

A Large Primary Retroperitoneal Synovial Sarcoma: A Case Report of a Huge Malignant Tumor

Anahita Ansari Djafari¹, MD;^{ORCID}
Mohammadreza Razzaghi¹, MD; Azadeh Rakhshan², MD; Saba Faraji³, MD; Amir Hossein Rahavian⁴, MD; Seyyed Ali Hojjati¹, MD^{ORCID}

¹Department of Urology, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran;

²Department of Pathology, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran;

³Department of Psychiatry, Roozbeh Hospital, Tehran University of Medical Sciences, Tehran, Iran;

⁴Andrology Research Center, Yazd Reproductive Sciences Institute, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Correspondence:

Seyyed Ali Hojjati, MD;
Department of Urology, Shohada-e-Tajrish Hospital, Tajrish Sq., Postal code: 19899-34148, Tehran, Iran

Tel: +98 21 22718001

Fax: +98 21 22829356

Email: sah_hojjati@yahoo.com

Received: 14 March 2021

Revised: 07 June 2021

Accepted: 09 July 2021

Abstract

Synovial Sarcoma (SS) is a rare soft-tissue malignancy. Only about 15% of SS originates from the retroperitoneum. Retroperitoneal SS (RSS) is usually diagnosed incidentally due to the anatomy of the retroperitoneum. The most common complaints of patients are abdominal and low back pain. Other common symptoms of RSS are palpable abdominal mass, weight loss, and anemia. In this study, we will describe a 29-year-old white Asian man with a diagnosis of RSS after radical nephrectomy. He was admitted to the Urology Department of Shohada-e Tajrish hospital, Tehran, Iran in March 2019. The distinguishing feature of this case is the size of the mass, which has never been reported so much for retroperitoneal synovial sarcoma. Radiologic imaging showed a huge retroperitoneal mass originating from the kidney. Based on the pathologic features and immunohistochemistry (IHC) study, the diagnosis was consistent with synovial sarcoma. Accurate diagnosis of RSS is usually based on the pathological findings. Therefore, in case of doubt, a biopsy can be employed. Surgical resection of the tumor and lymph nodes dissection is the main and most important part of the treatment. Aggressive resection with free margin is recommended. The role of adjuvant and neoadjuvant chemotherapy in RSS is not certain to date, but it is recommended according to the patient's condition.

Please cite this article as: Ansari Djafari A, Razzaghi MR, Rakhshan A, Faraji S, Rahavian AH, Hojjati SA. A Large Primary Retroperitoneal Synovial Sarcoma: A Case Report of a Huge Malignant Tumor. *Iran J Med Sci.* 2022;47(3):280-284. doi: 10.30476/IJMS.2021.90470.2141.

Keywords • Drug therapy • Retroperitoneal neoplasms • Synovial sarcoma

What's Known

- Primary Retroperitoneal Synovial Sarcoma is a rare malignant tumor, which presents with abdominal pain or abdominal mass or in some cases, weight loss. The main part of treatment is the aggressive surgical removal of the tumor. Chemotherapy is also useful in these patients.

What's New

- The new chemotherapy plan with new chemotherapy drugs has been applied to treat retroperitoneal synovial sarcoma. New immunohistochemistry markers also help us to diagnose this tumor faster and better.

Introduction

Synovial Sarcoma (SS) is a rare soft-tissue malignancy mostly affecting extremities (50%) particularly the lower thigh and knee region. Other primary sites are the trunk (10%-15%), head and neck (less than 10%), and retroperitoneum (about 15%). SS is the fourth most common subtype of soft-tissue sarcoma.¹ Retroperitoneal SS (RSS) affects both men and women, and its prevalence does not differ in different races. Its age of onset is usually lower than other primary cancers.¹ RSS is usually diagnosed incidentally on account of the anatomy of the retroperitoneum. The most common complaints of patients are abdominal and low back pain. It can also present with the signs of urinary obstruction or bowel obstruction. Other common symptoms of RSS are palpable abdominal mass, weight loss, and anemia.² RSS is usually detected through imaging techniques, such as Computerized Tomography (CT) and Magnetic

