Journal of BUON **17:** 138-142, 2012

ORIGINAL ARTICLE

Management of retroperitoneal sarcomas: main prognostic factors for local recurrence and survival

T. Theodosopoulos[1], V. Psychogiou[1], A.I. Yiallourou[1], G. Polymeneas[1], A. Kondi-Pafiti[2], I. Papaconstantinou[1], D. Voros[1]

[1]2nd Department of Surgery and [2]Department of Pathology, Aretaieion Hospital, University of Athens, Athens, Greece

Summary

Purpose: *Retroperitoneal sarcomas (RPs) are characterized by slow indolent growth and metastasize at a late point in their natural course. The purpose of this study was to review our experience in the management of RSs and identify prognostic factors for local control and survival.*

Methods: *Between January 1990 and December 2010, the hospital records of 75 patients with RSs were retrospectively studied. Sixty-four (85.3%) patients had undergone surgical resection in our hospital for primary RS, whereas 11 (14.7%) were referred to our department for recurrent disease.*

Results: *The patient median age was 57 years. Median tumor size was 18.5 cm. The most common histologic type was liposarcoma (44%) followed by leiomyosarcoma (17%), paraganglioma (10%), malignant fibrous histiocytoma (6.5%) and rare tumors such as 2 chondrosarcomas and 1 pecoma. Complete initial resection with negative macroscopic margins (R0) was achieved in 39 (60.9%) patients. En bloc resection of adjacent organs was required in 8 (12.5%) patients with primary RS and in 8 (72.9%) with recurrent disease. Mortality rate was 4%. For the group of patients initially treated in our hospital, 1-year recurrence rate was 34.3%. The 3- and 5-year overall survival rates were 56.2% and 53.1%, respectively. Satellite tumors were recognised in 13 (20.3%) patients treated for primary RS, from whom 11 (84%) recurred within one year. Seven patients received adjuvant chemotherapy.*

Conclusion: *Radical surgical resection is the treatment of choice for patients with primary and locally recurrent RSs.*

Key words: liposarcoma, mesenchymal tissue, retroperitoneum, sarcoma, satellite tumors, soft tissue

Introduction

Sarcomas are uncommon malignant tumors arising from mesenchymal stem cells residing in muscle, fat and connective tissues. Retroperitoneum is the less common site of origin accounting for approximately 10% of soft tissue sarcomas and less than 1% of all malignant neoplasms [1,2]. The most commonly encountered histologic subtypes are liposarcoma, leiomyosarcoma, and malignant fibrous histiocytoma [3-6].

Due to the fact that retroperitoneum is a large space, RSs are often diagnosed when they are large in diameter. When symptoms are present, they relate either to the mass effect of the tumor or to local invasion. *En bloc* surgical resection is the treatment of choice with removal of adjacent organs in order to obtain normal macroscopic and microscopic surrounding tissue [7,8]. The reported complete resection rate varies between 65-99% [4,5]. In some cases, satellite tumors have been identified in the surrounding sarcoma's fat, which may be quite far from the initial tumor and these may be responsible for local recurrence [9]. However, complete resection may be difficult to achieve, due to involvement of surrounding vital structures. The completeness of surgical resection is an important prognostic variable as it has been shown to reduce local recurrence rate and improve overall survival [7,10,11].

The role of adjuvant radiation therapy for RSs is less clear than for extremity sarcomas. One randomized trial using intraoperative radiation has shown an improvement in local control of RSs [12]. In addition, several retrospective and prospective studies suggest

Correspondence to: Anneza I. Yiallourou, MD. 76, Vassilissis Sofias Ave, 115 28, Athens, Greece. Tel: +30 6977678737, Fax: +30 210 7286128, E-mail: annyiallo@yahoo.gr

Received 21-06-2011; Accepted 26-07-2011

improved local control with the use of adjuvant radiation therapy for RSs [13-18].

The purpose of the current study was to review our experience in the management of retroperitoneal soft tissue sarcomas and identify prognostic factors for local disease control and overall survival.

Methods

Between January 1990 and December 2010, 75 patients with a diagnosis of RS were treated in our department. Eleven patients (14.7%) had undergone a previous surgical resection at another institution and were referred for recurrent disease. The medical records, including clinical notes, radiographic, operative data, as well as pathology reports were reviewed. Patient demographics included gender, age, and duration of symptoms. Tumors were characterized based on histopathologic type, size in greatest diameter and grade. Surgical resection was identified as either complete (R0: no microscopic residual disease and tumor more than 0.1 mm from margin) or incomplete (R1: macroscopically complete resection but with microscopic residual disease). The use of radiation therapy and chemotherapy was also assessed.

