

Management of Retroperitoneal Soft Tissue Sarcomas

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ABSTRACT:

BACKGROUND:

Most retroperitoneal tumors are malignant and about one third are soft tissue sarcomas. Sarcomas are uncommon malignant tumors arising from mesenchymal tissue. Retroperitoneal sarcomas account for approximately 10%-15% of soft tissue sarcomas and less than 1% of all malignant neoplasms. Surgery is the only curative treatment for retroperitoneal soft tissue sarcomas.

OBJECTIVE:

To define the best extent of surgery that would optimize the safe margins on retroperitoneal soft tissue sarcomas, where the recurrence of tumor greatly depends on feasibility of complete resection and the grade of tumor.

PATIENTS AND METHODS:

Between June 2007 and December 2010, 28 patients (female 16, male 12, mean age; 43.93 years, range 18-69 years) were evaluated for survival and response to therapy by gender, age, preoperative symptoms, symptoms duration, primary or recurrent tumors, the extent of surgical resection, or palliative procedures. Complete resection was defined as removal of gross tumor with histologically confirmed clean resection margins.

RESULTS:

Eighteen patients (64%) out of 28 patients underwent simple surgical resection, 5 patients (28%) underwent compartmental resection (systematic resection of noninvolved contiguous organs), 1 patient (3%) underwent enucleation of tumor, while debulking was done in 4 patients (15%). The surgical resection margin was involved only in one patient (due to tumor rupture during resection) of those patients who underwent compartmental resections, it was free in only 10/18 (56%) patients who underwent simple resection, while it was involved in all tumors removed with enucleation or debulking (incomplete resection).

The recurrence of tumor greatly depends on the state of surgical margin in the resected sample (p-value=0.001, significantly associated).

The histopathological grade of tumor on the other hand also proved an important factor in the recurrence of tumor where it was higher with high grade tumor versus low grade tumor (P-value=0.001, significantly associated).

CONCLUSION:

Complete compartmental surgery without tumor rupture should be performed when possible to achieve clear margins. Wide resection lowers the local recurrence and improves survival rate. Both the state of surgical margin and grade of tumor are the most important prognostic factors which determine the survival rate and recurrence of tumor.

KEYWORDS: retroperitoneal soft tissue sarcoma, compartmental resection.

INTRODUCTION:

Retroperitoneum is defined as the space between the posterior envelope of peritoneum and the posterior body wall. The retroperitoneal space is bounded superiorly by the diaphragm, posteriorly by the spinal column and iliopsoas muscles, and inferiorly by the

levator ani muscles^(1,2). The retroperitoneum contains a number of vascular and visceral structures in the form of gastrointestinal, genitourinary, musculoskeletal, nervous and lymphatic tissues. The multiplicity of structures within the retroperitoneum give rise to a variety of pathological conditions.

Most retroperitoneal tumors are malignant and about one third are soft tissue sarcomas. Sarcomas are uncommon malignant tumors arising from mesenchymal tissue.

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Retroperitoneal sarcomas account for approximately 10%-15% of soft tissue sarcomas and less than 1% of all malignant neoplasms.^(2,3)

The common histological types are liposarcoma, leiomyosarcoma, and malignant fibrous histiocytoma.

Most patients who have retroperitoneal sarcomas present with abdominal mass. Although neurological symptoms, pain, early satiety, and obstructive gastrointestinal symptoms or urological symptoms are also seen as presenting symptoms in some patients. Because of the typically silent nature of these tumors (until they are large enough to present as abdominal mass) most retroperitoneal sarcomas are large and advance when diagnosed⁽⁴⁾.

Recently it was shown that 77% of retroperitoneal sarcomas related death were caused by local recurrence without concomitant metastasis, local control is therefore essential in the treatment of patients with retroperitoneal sarcoma^(5,6).

Surgery is the mainstay of treatment, en bloc surgical resection is the treatment of choice.

This has been described recently as compartmental resection in which there is a systematic removal of adjacent organs to obtain a rim of normal tissue surrounding the tumor. Compartmental resection has been reported to have three fold lower rate of sarcoma recurrence in a recent study⁽⁷⁾.

