedifferentiated liposarcoma but not in those with leiomyosarcoma or grade 3 liposarcoma.[44]

Chemotherapy for Retroperitoneal Sarcoma

In the treatment of STS, the established role of chemotherapy as a neoadjuvant or adjuvant therapy has not been clearly defined for RPS. The potential for further surgical interventions in RPS through tumor downstaging remains uncertain. Neoadjuvant chemotherapy combined with regional hyperthermia demonstrated a significant increase in progression-free survival (PFS) and OS compared with neoadjuvant chemotherapy alone, especially for RPS patients undergoing R0/R1 resection, particularly those with tumors ≥ 5 cm and Fédération Nationale des Centres de Lutte Contre le Cancer grades of G2 to G3 with a high risk of recurrence, as indicated by the EORTC 62961 study.[45] The ongoing STRASS2 phase 3 clinical trial is evaluating neoadjuvant chemotherapy, followed by surgery versus surgery alone in individuals with high-risk RPS, specifically those with high-risk leiomyosarcomas or liposarcomas, with DFS as the primary endpoint. This trial aims to provide further evidence of the benefits of neoadjuvant treatments in this patient population. Currently, there is insufficient evidence to support the use of adjuvant chemotherapy after complete resection in patients with RPS, emphasizing the importance of participation in ongoing clinical trials as they arise.

Palliative chemotherapy is administered to patients with metastases or recurrence of incompletely resectable tumors to shrink and stabilize the tumor, alleviate symptoms, prolong survival, and enhance quality of life. However, due to the heterogeneity of STS and the severe toxic side effects of chemotherapy, palliative chemotherapy regimens must be individualized based on the specific pathologic type. There is no universally approved chemotherapy regimen for the second-line treatment of STS, and selection depends on the pathologic subtype. For instance, gemcitabine in combination with dacarbazine, gemcitabine in combination with doxorubicin, or trabectedin for leiomyosarcoma, trabectedin or eribulin for liposarcoma, high-dose isocyclophosphamide for synovial sarcoma, gemcitabine in combination with doxorubicin for undifferentiated pleomorphic sarcoma, and paclitaxel for angiosarcoma.[46,47] Eribulin, approved by the Food and Drug Administration (FDA) for second-line liposarcoma chemotherapy, demonstrated an increase in median OS from 8.4 to 15.6 months compared with dacarbazine.[48] Trabectedin, licensed by the FDA for second-line chemotherapy in leiomyosarcoma and liposarcoma, improved median PFS from 1.5 to 4.2 months compared with dacarbazine ($P < 0.001$), but it showed no effect on OS compared with dacarbazine.[49]

Targeted Therapy for Retroperitoneal Sarcoma

Novel therapeutic modalities, specifically anti-tumor–targeted medications, have demonstrated considerable success in treating various tumor types. Compared with traditional chemotherapy, targeted medications exhibit fewer adverse effects and enhanced tolerability. Over recent years, several targeted therapy drugs have been employed in the treatment of advanced or incurable STS. Notably, certain targeted therapeutic agents exhibit promise in addressing specific histologic subtypes of advanced STS. Pepozopanib, anlotinib, and regorafenib have been identified as potential second-line treatments for unresectable or advanced STS, although their use is not recommended for liposarcoma.[50]

Pepozopanib, a small molecule tyrosine kinase inhibitor targeting receptors associated with angiogenesis and tumor cell proliferation, has received FDA approval as a second-line therapy for chemotherapy-refractory metastatic STS, excluding liposarcoma. Pegaptanib, in a randomized controlled study (phase 3 PALETTE), significantly extended median PFS compared with placebo in patients with metastatic STS who had failed standard chemotherapy and not received angiogenesis inhibitors (4.6 vs 1.6 mo, HR: 0.35, $P < 0.0001$). However, there was no significant difference in OS between the two groups (12.5 vs 11 mo, $P = 0.25$).[51]