Results

Patient and tumor characteristics

Table 1 summarizes the demographic characteristics of 75 patients with primary and recurrent RSs included in this study. Sixty-four (83.7%) had primary tumors and were admitted to our hospital and 11 (14.7%) were referred for locally recurrent disease. The reason for this was incomplete resection at the initial operation. There was no sex predominance and the median age was 57 years (range 6-79). Twenty-five (33%) patients reported symptoms of < 6 months duration and 37 (50%) had symptoms for a longer period of time. Thirteen (17%) patients did not mention symptoms (Table 1). Presenting symptoms included pain, mass, abdominal distention, and constitutional symptoms. Liposarcoma was the most common histological type (44%), followed by leiomyosarcoma (17%), paraganglioma (10.5%), malignant fibrous histiocytoma (6.5%) and some rare tumors such as 2 chondrosarcomas and 1 pecoma. Median tumor size was 18 cm (range 6-55) with 60% of them being > 10 cm. Forty-four (58%) of the sarcomas were high grade and 31 (42%) low grade (Table 1).

Table 1. Patient characteristics, tumor characteristics and operative data of 75 patients

Characteristics	*N*	*%*
Gender		
Female	35	46
Male	40	54
Age (years)		
<57	19	25
>57	56	75
Duration of symptoms (months)		
<6	25	33
>6	37	50
Unknown	13	17
Histological subtype		
Liposarcoma	33	44
Leiomyosarcoma	12	17
Paraganglioma	7	10.5
Malignant fibrous histiocytoma	4	6.5
Other	19	29
Tumor size (cm, maximum diameter)		
<5	8	10
5-10	22	30
>10	45	60
Tumor grade		
Low	31	42
High	44	58
Resection		
R0	39/64	60.9
R1	25/64	39.9
Contiguous organs resected		
Kidney	16	21.33
Colon	10	13.33
Small bowel	7	9.33
Spleen	4	5.33
Ovary	4	5.33
Testis	1	1.33
Gallbladder	2	2.66
Uterus	3	4
Distal pancreas	2	2.66
Adrenal	2	2.66
Chemotherapy		
Adjuvant	7	9

Operative data

All patients underwent transabdominal retroperitoneal exploration. The majority (n=63) was through midline incision; 2 were thoraco-abdominal incisions, 8 midline incisions with transverse extension and 6 abdominoinguinal incisions. At the time of resection, 39/64 (60.9%) patients had complete resection with negative macroscopic margins (R0; Table 1). From the patients initially treated at our institution 8/64 (12.5%) had one or more organs removed to achieve a complete resection at the first operation (Figure 1), whereas for those referred for recurrent disease, simultaneous adjacent organ resection was necessary in 8/11 (72.9%) of them. The *en bloc* excised adjacent organs are shown in Table 1. In one pelvic schwannoma, difficult to resect at the first operation, ischemic embolization was performed and the tumor was completely removed after 1 week (Figure 2). A filter in the inferior vena cava (IVC) was inserted preoperatively

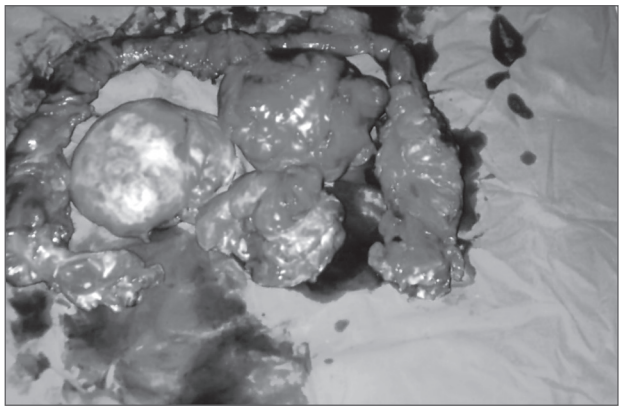

Figure 1. *En bloc* excision of a primary retroperitoneal sarcoma with subtotal colectomy; the right colon was invaded by the tumor and the left colon was connected to the mass due to dense adhesions.