Resonance Imaging (MRI).³ A biopsy can also be helpful in diagnosing and determining a treatment plan.¹ Since RSS is usually asymptomatic in the early stages, it can cause pulmonary and liver metastases.⁴ Therefore, Chest CT scan is required to check for lung metastasis.⁵ Differential diagnoses for this tumor include primary neoplasm of retroperitoneal organs, lymphoma, or metastatic lesions. Symptoms, such as testicular abnormality, B-symptoms, hematuria, or uncontrolled hypertension, can help us differentiate its various causes.¹ Local recurrence is common in RSS, and surgical therapy is the most effective curative treatment option. In addition, chemotherapy and radiotherapy are other useful options for treating RSS;⁵ yet, without surgery, other treatment techniques are useless.¹ Five-year survival rates for RSS are low, ranging from 20%-29%.⁶ Histologically, synovial sarcoma demonstrates a biphasic pattern with some epithelial components, namely the glands part and spindle cell components. Single-phase synovial sarcomas are composed only of spindle cells.⁵

Herein, we will describe a young patient with a large retroperitoneal mass, who was hospitalized, operated on, and proposed for the diagnosis of retroperitoneal synovial sarcoma. For retroperitoneal synovial sarcoma, a mass of this size has never been reported before, which makes our case novel.

Case Presentation

The patient is a 29-year-old white Asian man without any past medical history, who came to the urology clinic due to left low back pain. He did not have any urinary symptoms, but there were signs of microscopic hematuria in his laboratory data. In his physical examination, a large mass was palpable in his left flank area. He was admitted to the Urology Department of Shohada-e Tajrish hospital, Tehran, Iran, in

March 2019. Sonography revealed a huge solid-cystic well-defined mass measuring 243×150 mm in the left part of the abdomen with a compressive effect on the adjacent viscera causing the spleen to move upward and the left kidney to move downward. According to the claw sign, it seems to have originated from the upper pole of the left kidney.

Abdominopelvic CT scan with intravenous (IV) contrast revealed a large mass measuring 22 cm in the upper pole of the left kidney with cystic components and peripheral enhancement in favor of neuroblastoma (figure 1-A). Spiral chest CT scan showed no signs of metastasis.

Abdominopelvic MRI with and without IV contrast showed a well-defined solid-cystic mass with the enhancement of about 223×178 mm, which caused the displacement of stomach, colon, spleen, and bowel loops. Hemorrhagic areas were seen in solid components. Tumor thrombosis in the renal artery and vein was not observed (figure 1).

In terms of laboratory tests, blood routine tests were normal with a hemoglobin level of 13.1 g/L and a creatinine level of 1.3 mg/dL. The patient underwent a left radical nephrectomy with retroperitoneal lymphadenectomy.

Macroscopically, the specimen included a large creamy pinkish-red soft to elastic friable, heterogeneous mass measuring 20×18×9 cm attached to the upper pole of the right kidney. The mass weighed 8.5 Kg.

The mass had a thickened capsule that easily separated. On serial sections, the cut surface was creamy brown friable, and partially necrotic. No gross abnormality was found in the renal parenchyma.

Histopathological examination of the retroperitoneal mass demonstrated a closely packed proliferation of atypical spindle cells arranged in a short fascicular pattern with hemangiopericytoma-like vessels and areas of