Anlotinib hydrochloride, a multitargeted tyrosine kinase inhibitor with dual effects on tumor development and angiogenesis, demonstrated efficiency, a 12-week DFS rate, median PFS, and median OS in a phase 2 study for the second-line treatment of advanced STS.[52] Regorafenib, in a randomized phase 2 (REGOSARC) clinical trial with placebo control, showed improved PFS in doxorubicin-treated non-liposarcomas (4.0 vs 1.0 mo, $P < 0.0001$), with OS of 13.4 months and 9 months, respectively.[53]

A phase 1/2 clinical trial of larotrectinib in patients with inoperable or metastatic solid tumors who had failed standard therapy with *NTRK* fusion involved 55 patients ranging in age from 4 months to 76 years, 21 of whom were diagnosed with STS. The median time to remission and progression-free time had not been reached by the study cutoff time of the clinical trial, but the objective remission rate (ORR) for patients with *NTRK*-fused STS was 95%, and the duration of remission was prolonged, with 71% of patients maintaining remission after 1 year of the overall study (55 patients). The efficacy of larotrectinib in STS with *NTRK* fusion was significant and durable.[54]

In addition, specific targeted agents may be considered for the first or second-line treatment of particular unresectable or advanced sarcomas. Examples include *ALK* inhibitors for inflammatory myofibroblastoma with *ALK* gene fusions, *NTRK* inhibitors for sarcomas with *NTRK* gene fusions, EZH2 inhibitors for epithelioid sarcomas with *INI1* gene deletions, and *CDK4* inhibitors like palbociclib for highly differentiated/dedifferentiated liposarcomas with *CDK4* gene amplification.[55]

Immunotherapy for Retroperitoneal Sarcoma

Immunotherapy employing the immune checkpoint inhibitor programmed cell death protein 1/programmed death-ligand 1 antibody has demonstrated success across various tumors, particularly emphasizing its potential in STS. However, the current efficacy of immunotherapy is limited to specific sarcoma types, notably undifferentiated pleomorphic sarcoma and adenoid STS, while its effectiveness in others remains uncertain. A phase 2 multicenter, single-arm, open-label study (Sarcoma Alliance for Research through Collaboration-028) investigated the efficacy and safety of pembrolizumab for advanced STS, encompassing forty cases. The study included ten instances each of undifferentiated pleomorphic sarcoma, dedifferentiated liposarcoma, smooth muscle sarcoma, and synovial sarcoma. Notably, the undifferentiated pleomorphic sarcoma group exhibited a 40% ORR, with 4 effective cases, whereas, the dedifferentiated liposarcoma group demonstrated a 20% ORR with 2 effective cases.[56]

A 2017 single-center, phase 1 basket trial focusing on immunotherapy for advanced STS found that pembrolizumab was more effective in patients with adenoid STS, yielding 2 partial responses and 2 cases of stable disease out of 4.[57] Another single-center, single-arm, phase 2 study explored the efficacy of axitinib in combination with pembrolizumab for patients with progressive or metastatic STS who had previously failed at least one first-line therapy. The study, including 33 patients, observed an overall ORR of 26.7% and a PFS of 4.7 months in all evaluable patients. Subgroup analysis revealed a median PFS of 3.0 months in the nonadenoid STS group and an ORR of 54.5%, with a median PFS of 12.4 months in the adenoid STS group. The combination of axitinib with pembrolizumab exhibited more pronounced efficacy in adenoid STS.[58]

CONCLUSIONS

Surgery stands as the primary treatment modality for symptomatic benign RPT. In cases of malignant RPT and RPS, the combination of surgery, extensive resection involving multiple adjacent organs, and collaboration with a proficient medical team comprising radiologists, pathologists, and oncologists at a central hospital can significantly augment survival rates and mitigate the risk of local recurrence. Ongoing clinical trials are exploring avenues to further enhance treatment outcomes, encompassing radiotherapy, chemotherapy, targeted therapy, and immunotherapy. A comprehensive understanding of the biology of RPS, including its molecular underpinnings, necessitates in-depth exploration through fundamental and translational research, extending beyond the confines of clinical studies.

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