Several reports have identified histological grade and completeness of macroscopical resection, which proved to be free margin microscopically as the major prognosticators for survival⁽⁸⁾.

PATIENTS AND METHODS:

This is a prospective study of 28 patients with a primary retroperitoneal soft tissue sarcomas carried out at Baghdad teaching hospital and at Al-Kufa teaching hospital between June 2007 and December 2010.

Patients presented to us and treated during this time period for a retroperitoneal lymphoma, tumors of retroperitoneal parts of gastrointestinal tract, tumors of genitourinary tract or tumors of adrenal glands were excluded

from analysis. Patients were analyzed for survival and response to therapy by gender, age, preoperative symptoms, symptoms duration, primary or recurrent, the extent of surgical resection, or palliative procedures.

The histopathological analysis were made for characteristics of biopsy and this included the histopathological type, tumor grade, principle tumor origin, infiltration of adjacent organs and state of surgical margin with great concern given to effects of histopathological type, state of surgical margin and the tumor grade on recurrence of tumor and hence survival rate. Resection of tumor was regarded as complete only if all grossly visible tumor was removed with conformation of histopathologically clear margin.

Patients who underwent resection with grossly clear surgical margin would considered to be incomplete resection if the histopathological margin were to be involved.

This of course did not include unresectable tumor with just debulking surgery.

Role of adjuvant therapy whether radiotherapy, chemotherapy or combined in the treatment of retroperitoneal soft tissue sarcomas and their effects, and hence the response of these sarcomas to such modality of treatment will also be encountered.

These data were collected and analyzed and the results will shown in form of figures and tables with statistical analysis for importance factors (P-value).

our median follow up was twenty two months (rang from six to thirty six months) with patient conserved till death or their last follow up appointment, follow up performed by clinical consultation every three month and thoracoabdominal CT scan performed each six month or sooner if a new clinical sign or symptom appeared.

RESULTS:

In this study a 28 patients with primary retroperitoneal tumors were (16/28, 57.1%) female and (12/28, 42.9%) male.

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Table 1: Age distribution in 28 patients with retroperitoneal sarcomas.

Age (years)	Tumor No .	%
10-19	1	3.6
20 – 29	4	14.2
30 – 39	6	21.4
40 – 49	5	17.9
50 – 59	7	25
60 -69	5	17.9
Total	28	100

The mean age of patients were 43.93(+/-SD) the (50 -59) years age group in which we have with minimum age 18 years and maximum age (7/28 ,25%) patients . 69 years. The majority of patients were found in

Table 2: Duration of symptoms in 28 patients with retroperitoneal sarcomas.

Duration of symptoms	Frequency	%
More than 6 months	17	60.7
Equal or less than 6 months	11	39.3
Total	28	100

Eleven (39.3%) patients reported symptoms of less than 6 months duration and (17/28 ,60.7%) had symptoms for longer period of time.

Table 3 :Clinical presentations in 28 patients with retroperitoneal sarcomas.

Clinical symptoms	No.	%
Abdominal mass	16	57
Gastrointestinal obstructive symptoms	6	21
Abdominal pain	6	21
Urinary obstructive symptoms	3	10.7
Vascular compression symptoms	2	7
Neurological pressure symptoms	1	3.5

The majority of patients (16/28,57%) presented with abdominal mass .

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Table 4 : Diagnostic modalities in 28 patients with retroperitoneal sarcomas .

Diagnostic method and its results	No	%
Plain abdominal X-Ray		
Soft tissue shadow	8	28.5
Calcification	2	7
Abdominal U\S examination		
Solid lesions	22	78.5
Solid- cystic lesions (necrotic areas)	6	21.5
Hydronephrosis (unilateral)	5	18
Hydronephrosis (bilateral)	2	7
CTscan\MRI		
Solid lesions	20	71.5
Solid- cystic lesions(necrotic areas)	8	28.5
GIT compression	9	32
Hydronephrosis (unilateral)	5	18
Hydronephrosis (bilateral)	2	7
Inferior vena cava compression	4	14

Fine needle aspiration under image guidance used in 2 patients was attempted to obtain tissue diagnosis prior to surgery but unfortunately was inconclusive.