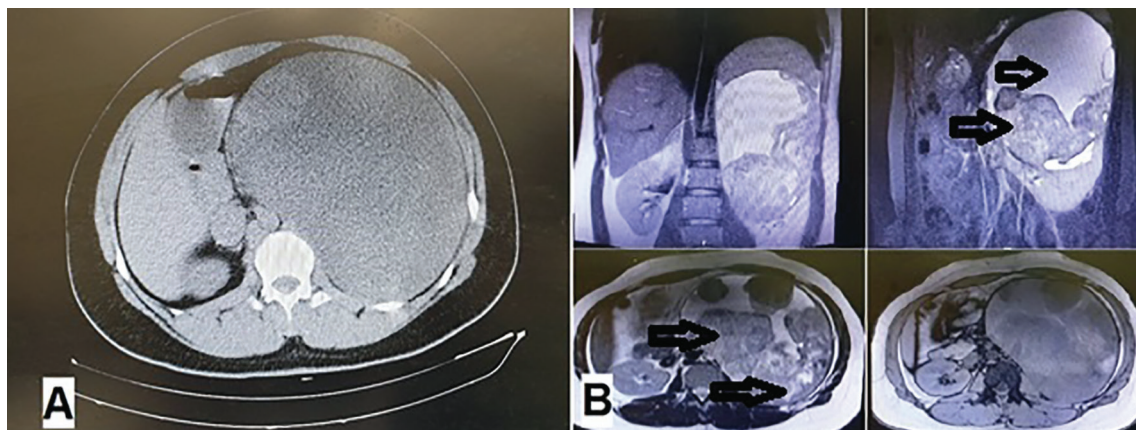


Figure 1: Abdominopelvic CT scan with IV contrast (A) and Abdominopelvic MRI with and without IV contrast (B) demonstrate a well-defined solid-cystic mass.

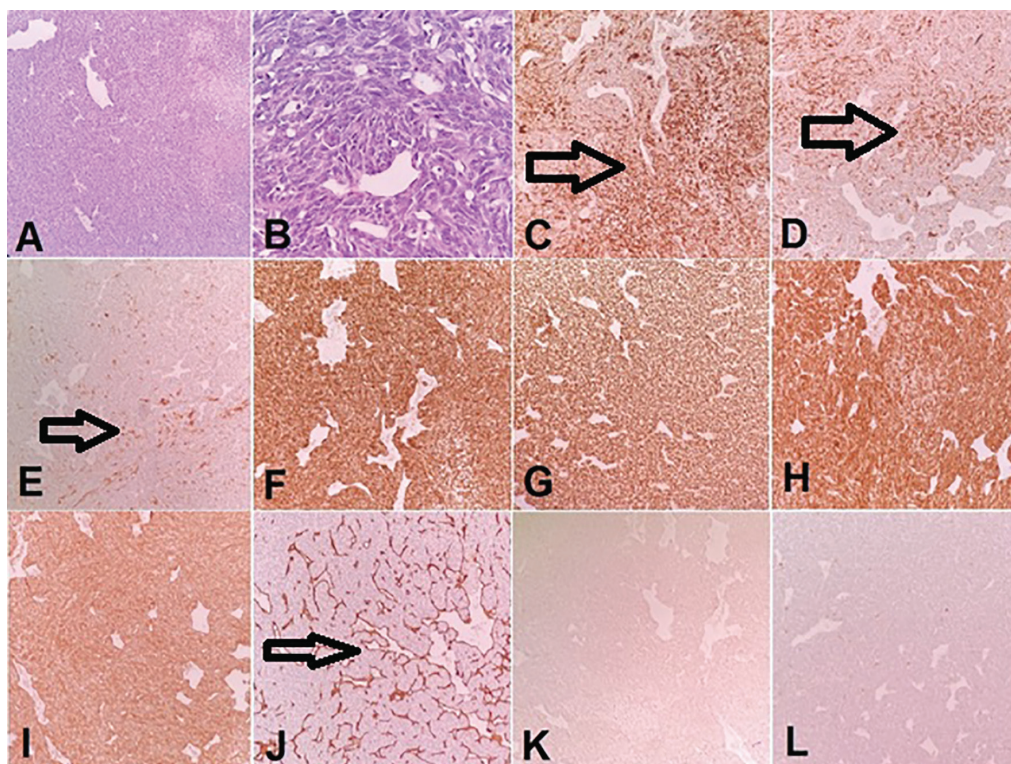


Figure 2: H&E stain (A-B), Positive IHC results for CKAE1/AE3 (C), CK7 (D), EMA (E), WT-1 (F), TLE-1 (G), Bcl-2 (H), CD99 (I), and Negative IHC results for CD34 (J), Desmin (K) and S-100 (L) are all in favor of Synovial Sarcoma.

necrosis (figure 2-A, x10 objective, hematoxylin and eosin (H&E) stain). The kidney showed patchy lymphocytic infiltration without tumoral involvement. Frequent mitotic figures, including atypical forms, are also present (figure 2-B, x40 objective, H&E stain). Immunohistochemically (IHC), the specimen was positive for cytokeratin (CK) AE1/AE3, CK7, and epithelial membrane antigen (EMA), as well as diffuse positive reaction for Wilms' tumor-1 (WT-1), transducin-like enhancer of split-1 (TLE-1), B-cell lymphoma-2 (Bcl-2), and a cluster of differentiation-99 (CD99).

