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Real-Life Results of a Cohort of Retroperitoneal Sarcomas (RPS): Management at Hassan II University Hospital in Fes

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Abstract

Retroperitoneal sarcomas (RPS) pose a challenge in treatment due to their rarity and complex nature. This retrospective study aimed to analyze the epidemiological, clinicopathological characteristics, and survival outcomes of RPS patients treated over an 11-year period. Seventeen patients diagnosed with RPS were included, with leiomyosarcoma being the most prevalent subtype. Surgical excision was the primary treatment modality, often complemented by radiotherapy and chemotherapy. The 5-year and 10-year overall survival rates were 56% and 46.9%, respectively, with a median progression-free survival of 10 months. Discussion highlights the importance of complete surgical resection and tumor grade as prognostic indicators. Local recurrence remains a significant concern despite advancements in treatment modalities. The role of radiotherapy in reducing local recurrence risk is acknowledged, particularly in the preoperative setting. For metastatic RPS, a multidisciplinary approach integrating surgery and systemic therapy is crucial. Patient selection for surgical interventions considers tumor biology, disease burden, and response to chemotherapy. Chemotherapy, primarily anthracycline-based, remains a cornerstone in managing unresectable or metastatic disease, with emerging agents showing promise in clinical trials. Overall, a tailored treatment approach emphasizing radical resection and adjuvant therapies offers the best chance for long-term survival in RPS patients.

Subject Areas

Oncology

Keywords

Retroperitoneal Sarcomas (RPS), Multidisciplinary Approach, Chemotherapy, Metastatic Disease

1. Introduction

Retroperitoneal soft tissue sarcomas (RSTS) comprise only about 15% of all soft tissue sarcomas (STS), but represent about 45% of all retroperitoneal tumors [1]. Given their rarity, establishing an optimal treatment strategy is challenging. Currently, radical surgery is the standard treatment with a significant impact on overall survival. Patients mostly succumb to either locoregional progression or distant metastasis. Radiotherapy substantially affects locoregional control, but its effect on survival is not clearly established. Chemotherapy remains the standard treatment for locally advanced and/or unresectable metastatic or recurrent forms.

2. Methods

2.1. Setting and Type of Study

This is a descriptive, monocentric retrospective study of 11 consecutive cases of retroperitoneal sarcoma managed at CHU Hassan II Fes, MOROCCO, over an 11-year period from June 2010 to June 2021. A thorough search of the PubMed and Google Scholar databases was carried out to find the bibliographic sources that will enable us to discuss the results found and write up this study.

2.2. Study Participants

Data were collected from the patient files of the medical oncology department, CHU HASSAN II FES, for all cases included during the study period. For each patient, we collected the following data: age at diagnosis, sex, location, anatomopathological and immunohistochemical characteristics, therapies received and evolutionary aspects of the disease. An evaluation form was used to collect data from each of the included files.

2.3. Inclusion Criteria

All patients over 18 years of age, followed for histologically confirmed Retroperitoneal Sarcomas, managed within the department during this period,

2.4. Exclusion Criteria

All patients admitted to the department for tumors other than retroperitoneal sarcomas, age less than 18 years, incomplete files, patients without histological evidence.

The primary endpoints were objective response, progression-free survival, and toxicity.

3. Results

Over an 11-year period spanning from June 2010 to June 2021, 17 patients treated for RPS were identified. The median age at diagnosis was 51 years (range, 22 - 80).

Leiomyosarcoma was the most common variant among 12 patients, followed by well-differentiated liposarcoma in 3 patients and Ewing's sarcoma in two patients (Figure 1).

Ten patients had a high grade, and 7 patients had an intermediate grade.

The median tumor size was 16 cm (range, 9 - 20 cm).

Treatment included surgery (14 patients), radiotherapy (9 patients), and chemotherapy (7 patients) (Figure 2).

Ten patients were initially metastatic, and seven patients had unresectable locally advanced tumors (Figure 3).

In monotherapy, the drugs used in our series were doxorubicin, ifosfamide, gemcitabine, and dacarbazine.

Polychemotherapy is based on the combination of drugs effective in monotherapy.