In the treatment of our patients ,all of them were submitted for surgical resection with

compartmental enbloc resection done in(5/28 ,18%), simple resection of tumor in (18/28 ,64%) macroscopically ,enucleation of tumor in (1/28 ,3%),while debulking of tumor in (4/28 ,15%). As shown inFig . (1) : Types of surgical procedures.

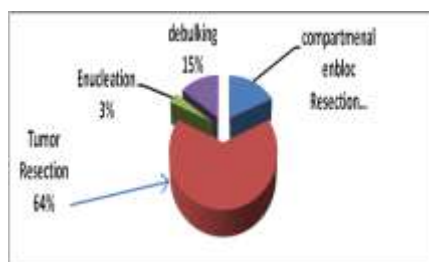


Fig 1 : Types of surgical procedures

Table 5 : Postoperative histopathological diagnosis (types)in 28 patients with retroperitoneal sarcomas.

Histopathology	No.	%
Differentiated liposarcoma	8	28
Lieomyosarcoma	6	22
Malignant fibrous histocytoma	4	14
Rabdomyosarcoma	3	11
Myxoidliposarcoma	3	11
Malignant schwanoma	3	11
Myoliposarcoma	1	3

Table (5) classified the patients according to the post operative histopathology of resected samples and this revealed differentiated liposarcoma in (8/28, 28%) is most common one.

Histopathological grading for the resected tumor in our patient sample the figure (3) showed high grade tumor in (17/28 ,61%)and low grade tumor in (11/28 ,39%) .as shown in Fig.(2) .

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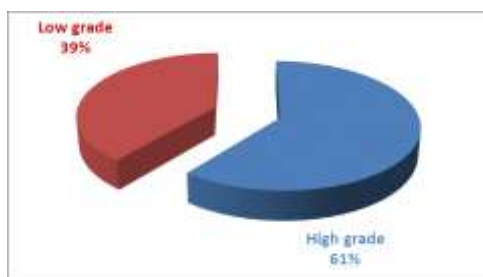


Fig 2: Histopathological grading in 28 patients with retroperitoneal sarcomas.

The state of surgical margin which was free of tumor and hence complete resection in (14/24,58%) and involved in (10/24 ,42%)which considered incomplete resection .These results

not include those 4 patients in whom the margins already involved due to incomplete resection(debulking). As shown in Fig.(3).

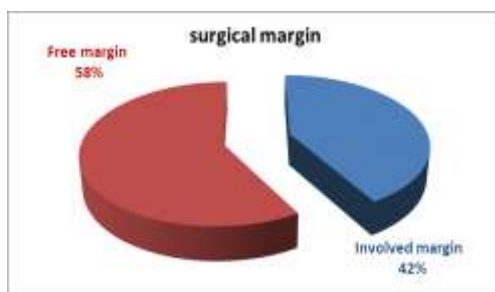


Fig 3: The state of surgical margin of resected tumors in 24 patients with retroperitoneal sarcomas.

Only three patients died at post operative period (3/28 ,11%) all of them were elderly with advanced tumor and just debulking procedures with comorbidies (cardiopulmonary problems) .

Regarding the number of recurrence of tumor in our patient sample were (12/24 ,50%) . as shown in Fig.(4).

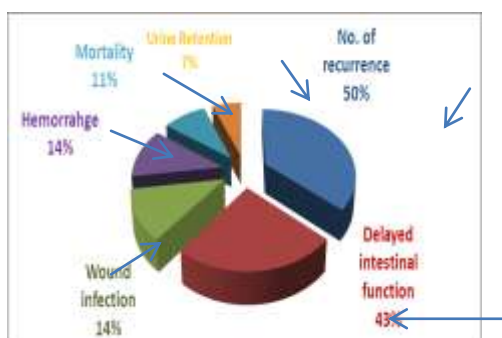


Fig 4: Postoperative complication (morbidity) and mortality.

