



# Nephrectomy in the treatment of retroperitoneal sarcoma

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## ■ ABSTRACT

**Introduction.** Complete retroperitoneal sarcoma resection requires the inclusion of adjacent organs, the kidney being the most frequent. **Objective.** To analyze the role of nephrectomy in the treatment of retroperitoneal sarcoma.

**Patients and Methods.** A retrospective study of nephrectomies in retroperitoneal sarcoma performed at the Mixed Tumor Unit of the Oncology Service at the *Hospital General de Mexico* was carried out from January 1999 to December 2002. Factors associated with survival were analyzed statistically.

**Results.** From a total of 59 patients presenting with retroperitoneal sarcoma, 11 (18.6%) required nephrectomy - 6 men (54.5%) and 5 women (45.5%). Mean age was 47 years (range of 17-75 years) with 5 patients older than 50 years of age (45.5%). Liposarcoma was found in 45.5% of patients and leiomyosarcoma in 27.2%. Tumor grade was high in 7 cases and low in 4. Complete resection was performed in 8 patients (72.7%) and partial resection in 3. There was no disease invasion in 4 kidneys (36.6%), 6 presented with capsular invasion (54.5%) and 1 presented with invasion of the parenchyma (9%). Complete resection was associated with a higher survival rate of 72.7% at 1 year (72.7%), while incomplete resection was associated with a survival rate of 27.7%. Mean survival rate was 60

## ■ RESUMEN

**Introducción:** La resección completa del sarcoma retroperitoneal requiere inclusión de órganos adyacentes; el riñón es el más frecuente.

**Objetivo:** Analizar el papel de la nefrectomía en el tratamiento de sarcomas retroperitoneales.

**Pacientes y métodos:** Estudio retrospectivo de nefrectomías en sarcoma retroperitoneal operadas en la Unidad de Tumores Mixtos, Servicio de Oncología del Hospital General de México, entre enero de 1999 y diciembre del 2002. Se analizan estadísticamente factores asociados a la sobrevida.

**Resultados:** De 59 pacientes con sarcoma retroperitoneal 11 (18.6%) requirieron nefrectomía, 6 hombres (54.5%) y 5 mujeres (45.5%). La edad promedio fue de 47 años (rango 17-75), 5 mayores de 50 años (45.5%). Encontramos liposarcoma en 45.5% y leiomyosarcoma en 27.2%; el grado de diferenciación fue alto en 7 casos y bajo en 4. Hubo resección completa en 8 (72.7%) y parcial en 3. Cuatro riñones resultaron sin invasión (36.6%), seis con invasión capsular (54.5%) y uno a parénquima (9%). La resección completa fue asociada a mayor sobrevida a 1 año (72.7%), mientras en la incompleta 27.7%. La supervivencia promedio fue de 60 meses para tumores de bajo grado frente a 12 meses para alto grado. Las recurrencias fueron locales en 50% con resección completa y las metástasis a distancia en hígado

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months for low-grade tumors compared with 12 months for high-grade tumors. There was local recurrence and distance metastasis in liver and lung in 50% of patients having undergone complete resection. Adjuvant therapy showed no benefit for survival.

**Conclusions.** When kidney involvement is suspected, the performance of nephrectomy during complete resection of retroperitoneal tumor improves survival rate.

**Key words:** Retroperitoneal sarcoma, Nephrectomy, Survival

y pulmón. La terapia adyuvante no mostró beneficio en la sobrevida.

**Conclusiones:** En sospecha de involucro a riñón, se realizará nefrectomía durante la resección completa del tumor retroperitoneal, lo que mejorará la sobrevida.

**Palabras clave:** sarcomas retroperitoneales, nefrectomía, sobrevida.

## ■ INTRODUCTION

Retroperitoneal sarcomas are not very common tumors and they represent less than 1% of neoplasms in adults and approximately 15% of all soft tissue sarcomas (1-3). The highest incidence occurs between the fifth and sixth decades of life and is associated with various genetic pathologies such as Li-Fraumeni syndrome, von Recklinghausen disease and Gardner's syndrome. A history of pelvic or abdominal radiotherapy is a known risk factor (4-6).

The most frequently reported histological types reported in the literature are liposarcoma (31.5%) and leiomyosarcoma (28.4%), followed by fibrosarcoma (10.3%), malignant fibrous histiocytoma (9.1%), neurogenic sarcoma (5.1%), angiosarcoma/hemangioma pericytoma (2.3%) and others (13.4%) (5,7,8).