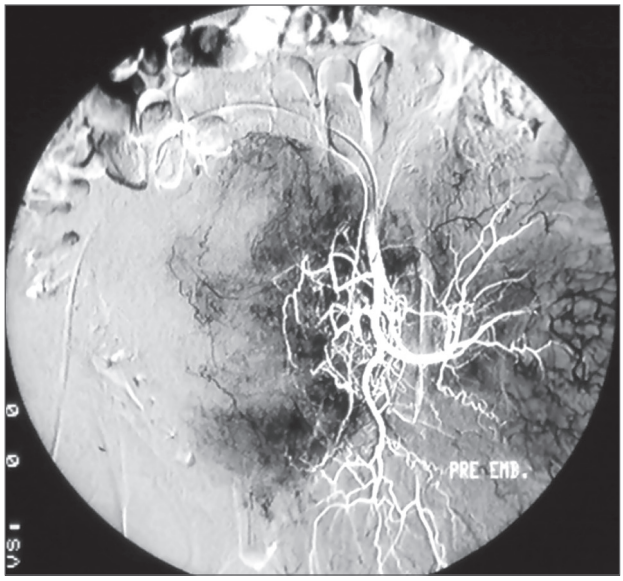

Figure 2. Pre-embolism angiography of a retroperitoneal sarcoma depicting the tumor's vascularity. A complete embolization of the tumor was performed which resulted in decrease of its size.

to minimize the possibility of pulmonary embolism as the patient already presented with deep vein thrombosis (Figure 3). In 13/64 (20.3%) patients, satellite tumors were revealed at the pathology report, not always recognised preoperatively, of which 11 (84%) recurred in one year (Figure 4). Seven patients received adjuvant chemotherapy. Median follow up was 60 months (range 24-80).

Survival

Mortality rate was 4% (3/75). One patient died due to myocardial infraction, the second one due to multiorgan failure secondary to sepsis (with proven intestinal anastomotic leakage) and the third one due to uncontrolled hemorrhage during the operation.

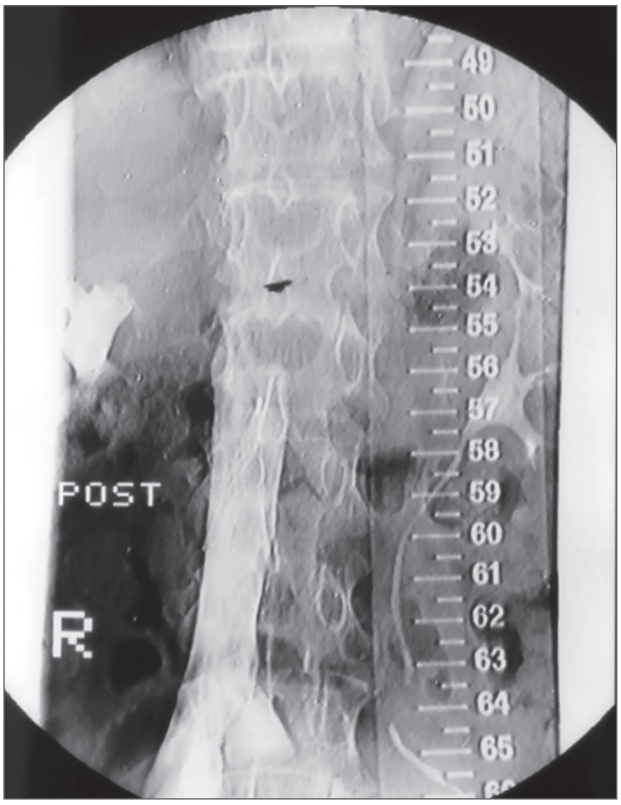

Figure 3. Preoperative inferior vena cava filter placement for pulmonary embolism prevention.

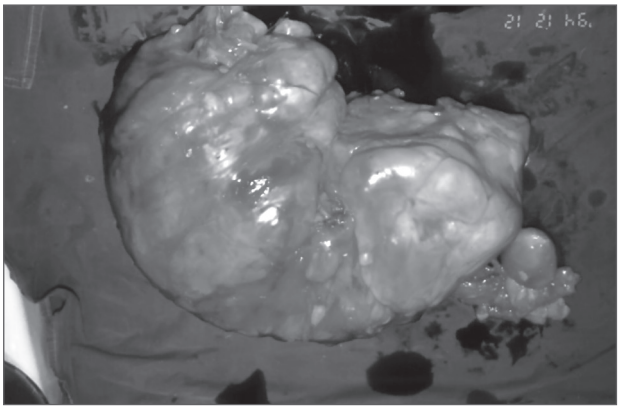

Figure 4. Satellite tumors in the surrounding fat of the primary retroperitoneal sarcoma.