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Table 6: The correlation between the recurrence of tumor and type of surgery in 24 patients with retroperitoneal sarcomas.

Recurrent of tumor	Type of surgery						Total	%
	Compartmental Enbloc resection	%	Simple resection of tumor	%	Enucleation of tumor	%		
present	1	20	10	55	1	100	12	50
absent	4	80	8	45	0	0	12	50
Total	5	100	18	100	1	100	24	100

The P-value=0.038(significant)

the recurrence of tumor was less with compartmental enbloc resection which occurred in (1/5,20%) , the recurrence of tumor was definitive when the surgery was incomplete as with enucleation (1/1,100%),while with resection of tumor that appear macroscopically completed resection was (10/18,55%) .

Table7: The correlation between the recurrence of tumor and state of the surgical margin in 24 patients with retroperitoneal sarcomas.

Recurrence of tumor	Surgical margin				Total	%
	Involved	%	Free	%		
present	9	90	3	21	12	50
absent	1	10	11	79	12	50
total	10	100	14	100	24	100

The P-value=0.001 (significant).

This variation of recurrence rate with type of surgical resection greatly reflected the state of surgical margin in resected sample. As shown in table (7) where the P-value was significant (0.001).

Table 8: Show the relation between the recurrence of tumor and histopathological grading of the resected tumor in 24 patients with retroperitoneal sarcomas.

Recurrence of tumor	Histopathological grade of tumor				Total	%
	High grade	%	Low grade	%		
present	10	77	2	19	12	50
absent	3	23	9	81	12	50
Total	13	100	11	100	24	100

The P- value=0.001(significant)

The histopathological grade of tumor on other hand also appear an important factor in the recurrence of tumor as show as in table (8) .

Table 9: Show the correlation between the duration of symptoms and type of surgery done in 28 patients with retroperitoneal sarcomas.

Duration of symptom	Type of surgery								total
	Compartmental Enbloc resection	%	Resection of tumor	%	Enucleation	%	Debulking	%	
More than 6months	1	20	12	66.7	1	100	3	17	60.7
Equal or less than 6months	4	80	6	33.3	0	0	1	11	39.3
total	5	100	18	100	1	100	4	28	100

The p-value=0.193(not significant).

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There was no significant relation between the extent of surgical procedure that could be done to the retroperitoneal sarcoma and duration of symptoms and this probably related to histopathological type and grade of tumor .

Regarding the postoperative adjuvant therapy ,(4/25, 16%) patients did not receive adjuvant therapy owing to free margin and low grade tumor and no recurrence of tumor had occurred in these 4 patients.

(6/25,24%) of patients had received combined chemoradiotherapy and the recurrence occurred in (5/6, 84%) where all of these 5 patients had either

involved surgical margin or high grade tumor (or both) and the last 6th who only had debulking of tumor exhibited regrowth of residual tumor in spite of chemoradiotherapy courses .

On other hand (15/25, 60%)received only chemotherapy and the recurrence of tumor occurred in (7/15, 47%). Again these 7 patients either had involved margin or high grade(or both) .

The total recurrence number in our patients sample were (12/24, 50%)only(7/12, 58%)submitted for another surgical intervention with complete resection done in (1/7,14.3%). As shown in Fig(5).

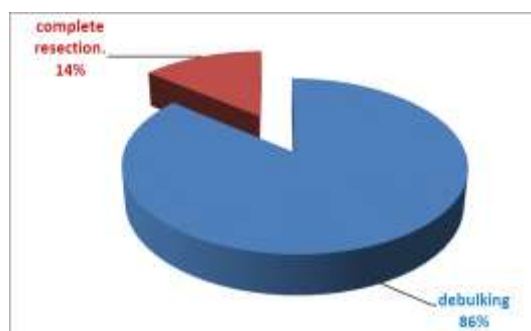


Fig. 5 : Type of surgical re-excision for 7 patients with recurrent retroperitoneal sarcomas.

DISCUSSION:

In our result ,we found no significant difference in gender distribution as shown in figure (1)and this agree with other studies 3,6,7,9,10,11 , but disagree with S.Singer et al⁽¹²⁾ who found that there is significant preponderance of male population while L. Gilbeau et al⁽¹³⁾ found female affection significantly higher than male (64%)versus (36%).