The cardinal symptom is non-specific abdominal pain in 40-60% of patients. There may be neurological symptoms related to nerve compression or involvement in 30%. Symptoms that are less frequent are weight loss (<15%), gastric plenitude (<10%), nausea and vomiting (<10%) or varicose veins in the pelvic members (<10%) (9-11). Clinical examination shows a palpable increase in volume in 45-75% of patients with variation in firmness depending on tumor grade (12).

Total extirpation of the tumor with free microscopic edges is the basis of treatment. It often requires a number of multi-organ and *en bloc* resections (53-83%). The kidney is the most frequently involved organ (46%), and ipsilateral nephrectomies are carried out in more than 33% of the cases. Following the kidney are the colon (24%), the suprarenal glands (18%), the pancreas (15%) and the spleen (10%) (9, 13-16).

The objective of this study is to analyze the clinical presentation of patients presenting with retroperitoneal sarcoma who underwent nephrectomy as part of their surgical treatment and to analyze the prognostic survival

factors based on experience with these patients at the Oncology Service of the *Hospital General de México*.

## ■ PATIENTS AND METHODS

A descriptive retrospective study was carried out. Case records of all patients presenting with preoperative retroperitoneal tumor having undergone surgery at the Oncology Unit of the *Hospital General de México* from January 1990 to December 2002 were reviewed and analyzed. All cases with a histopathological report of sarcoma were selected. Patients above 16 years of age, of both sexes and who were preoperatively diagnosed with primary retroperitoneal sarcoma were included in the study. Patients presenting with benign cysts and tumors, germ cell tumors, lymphomas or primary tumors extending to the retroperitoneum were all excluded. Patients presenting with sarcomas arising in the gastrointestinal tract, genitourinary tract, bone or embryonic remnant were also excluded along with patients who were not operated on in the unit or who presented with recurrent or metastatic disease at the time of the study. Study elimination criteria were incomplete follow-up and non-conclusive histopathological reports for retroperitoneal sarcoma.

Histological type and differentiation grade were analyzed in all surgical patients requiring nephrectomy as part of their treatment. The reason for nephrectomy as part of the treatment for retroperitoneal sarcoma was also determined. Histopathological report was analyzed to determine the degree of kidney invasion by the sarcoma. All surgeries were statistically analyzed and the nephrectomy subgroup was not included due to its small size. Kaplan-Meier method was used to evaluate disease-free survival rate.

Prognostic factors were age, sex, differentiation grade, histological type, resectability and tumor size

**Table 1.** Tumor pathological characteristics

Parameter	N	%
<b>Histopathological Report</b>		
Liposarcomas	5	45.5
Leiomyosarcoma	3	27.2
Malignant Fibrous Histiocytoma	2	18.1
Malignant Schwannoma	1	9.1
<b>Differentiation Grade</b>		
High	7	63.6
Low	4	36.3
<b>Tumor Size</b>		
<10cm	1	9.1
10-20cm	2	18.1
>20cm	8	72.7

**Table 2.** Nephrectomies during retroperitoneal sarcoma surgical treatment.

Nephrectomy	N	%
Primary Resection	8	72.7
First Recurrence	2	18.1
Second Recurrence	1	9.1

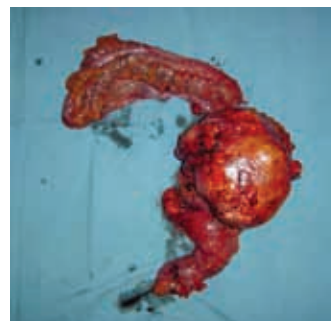
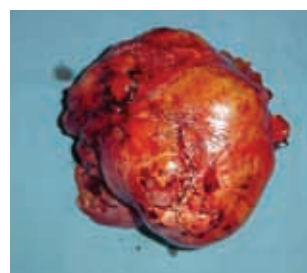
and they were evaluated by univariate analysis. For multivariate analysis the Cox proportional risk model was used for recurrence and survival rates. Descriptive statistics were used to analyze data with Windows SPSS/PC version 10.01 software. Statistical significance was defined when  $P < 0.05$ .

## RESULTS

From January 1990 to December 2002, 176 retroperitoneal tumor cases were operated on. A total of 33.5% were soft tissue sarcomas, 31.2% were urogenital neoplasms, 11.5% were lymphomas and the rest were benign neoplasms, gastrointestinal tract tumors extending to the retroperitoneum and metastatic disease.

Fifty-nine patients presenting with soft tissue retroperitoneal sarcoma, 11 of whom (18.6%) required nephrectomy as part of their treatment, were included in the study. Six of those patients were men (54.5%) and 5 were women (45.5%). Mean age was 47 years (range 17-75 years). Five patients were over 50 years of age (45.5%) and 6 were under 50 years of age (54.5%).