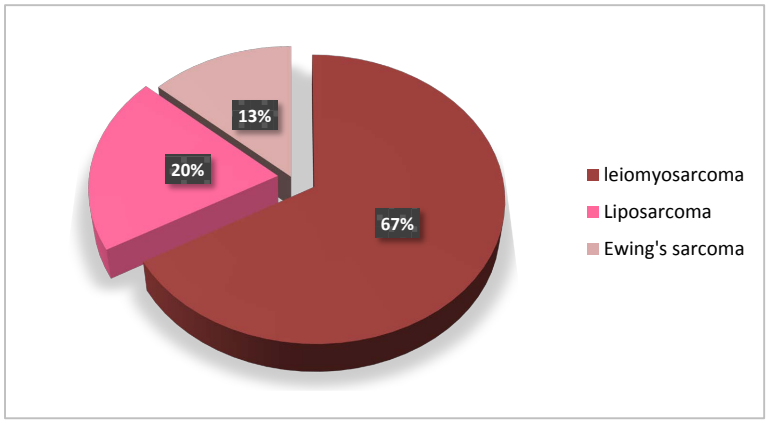

Figure 1. Population distribution by histological type.

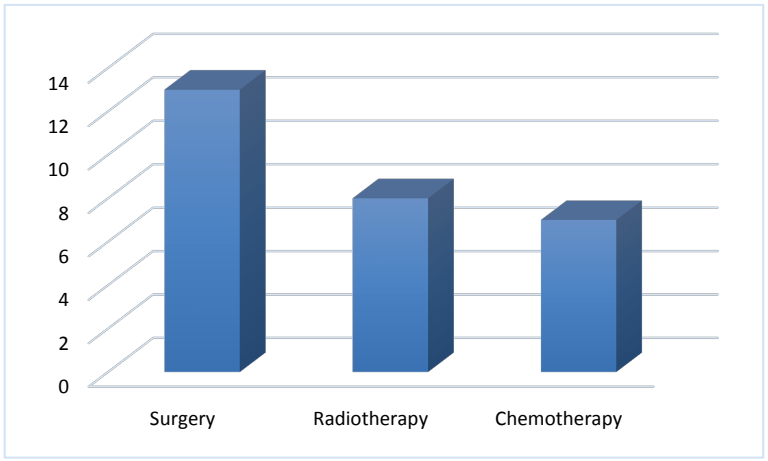

Figure 2. Population distribution by therapeutic management.

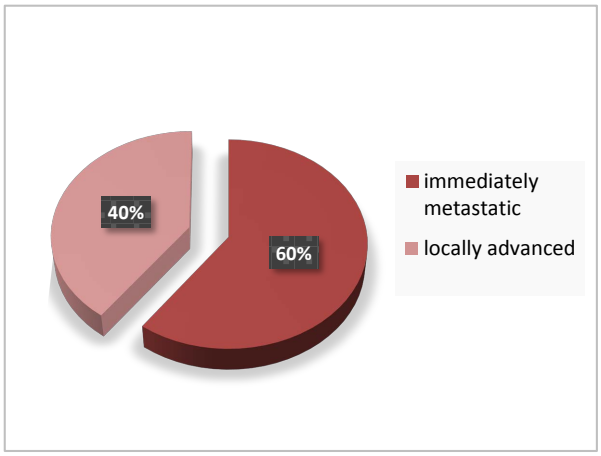

Figure 3. Population distribution by Tumor stage.

The 5-year overall survival rate was 56%, and the 10-year survival rate was 46.9%.

The median progression-free survival was 10 months.

4. Discussion

The majority of retroperitoneal tumors are malignant, with approximately 30% being sarcomas [2]. The slow increase in tumor size and the compliance of the retroperitoneal space explain the asymptomatic nature and large dimensions of these tumors. In our series, all tumors measured over 10 cm. The presence of an abdominal mass is the most frequently observed sign, present in 45% to 75% of patients [3].

CT scans and MRI are important in assessing the extent of retroperitoneal tumors to evaluate their relationships with intra-abdominal viscera, major vessels, and extension through anatomical passages, allowing for the selection of the most appropriate surgical approach. This imaging also allows for biopsies and preoperative histological diagnosis, thus avoiding unnecessary surgery in some cases (germ cell tumors, lymphoma).

Tumor excision, along with involved viscera en bloc without tumor rupture, is the standard treatment. The rate of complete resection varies in series from 38% to 74% [4] [5]. The quality of excision is consistently the determining prognostic factor in all multifactorial studies [6]. Thus, this surgery conditions survival and the risk of local or distant recurrence independently of tumor size and the extent of resection involving neighboring organs [7].