Regarding the age group distribution ,we found that the (50-59 years)age group had the highest number of patients presented with retroperitoneal sarcomas and these result in accord with H. Al-Obaidi et al⁽²⁾ ,and I. Robert et al⁽¹⁴⁾ who stat that retroperitoneal sarcomas are most prevalent from fifth to the seventh decade of life.

In respect to the duration of symptoms, in our patient sample our result similar to that found by A.Chiappa et al⁽¹⁵⁾ but not agree with S.Gholami et al⁽³⁾ who found most patients had symptom for less than 6 month duration (61%) .

Most our patients who had a retroperitoneal sarcomas presented with abdominal mass and because of typically silent nature of these tumor until they were large enough to present as an abdominal mass ,most retroperitoneal sarcomas were large and locally advanced when diagnosed

,this result agree with M.T.Hueman et al⁽⁴⁾ and A. Chiappa et al⁽¹⁵⁾ who conclude that late presentation as a feature of retroperitoneal sarcomas is due to their presence in potential growing space.

On other hand our result not agree with S.Gholami et al⁽³⁾ and I. Hassan et al(16) ,both of them found that most common presenting symptom is abdominal pain (21.5%, 57%) respectively while in our patients sample the abdominal pain was presenting symptom in only (21%).

Concerning the diagnostic modalities , by which our patients were investigated ,it's important to note that although the plane abdominal X-ray is not so helpful in the diagnosis of retroperitoneal sarcomas ,but one peculiar finding was the calcification within the soft tissue shadow presented in two patients which proved later to be Liposarcoma on histopathology and this result in accord with that of T. Ferrario et al⁽¹⁷⁾ who demonstrated calcification in retroperitoneal Liposarcoma.

Despite the great advancement in our experience with the usage of modern imaging modalities in reaching the diagnosis still most retroperitoneal sarcoma are detected as locally advanced tumor

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and this agree with I. Hassan et al⁽¹⁶⁾, who stated that in spite the increase in incidence of asymptomatic retroperitoneal sarcomas due to increase use of CT scanning as a diagnostic tool by medical profession, but still most sarcomas are locally advanced when detected.

One of great challenge in our management of retroperitoneal sarcomas is the limitation in obtaining a preoperative tissue diagnosis under image guidance prior to surgery.

In fact we tried for this in two patients and both were inconclusive and end with complication and this is not similar to what obtained by S. Bonvalot et al⁽⁷⁾ who found the percutaneous preoperative biopsy lead to diagnosis of sarcomas in same proportion as the surgical biopsy with frozen section and C. M.G Keyzer et al⁽¹⁸⁾ who had got preoperative tissue diagnosis for 14 patients by large core needle biopsy.

We thought the reasons behind this limitation in our center are:

The above two studies done in tertiary centers with long term experience curve line and because most solid retroperitoneal mass are malignant, and most of them required surgical intervention for reason or other, most surgeons and radiologists do not pay significant attention to get a preoperative tissue diagnosis. Lastly paucity of more advance imaging machines (CTS, MRI) and long term appointment to get imaging make the experience to obtained tissue sample percutaneously limited.

In our patients sample, the most common histopathological type was differentiated Liposarcoma and next is Lieomyosarcoma and this agree with other studies 3,7,16,17,19, but disagree with A.Chiappa et al⁽¹⁵⁾ who had found the Lieomyosarcoma is the most common histopathological type.

Regarding the grading of tumor, our results show significant variation between high grade tumor (61%) and low grade tumor (39%) and this agree with S.Gholami et al⁽³⁾, A.Gronchi et al⁽¹¹⁾ and M.T.Ballo et al⁽¹⁹⁾ who found higher percentage of high grade tumor (59%, 64.7%, 61%) respectively, but our result apposite to that found by S.Bonvalot et al⁽⁷⁾ and A.Chiappa et al⁽¹⁵⁾ that had higher percentage of low grade tumor than high grade tumor (66%, 58%) respectively.