The most common histological results were liposarcoma in 5 patients (45.5%) and leiomyosarcoma in 3 (27.2%) followed by malignant fibrous histiocytoma

**Image 1.** Retroperitoneal sarcoma en bloc resection.**Image 2.** Retroperitoneal sarcoma surgical specimen, unidentifiable kidney (encapsulated).

in 2 (18%) and malignant schwannoma in 1 patient (9%). Differentiation grade was high in 7 cases (63.6%) and low in 4 (36.3%) with a significant difference for liposarcomas ( $P < 0.05$ ). Tumor diameter was a mean 25.9 cm with a range from 10 to 80 cm. Tumors larger than 20 cm were found in 8 patients (72.7%) (**Table 1**).

Nephrectomy was performed on 8 patients (72.7%) during surgical treatment for primary retroperitoneal sarcoma and in 3 cases (27.2%) for tumor recurrence (**Table 2**). Complete or negative microscopic border resection was carried out in 63.6% of cases ( $n=7$ ) performing *en bloc* resection of the adjacent organs including the kidney, colon or small intestine (**Image 1**). Incomplete resection was reported in 36.3% of cases ( $n=4$ ) in which macroscopic residual was evident or suggestive of microscopic disease. During the operation in 6 cases (55.4%) the sarcoma completely surrounded the kidney rendering it unidentifiable (**Image 2**). It was densely adhered to the kidney in 3 cases (27.2%) and had invaded the kidney in 2 cases (18%) (**Table 3**). Of the 6 kidneys that were unidentifiable during surgery, 3 were histologically normal (50%), 2 presented renal capsule invasion (33.3%) and 1 presented renal parenchyma invasion (16.6%). Of the 3 cases of dense adhesion to the kidney during surgery, 1 case (33.3%) presented with normal histological characteristics

**Table 3.** Surgical indication for nephrectomy in retroperitoneal sarcoma.

Indication	N	%
Sarcoma that surrounds the kidney (encapsulated)	6	54.54
Sarcoma densely adhered to the kidney	3	27.27
Renal parenchymal invasion	2	18.18

**Table 4.** Surgical specimen histopathological report.

Microscopic description	N	%
Without invasion	4	36.36
Capsular invasion	6	54.54
Parenchymal invasion	1	9.10

**Table 5.** Postoperative complications.

Complication	N
Sepsis	2
Hemorrhage	1
Atelectasia	1
Intestinal Fistula	1

and the other 2 with capsular invasion (66.6%). The 2 cases of kidney invasion during surgery presented with capsular invasion.

Histopathological study of the surgical specimens from the 11 nephrectomies performed revealed that 4 kidneys did not present with invasion (36.36%), 6 presented with capsular invasion (54.54%) and 1 with parenchymal invasion (9.10%) (Table 4).

The main surgical complications were sepsis, surgical bed hemorrhage, atelectasis and intestinal fistula. In these cases multi-organ resection including kidney and intestine were carried out (Table 5).

Patients who underwent complete primary tumor resection were associated with improved survival rate at 1 year (72.7%) compared with patients with incomplete resection (27.7%). According to univariate analysis factors associated with better survival prognosis were low-grade sarcomas ( $P=0.01$ ) and histological report of liposarcoma ( $P=0.01$ ). In the multivariate analysis incomplete resection, high-grade sarcomas, leiomyosarcoma histological classification, and age above fifty years were considered poor prognosis factors. Sex, neoplasm size and adjuvant treatment were not shown to have prognostic significance in relation to survival rate. Mean survival period was 60 months for patients presenting with low-grade tumor compared to 12 months for patients presenting with



**Image 3.** Cat of retroperitoneal sarcoma adhered to left perirenal fat.

high-grade tumors. Complete resection was associated with a mean survival period of 62 months ( $P=0.01$ ) and partial resection with 17 months. Mean follow-up duration was 3 years for all patients. Four high-grade tumor patients presented with mainly local recurrence (50% with complete resection) and the principal distance metastasis sites were the liver and lung.

## DISCUSSION

Retroperitoneal sarcomas are rare neoplasms with non-specific symptoms. Diagnosis is established when tumors are voluminous. CAT is used to determine tumor extension (Image 3) and guided needle biopsy is performed in neoadjuvant treatment or when lymphoma or germ cell tumors are suspected. Magnetic Resonance Imaging (MRI) with gastrointestinal and intravenous (IV) contrast can help to determine resectability by knowing the origin and limits of the tumor and the degree of necrosis. Extension studies are radiography and thorax CT to rule out distance extension (5). Retroperitoneal lymphadenectomy is not indicated as part of the treatment because there is tumor involvement in less than 5% of cases (5).