Immunostaining for CD34, Desmin, and S-100 were negative (figure 2).

According to histology and IHC study findings, the diagnosis was malignant neoplasm with spindle cell features consistent with poorly differentiated synovial sarcoma. Renal parenchyma was tumor-free.

After surgery and according to the pathology result, the patient underwent six courses of chemotherapy with Adriamycin and ifosfamide (Pfizer, United States of America) (AI regimen). AI regimen included four days of Adriamycin

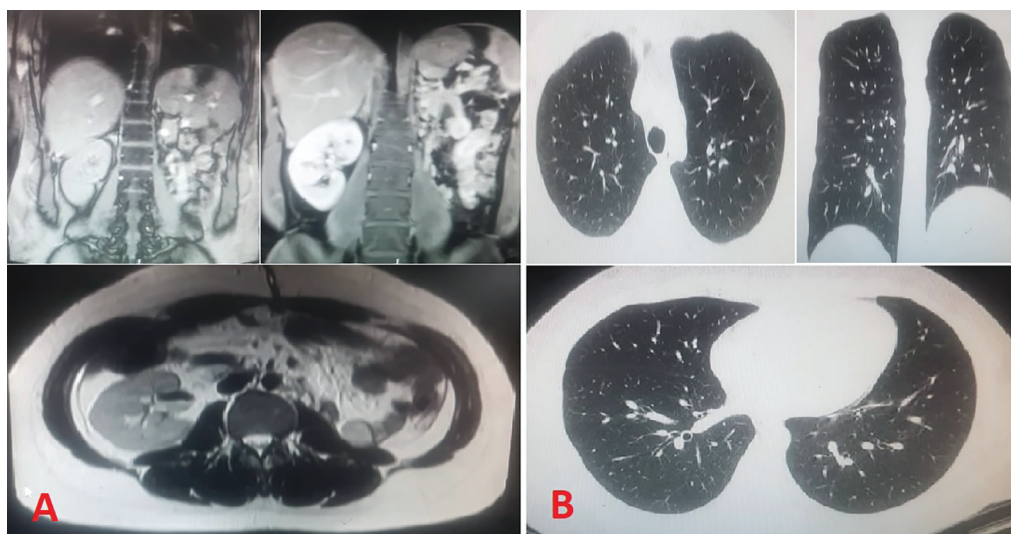


Figure 3: Abdominopelvic MRI with and without IV contrast (A) and spiral chest CT scan (B), show no signs of metastasis or recurrence six months after surgery.

with a dosage of 20 mg/m² and ifosfamide with a dosage of 1500 mg/m². According to the discretion of the oncologist, radiotherapy was not required.

An Abdominopelvic MRI with and without IV contrast and spiral chest CT scan were performed on the patient six months after chemotherapy. Both were normal without any signs of tumor recurrence or metastasis (figure 3).

Written and signed informed consent was obtained from the patient to publish the manuscript and was approved by the ethics committee of Shahid Beheshti University of Medical Sciences. The patient's personal information remained confidential to the researchers.

Discussion

SS is an uncommon type of soft-tissue sarcoma.⁷ RSS can be very large due to the anatomical nature of the retroperitoneal space.² RSS is usually asymptomatic, and after increasing its size, it has a compressive effect on the surrounding organs and causes clinical symptoms, the most common of which are low back and abdominal pain.² As in previous studies, our patient was also referred for mass enlargement and pain due to its compressive effects.

According to the radiological findings of our patient and the extent of the mass, the most common differential diagnosis was retroperitoneal sarcomas. Previous studies have shown that metastases are not common at the time of diagnosis. Our patient's preoperative radiological examination also confirmed this.

Histologically, we have three types of SS: Monophasic type, Biphasic type, and poorly differentiated type. The biphasic histologic pattern has a better prognosis than the monophasic type and poorly differentiated type. Among these three types of pathology, the poorly differentiated type has the worst prognosis and accounts for only 20%-36% of synovial sarcomas.⁸ Due to the abundance of mitosis and the presence of necrosis and hemangiopericytoma-like appearance, our patient was in the poorly differentiated group and consequently had a worse prognosis than other types of SS.