Regarding the surgical margin of resected tumor in our patients sample it was involved in (42%) of resected tumor and this rate is similar to that

obtained by S.Singer et al⁽¹²⁾ (37%), M.T.Ballo et al⁽¹⁹⁾ (47%) and J.O.Park et al⁽²⁰⁾ (49%).

The state of surgical margin is greatly reflected the extent of surgical resection and hence recurrence of tumor or development of systematic recurrence, where it was involved in one patient with enbloc compartmental resection group (owing to tumor rupture) and in 8 patients of simple tumor resection group, so that recurrence of tumor with enbloc compartmental resection is the least as shown in table⁽⁶⁾ and table (7).

While symptomatic recurrence of incompletely resected tumor was definitive and rapidly occurred as compared with other type of resection and this agree with S.Gholami et al⁽³⁾, S.Bonvalot et al⁽⁷⁾, A.S.Sogaard et al⁽⁹⁾, I.Ardoino et al⁽¹⁰⁾, S.Singer et al⁽¹²⁾ and M.T.Ballo et al⁽¹⁹⁾, who all of them stated that the surgical margin is the most important prognostic factor in determined of survival and recurrence rate and its greatly depend on the extent of surgical resection with best result obtained with compartmental systematic resection.

Concerning the recurrence of tumor, or rate of growth of macroscopically residual tumor, they appear to depend on grade of tumor, where its highest with high grade tumor (77%) and this agree with that mentioned by S.Gholami et al⁽³⁾, T.Lehnert et al⁽⁶⁾ and T.ferrario et al⁽¹⁷⁾.

The most common early postoperative complication in our patient sample was delayed intestinal recovery (paralytic ileus 43%) and this agree with H.Al-Obaidi et al⁽²⁾ and A. S.Sogaard et al⁽⁹⁾, but disagree with S.Gholami et al⁽³⁾ and A.Chiappa et al⁽¹⁵⁾ where both had the most common early complications were chest infection and frequent blood transfusion respectively.

While the most remote complication is recurrence of tumor (50%) and this agree with S.Bonvalot et al⁽⁷⁾, A.S.Sogaard et al⁽⁹⁾, and A.Chiappa et al⁽¹⁵⁾.

Regarding the adjuvant therapy, our results show that the adjuvant therapy had no significant impact on overall recurrence rate and free survival and this similar to that found by S.Gholami et al⁽³⁾, L.Gilbeau et al⁽¹³⁾ and M.T.Ballo et al⁽¹⁹⁾ who found that the high rate of local relapse does not demonstrate the usefulness of adjuvant therapy at the level of a given dose use.

On other hand A. Chiappa et al⁽¹⁵⁾ found improvement for both primary and recurrent retroperitoneal sarcoma for multicenter trials examining the effect of preoperative radiotherapy ,intraoperative chemotherapy and immune therapy regimens .

In respect to re-excision for recurrent tumors ,only 7 patients underwent further surgical intervention and of those only one patient (14%) got complete resection with microscopically free surgical margin while the remainder 6 patients (86%) just debulking and palliative measures done.

These results far away from that obtained by S.Gholami et al⁽³⁾ ,A.S.Sogaard et al⁽⁹⁾ and A.Chiappa et al⁽¹⁵⁾ , where they stated that patients with recurrence have an equally good prognostic chance as those with primary sarcomas and such surgery should not be considered only palliative efforts as much as possible and this preferentially to achieve in specialized tertiary centers, where they could achieved complete resection in the range of (70-85%) and this much higher than our results in which complete resection obtained only in (14%) as mentioned above .

CONCLUSION:

Surgical resection is the best modality of treatment for both curative and palliative attention.The survival rate and curative rate are greatly depend on the state of surgical margin (involved or not) and the histopathological grading of sarcomas (high or low grade),so they are the most important prognostic factors.Wide resection lower the local recurrence and improves survival rate, so complete compartmental resection without tumor rupture should be performed when possible to achieved clear margins.Adjuvant therapy (whether radiotherapy or chemotherapy) does not alter the survival rate or disease free period rate.

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