For the group of patients initially treated in our hospital, 1-year recurrence rate was 34.3%. The 3- and 5-year overall survival rates were 56.2% (36/64) and 53.1% (34/64).

Discussion

RSs constitute a rare clinical entity, comprising approximately 12-15% of all soft tissue sarcomas. Al-

though most extravisceral large masses in the retroperitoneum represent a RS, a differential diagnosis including lymphomas, germ cell tumors, desmoids, adrenal, renal and pancreatic tumors and gastrointestinal tumors, should be considered. At diagnosis, RSs are probably the largest tumors found in the human body. They arise from the connective tissues posterior to the posterior peritoneum. Patients typically present with chronic non specific symptoms related to tumor compression rather than infiltration, including abdominal distension and pressure, early satiety and anorexia, changes in bowel or bladder habits and peripheral edema.

Interestingly, they rarely metastasise, as they are characterized by slow, indolent growth and achieve metastatic potential at a late point in their natural course. Only 11-12% of patients with primary RSs are found with metastasis at initial presentation. In general, hematogeneous spread is the primary route of metastasis for RSs. However, when metastasis does occur, the most common sites are the liver and lungs. This metastatic rate is unexpectedly low considering the high proportion of patients who present with very large tumors and who do not achieve local control.

The most common histologic subtypes found in the literature are liposarcomas, leiomyosarcomas, and malignant fibrous histiocytoma [3-6], which are consistent with the previously mentioned results of the present study. The majority of RPs are characterised as low grade and this could explain the lower incidence or delayed appearance of metastases and their better prognosis compared with high grade RPs. Tumor size has not been shown to influence survival, local failure or distant failure rates. This reflects the fact that RPs are always large in diameter, most being > 10 cm (60% in our series).

The only treatment factor that consistently predicts improved survival is a macroscopically complete tumor resection at the first operation. Complete resection rates reported are < 70%, with survival rates at 5 and 10 years approximately 60 and 25%, respectively. Aggressive surgical approach that includes resection of involved viscera and other structures, improves complete resection rates to 80-95% in some series. Karakousis et al. report a complete gross resection rate of 96% and associated 5 and 10 years survival rates of 63 and 46%, respectively [17] whereas Gholami et al. reported an initial complete resection rate of 93% [2]. To attain a complete resection, contiguous organs were removed in 68% of the patients, resulting in an estimated 5-year overall survival (OS) of 46%. However, complete surgical resection is often technically challenging and limited by invasion of adjacent nerves, blood vessels, and organs. Rates of resection of visceral organs at the time of resection of RPs reported to date vary significantly from approximately 34 to 75% [19]. Because disease control outcomes depend significantly on the adequacy of resection, this approach has also been extended to the setting of vascular involvement [16]. In our series of the 64 patients with primary RSs, an initial complete resection rate of 60.9% was achieved. To attain a complete resection, contiguous organs were removed in 12.5% of the patients, resulting in an estimated 5-year OS of 53.1%. This is comparable to a report in which the 5-year overall survival for high-grade sarcomas was 50% following complete resection [7], and also to other reported series with results ranging from 35-63% [12,13,18,20] in which complete surgical resection was associated with improved survival. Of the 11 patients referred with recurrent disease because of incomplete initial resection, contiguous organs were removed in 72.9% to achieve R0 resection. The resectability dramatically decreases with each reoperation, from 80% for primary tumors, to 57% in first recurrence, 33% in the second and 14% in the third.

In 13/64 patients (20.3%) satellite tumors were recognised at the pathology report, not always known preoperatively, from which 11 (84%) recurred in one year. Some of these were seen in the preoperative CT scan. These satellite tumors are small sarcomatous tumors in the fat surrounding the main tumor, that could be even some centimetres away from it, and which, if they remain, could trigger local recurrence; this calls for meticulous search for them either preoperatively or intraoperatively [9].

The use of adjuvant therapy to reduce the probability of recurrence and distant metastases has long been a matter of dispute. Some studies have suggested that adjuvant radiation therapy may decrease the likelihood of local recurrence [7,13,14]. Newer radiation techniques including intensity modulated radiation therapy, respiratory guided therapy, image guided radiation therapy, proton or heavy ion radiation therapy, and stereotactic radiation therapy should permit a higher dose of radiation to be given with less toxicity to normal tissues. The benefits of chemotherapy in RSs are even less clear. In our series, chemotherapy was beneficial in only a small number (n=7) of patients. Although randomized trials suggest benefit from adjuvant chemotherapy for extremity sarcomas, no trial shows a clear improvement in outcome for RSs [18,19].