Grade constitutes the second independent prognostic factor found in the literature. It assesses the risk of local recurrence and metastatic dissemination [8] [9] [10]. Singer *et al.* showed that the risk of death was multiplied by eight in patients with high-grade retroperitoneal sarcoma compared to those with low-grade sarcoma. In a retrospective study of 40 patients treated for retroperitoneal sarcoma in four Languedoc centers, high grade (grades 2 and 3), involvement of section edges, and bilaterality were independent prognostic factors for local re-

currence [11].

The major risk of retroperitoneal sarcomas is local recurrence, and patients most often die from this local progression. The rate of local or peritoneal recurrences varies from 44% to 85%. The treatment of recurrences involves iterative surgery after radiological exploration, with the possibility of achieving macroscopically complete resection [12].

The contribution of radiotherapy is not yet clear. Postoperative radiotherapy reduces the risk of local recurrence and death [13] [14]. A study conducted by the FNCLCC on 145 patients treated for retroperitoneal sarcoma showed a threefold reduction in the risk of local recurrence in patients who received radiotherapy after complete surgery. The major drawback remains digestive toxicity, which can be prevented by displacing the digestive tract either by epiploplasty or by the placement of a prosthesis [15]. Currently, radiotherapy is preferred in the preoperative setting.

In patients with RPS metastatic disease, a tailored treatment should be designed in a multidisciplinary setting. Surgical and systemic treatment options should consider the histopathological subtype and its behaviour, as well as the patient's symptoms and status. In general, the complete radicalisation of the disease with resection surgery is the treatment that leads to the best long-term survival outcome. In patients with metastases, the primary surgery can be performed in selected cases to reduce the local disease burden or practice a complete local radicalisation, reduce symptoms, and facilitate any resection surgery on possible recurrences.

Surgery on liver or lung metastases can be considered with the sense of completely radicalising the disease in selected patients with good performance status and a high life expectancy. Patient selection based on favourable tumour biology should consider the low-volume disease, DFS time greater than 12 months, and response or prolonged stability to systemic chemotherapy [16]. Local therapies, such as radiofrequency or microwave ablations, can be important in the resection strategy and control of the disease, variously combined with surgery [17] [18].

Metachronous lung metastases (DFS ≥ 1 year) can be resected if radicalisation of the disease can be achieved [19]. Synchronous lung metastases should be treated with chemotherapy, reserving surgery for resectable residual lung lesions [20]. Extrapulmonary disease is not a contraindication to curative multiorgan resection, as long the radicalisation can be achieved, and the patient's status is adequate. Extrapulmonary metastases can be treated with chemotherapy first, and surgery should be offered for responding metastases in selected patients.

In large-volume liver metastatic disease, arterial embolisation or chemoembolisation can be considered [21] [22].

Intra-abdominal multifocal metastases can be treated with surgical resections, which may confer symptoms control, but incomplete resections do not have any benefit on survival. The recurrent metastatic disease should be approached with surgery only if the biology of the tumour is favourable: low-grade histology,

low-volume disease (in number and size) and high DFS time [23] [24]. RT could be an option for palliation of pain or symptoms of spinal compression.

Chemotherapy is usually the first approach in synchronous metastatic disease or non-resectable disease, especially if poor prognostic factors are present (high grade and high number of lesions). Administration of chemotherapy before surgery helps assess the response and modulate the treatment: regression or stable disease over 6 months may be a good factor for considering surgery [25]. In unresectable metastatic disease, systemic therapy should aim at retarding the growth of the mass, prolonging life expectancy as much as possible and ensuring a decent quality of life.

Anthracycline-based chemotherapy (doxorubicin or epirubicin) is the first-line treatment and the association with ifosfamide or dacarbazine can be considered [26] [27] [28] [29]. A combined therapy with dacarbazine is preferred for LMS and SFT [30] [31]. Recently the phase 3 ANNOUNCE trial showed there was no difference in OS with the addition of olaratumab to doxorubicin. More agents can be considered as a second-line treatment, or in case anthracyclines are contraindicated [32].

5. Conclusion

Our study has certain limitations: the various histological types and the limited number of treated patients, nonetheless, the quality of initial management directly impacts recurrence-free survival and overall survival.

Conflicts of Interest

The authors declare no conflicts of interest.

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