In some reports adjuvant radiotherapy is not part of standard retroperitoneal sarcoma treatment because its usefulness has not been clearly demonstrated (17, 18). However other studies support its use in clinical trials or in non-resectable tumors (5, 19-21). Current National Comprehensive Cancer Network (NCCN) recommendations for radiotherapy treatment in retroperitoneal sarcoma are: External Postoperative Radiotherapy (RT) in completely resected high-grade tumors (adjuvant), Intraoperative Radiotherapy (IORT) in completely resected high-grade tumors, Postoperative RT in incomplete resection, neoadjuvant RT in non-resectable tumors or when there is metastasis. Radiotherapy must be evaluated in the case of recurrent disease. A Phase III study is presently in process in which the role of surgery with and without preoperative radiotherapy in retroperitoneal

sarcoma patients is being evaluated. The study's objective is to determine whether survival with no recurrent disease is prolonged with preoperative radiotherapy. There is little information available evaluating the use of combined RT and chemotherapy (22).

The role of chemotherapy, whether neoadjuvant or adjuvant, is not yet well-defined in current treatment (5, 18, 23).

Present NCCN recommendations for chemotherapy in retroperitoneal sarcomas are: adjuvant treatment in non-resectable tumors, disease progression, disease recurrence and metastatic disease. The most commonly used drugs are separate or combined regimens of doxorubicin and ifosfamide (22). Neoadjuvant chemotherapy with doxorubicin and ifosfamide is presently being studied (5). For recurrent or persistent disease a Phase II study is in progress that is evaluating the use of gemcitabine versus gemcitabine followed by docetaxel (22).

Different articles have demonstrated that prognosis depends on total resection of the tumor and its wide macroscopic margins and on tumor grade (24, 25). A 41-46% recurrence rate at 5 years and a 29-58% survival rate at 5 years have been observed (8). The determining survival factor in retroperitoneal sarcoma patients is complete resection of the tumor and the involved adjacent organs (9, 13-16, 24-26).

The kidney is the most commonly resected organ and nephrectomy is mentioned in 46% of cases in the medical literature (13, 26).

According to a report from the Mayo Clinic in Rochester, Minnesota, there is a 35% nephrectomy frequency during retroperitoneal sarcoma resection (27). In Mexico, the National Cancer Institute (INCAN) has reported a nearly 40% frequency (28) and the *20 de Noviembre* National Medical Center has reported a 21% frequency (29). In the Oncology Service at the *Hospital General de México*, nephrectomy frequency is 18.3% which is less than that reported in the literature. This is due to the fact that 79.7% of the tumors in our service are larger than 20 cm in diameter with a mean 25.9 cm (10-80 cm range) and are non-resectable because of large vessel and mesenterium involvement or peritoneal dissemination (30).

There are only a few studies that specify the degree of resected kidney involvement and its impact on survival. A study from the Memorial Sloan-Kettering Cancer Center is the most complete in this respect and mentions a nephrectomy frequency of 20% (26), similar to the 18.3% found in our study. The Sloan-Kettering study found direct kidney affectation in only 27% of nephrectomized kidneys while in our study the figure was 63.4%. No statistically significant difference in

survival related to the degree of kidney involvement and tumor grade was found in the Sloan-Kettering study in which at 18-month follow-up there was 49% mortality and at 5-year follow-up there was 50% mortality. Our report showed a 72% survival rate at 1 year follow-up and 50% survival rate at 5-year follow-up in cases of complete tumor resection. The retroperitoneal sarcoma surgical management experience of the Oncology Service at the *Hospital General de México* shows a low nephrectomy percentage compared with that previously reported in the literature. In general the tumors are large – 70% are larger than 20 cm – and present with direct kidney invasion in which *en bloc* resection is done in order to guarantee microscopic negative margins. Histopathological report shows direct kidney affectation in 63.6% that can be in the parenchyma or renal capsule. Compared with the report by Russo et al (26), we found a greater invasion percentage in patients at the *Hospital General de México*. In other words, nephrectomy frequency is lower but kidney invasion percentage is higher. This could be due to clinicopathological characteristics of those patients: the tumors are large, high-grade, with an elevated recurrence pattern and a high level of non-resectability.

## ■ CONCLUSIONS

Nephrectomy during retroperitoneal sarcoma treatment is completely justified when kidney involvement is suspected. Even if involvement is not corroborated by the final microscopic report, nephrectomy guarantees complete tumor resection and is a favorable prognosis factor for local control and survival.

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