The evaluation and treatment of soft tissue RSs remains a challenging problem that requires multidisciplinary approach. Complete surgical resection, especially when dealing with primary tumors, is the most important predicting factor. Satellite tumors affect prognosis, therefore their careful identification during the preoperative imaging workup as well as the intraoperative surrounding tumor's fat exploration is crucial.

References

1. Jernal A, Siegel R, Ward E et al. Cancer statistics, 2007. CA Cancer J Clin 2007; 57: 43-66.
2. Gholami S, Jacobs CD, Kapp DS, Parast LM, Norton JA. The value of surgery for retroperitoneal sarcoma. Sarcoma 2009; [1]: 1-6.
3. Lewis JJ, Brennan MF. Soft tissue sarcomas. Curr Probl Surg 1996; 33: 817-872.
4. Ballo MT, Zagars GK, Pollock RE et al. Retroperitoneal soft tissue sarcoma: an analysis of radiation and surgical treatment. Int J Radiat Oncol Biol Phys 2007; 67: 158-163.
5. Ferrario T, Karakousis CP. Retroperitoneal sarcomas: grade and survival. Arch Surg 2003; 138: 248-251.
6. Lewis JJ, Leung D, Woodruff JM, Brennan MF. Retroperitoneal soft-tissue sarcoma: analysis of 500 patients treated and followed at a single institution. Ann Surg 1998; 22: 355-365.
7. Pawlik TM, Pisters PW, Mikula L et al. Long-term results of two prospective trials of preoperative external beam radiotherapy for localized intermediate- or high-grade retroperitoneal soft tissue sarcoma. Ann Surg Oncol 2006; 13: 508-517.
8. Bonvalot S, Rivoire M, Castaing M et al. Primary retroperitoneal sarcomas: a multivariate analysis of surgical factors associated with local control. J Clin Oncol 2009; 27: 31-37.
9. Voros D, Theodorou D, Ventouri K, Prachalias A, Danias N, Gouliamos A. Retroperitoneal tumors: Do the satellite tumors mean something? J Surg Oncol 1998; 68: 30-33.
10. van Dalen T, Plooij JM, van Coevorden F et al. Long-term prognosis of primary retroperitoneal soft tissue sarcoma. Eur J Surg Oncol 2007; 33: 234-238.
11. van Dalen T, Hennipman A, van Coevorden F et al. Evaluation of a clinically applicable post-surgical classification system for primary retroperitoneal soft-tissue sarcoma. Ann Surg Oncol 2004; 11: 483-490.
12. Sindelar WF, Kinsella TJ, Chen PW et al. Intraoperative radiotherapy in retroperitoneal sarcomas: final results of a prospective, randomized, clinical trial. Arch Surg 1993; 128: 402-410.
13. Catton CN, O'Sullivan B, Kotwall C, Cummings B, Hao Y, Fornasier V. Outcome and prognosis in retroperitoneal soft tissue sarcoma. Int J Radiat Oncol Biol Phys 1994; 29: 1005-1010.
14. Hueman TM, Heraman MJ, Ahuja N. Management of retroperitoneal sarcomas. Surg Clin N Am 2008; 88: 583-597.
15. Heslin MJ, Lewis JJ, Nadler E et al. Prognostic factors associated with long-term survival for retroperitoneal sarcoma: implications for management. J Clin Oncol 1997; 15: 2832-2839.
16. Mendenhall WM, Zlotecki RA, Hochwald SN, Hemming AW, Grobmyer SR, Cance WG. Retroperitoneal soft tissue sarcoma. Cancer 2005; 104: 669-675.
17. Karakousis CP, Gerstenbluth R, Kontzoglou K, Driscoll DL. Retroperitoneal sarcomas and their management. Arch Surg 1995; 130: 1104-1109.
18. Frustaci S, De Paoli A, Bidoli E et al. Ifosfamide in the adjuvant therapy of soft tissue sarcomas. Oncol 2003; 65(Suppl 2): 80-84.
19. Sogaard AS, Laurberg JM, Sorensen et al. Intraabdominal and retroperitoneal soft-tissue sarcomas-outcome of surgical treatment in primary and recurrent tumors. World J Surg Oncol 2010; 8: 81-85.
20. Petrioli R, Coratti A, Correale P et al. Adjuvant epirubicin with or without ifosfamide for adult soft-tissue sarcoma. Am J Clin Oncol 2002; 25: 468-473.