Foo and colleagues proved that synovial sarcoma exhibits TLE1, AE1/AE3, AE7, AE19 cytokeratins (such as CK7, CK8, CK14, CK18, CK19), EMA, BCL2, CD56, CD57, CD99, calretinin, S100, New York esophageal squamous cell carcinoma-1 (NY-ESO-1), and SYT. Negative results for CD34, Desmin, WT1, Myogenin, Friend leukemia virus integration 1 (FLI1), Myogenic Differentiation Antigen 1

(MyoD1), h-Caldesmon, SRY-related HMG-box 10 (SOX10), and integrase interactor 1 (INI1) are valuable for definitive diagnosis of SS.⁹ Moreover, t(X;18)(p11;q11) chromosomal translocation was found in more than 90% of RSS, which can help us differentiate RSS from other retroperitoneal masses.⁹ Immunohistochemistry tests of the patient are in accordance with the findings of previous studies and have proven these cases.

Surgical resection of the tumor and lymph nodes dissection is the main and most important part of the treatment of RSS. Removal of the organs involved around the mass is also usually recommended.¹⁰ Accordingly, our patient underwent extensive resection of the mass with free margins.

To date, the role of adjuvant and neoadjuvant chemotherapy in RSS is not certain. However, in large and high-grade tumors, neoadjuvant chemotherapy makes surgery easier by reducing the size of the mass. In practice, adjuvant chemotherapy is usually taken into consideration in high-risk patients and patients with distant metastasis. Radiotherapy is not recommended, if there is a possibility of damage to adjacent organs. In RSS, the proven effects of chemotherapy are greater than those of radiotherapy, although in most previous studies, preoperative chemotherapy was recommended for enlarged masses. One of the novelties of this study is that our patient did not undergo chemotherapy before the operation at the discretion of the surgeon and fortunately, the patient's outcome has been satisfactory so far. The most common and useful drug in chemotherapy is ifosfamide. There is no conclusive evidence that doxorubicin is useful.^{5, 8} The role of new therapies, such as pazopanib, Tazemetostat, and T-cell receptor-based immunotherapy directed towards NY-ESO-1 in human leukocyte antigen (HLA) -A*0201+ patients are still undecided and under investigation.¹⁰

Palmerini and others showed that some features could cause poor prognosis in SS patients, including SS18-SSX1 translocation, monophasic and poorly differentiated subtypes, male gender, older age at diagnosis, size ≥ 5 cm, non-extremity location, a high percentage of tumor necrosis, mitotic activity ≥ 10 /HPF or higher ki67 activity, tumor grade, IHC expression of chemokine receptor type 4 (CXCR4) and insulin-like growth factor 1 receptor (IGF-1R), positivity for WT1, positive surgical margins, H3K27me3, and vascular endothelial growth factor (VEGF) expression and deep-seated tumor.¹⁰ Our patient definitely has at least six of the above, but fortunately, 1.5 years of follow-up is hopeful, and no recurrence or metastasis has been seen so far.

The advantage of this paper was that it provided a comprehensive study on the causes, diagnosis, and treatment of RSS. The limitation of this work was the amount of follow-up time of the case, which requires to be increased. Owing to the good results in our patient, the lack of preoperative chemotherapy can be further investigated, and the patient can avoid the dangers of chemotherapy prior to surgery.

Conclusion

Based on the results of the current work and similar studies, surgical resection of the tumor and lymph nodes dissection is the main and most important part of the treatment. Accurate diagnosis of RSS is usually based on pathological findings. Therefore, in case of doubt, a biopsy can be applied. Preoperative chemotherapy is usually recommended. However, in the case of our patient, preoperative chemotherapy has not been performed, and the patient's outcome has been adequate so far. Owing to the good outcome of our patient, the role of preoperative chemotherapy will be debatable, and further studies are needed to prove its ineffectiveness before surgery.

Acknowledgment

We thank the staff at Shohada-e-Tajrish hospital operation room.

Authors' Contribution

A.A.D: conception and design of the work - Drafting the manuscript; M.R.R: Acquisition of the data - revising the manuscript critically for important intellectual content; A.R: Substantial contributions to the conception and design of the work - revising it critically for important intellectual content; S.F: Analysis of data - Drafting the manuscript; A.H.R: Interpretation of data for the work - revising the manuscript critically for important intellectual content; S.A.H: conception and design of the work - Drafting the manuscript; All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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