

High-grade undifferentiated pleomorphic sarcoma of the pelvis: A case report and review of literature

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Abstract

High-grade spindle cell sarcomas are rare undifferentiated pleomorphic cancers that present a treatment challenge to urological practices, especially when they present in the pelvis. We report a 46-year-old male patient who presented to our urology clinic with urinary retention after having a Foley catheter placed at an outlying facility. A voiding trial was attempted, but the patient failed this trial. This failure resulted in cystoscopy with bilateral retrograde pyelograms, which revealed a compressed bladder due to extrinsic compression. This finding had been evaluated with a computed tomography (CT) scan with and without intravenous contrast that showed a 14 cm pelvic mass with bladder displacement and compression. A fine needle aspiration was done at this outlying facility, prior to referral to our office, and it confirmed spindle cell pathology. The mass was surgically excised with the histology revealing a pelvic spindle cell sarcoma with positive surgical margins. Further, metastatic work-up with CT/positron emission tomography revealed bone and lung metastasis. The patient is currently undergoing chemotherapy and radiation. In this case study, we will review staging, management, differential diagnosis, chemotherapy, and radiation.

Key Words: Pleomorphic sarcoma, retroperitoneum, soft tissue sarcoma, spindle cells

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INTRODUCTION

High-grade spindle cell sarcomas of the pelvis are rare, undifferentiated, pleomorphic sarcomas previously known as malignant fibrous histiocytomas that are rarely found, and present difficult diagnostic and treatment options to urologists who encounter these lesions in clinical practice. Retroperitoneal sarcomas represent about 15% of soft tissue sarcomas (STSs) that occur annually, and about 10% of these cases will present with metastatic disease, with liver and lung being the most common sites of metastasis.^{(Campbell's}

Urology — ch 52, page 1506). We will review our pitfalls and recommendations for a 46-year-old male patient who was presented to our urology clinic with urinary retention and was found to have a pelvic mass displacing his bladder on computed tomography (CT) imaging.

CASE REPORT

A 46-year-old male presented to our urology clinic because of referral from an outlying hospital for urinary retention for a

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prolonged period of time that required Foley catheter placement and a pelvic mass. Computerized tomography (CT) scan with and without intravenous contrast was reviewed showing a 13.9 cm × 14.6 cm × 11.6 cm mass in the retroperitoneum with some extension into the left groin [Figure 1]. The CT scan also showed bilateral hydronephrosis and a compressed, displaced urinary bladder. Furthermore, fine needle aspiration (FNA) was done at the referring facility, which showed histologically that the mass was of spindle cell origin.

The patient's history and physical examination was done. The patient denied any other complaints other than urinary retention and slight tenderness in his left, lower quadrant. He denied smoking, alcohol, or illicit drug usage. He denies any recent radiation or toxin exposure. No histories of unintentional weight loss, fevers, chills, or hematuria were noted. His medical history included essential hypertension and a clavicle fracture. His surgical history included recent FNA of pelvic mass, CT guided biopsy of hepatic lesion, and soft tissue resection of lesion of finger and hand. His family history was insignificant for urological disease, but there was a family history of diabetes, hypertension, chronic obstructive pulmonary disease, and his mother had breast cancer. Review of systems was negative except for urinary retention, and a recent decrease in appetite. Physical examination revealed tenderness in the left, lower quadrant of the abdomen and a benign feeling, enlarged prostate on digital rectal exam.

The patient was scheduled for cystoscopy with bilateral retrograde pyelograms. Cystoscopy revealed a bladder displacement to the right with difficulty in evaluating the right ureteral orifice [Figure 2].

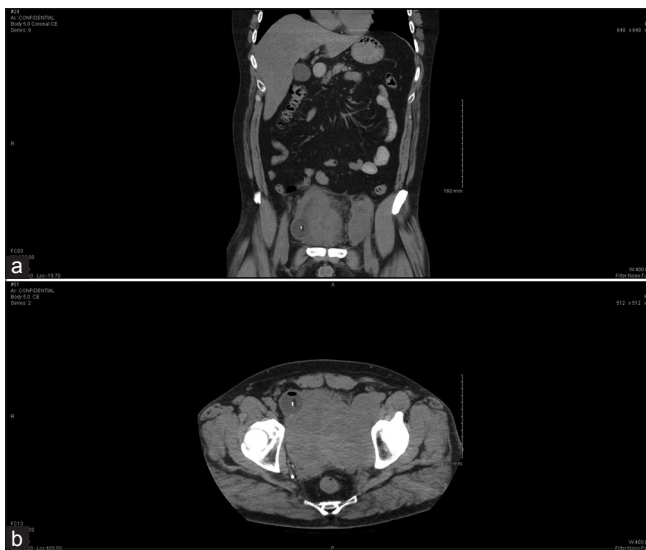


Figure 1: (a) Coronal view on computed tomography demonstrates a mass measuring 13.9 cm × 14.6 cm × 11.6 cm in the retroperitoneum. (b) Axial view on computed tomography demonstrates the mass and the Foley catheter shifted to the right pelvic region

The patient underwent abdominal and pelvic exploration with surgical excision of the pelvic sarcoma with bladder-sparing. There was no involvement of the left ureter. Surgical pathology revealed spindle cell sarcoma consistent with undifferentiated pleomorphic sarcoma. Pathologic staging was initially pT2b, pNX, and pMX, later to be changed to pM1 after further radiographic imaging with positron emission tomography (PET)/CT which showed hypermetabolic osseous lesions in the distal sternum, left pelvic bone, and a displaced fracture of the right clavicle with adjacent soft tissue mass/stranding with intense hypermetabolic activity. A lung lesion was also noted. Histologically, the pathology was grade 3 with >50% necrosis noted. Immunohistochemistry was as follows: Positive for smooth muscle actin, negative for desmin, desmin D33, s100, CD34, cytokeratin cocktail, and CD117.

DISCUSSION

STSs of the pelvis present a urological dilemma. Patients usually present with urinary symptoms due to its aggressive nature and space occupying nature within the pelvis that displaces organs (i.e., bladder).

STS are rare malignant tumors deriving from cells of mesenchymal origin (muscle, nerve, lymphatic, fibrous, and adipose origin) and represent only 1% of all malignant neoplasms and nearly 15% of the STSs that occur annually and thus account for approximately 2000 cases/year.^[1,2] Data from the U.S. National Cancer Institute have identified 2.7 cases/100,000 individuals at a steady rate over the past 30 years.^[3] Fewer than half of all retroperitoneal tumors are sarcomas. Lipomas, pelvic lipomatosis, myelolipoma, leiomyoma, and hemangiopericytoma, which are benign masses, represent 15–20% of the retroperitoneal tumors, which the remainder that consists of primary lymphoma or primary urologic tumors such as germ cell lesions.^[4]



Figure 2: Cystoscopy with bilateral retrogrades demonstrates a shifted ureteral orifice and bladder to the right pelvic area

Some of the epidemiology statistics include male predominance and two-thirds of patients have high-grade malignancy. Presentation is approximately in the sixth decade, but the age range can vary widely.^[5,6]

The etiology of retroperitoneal sarcoma is poorly defined and understood. History of radiation and toxins exposure could contribute to the development, yet this is difficult to account for in the majority of cases.

Scientists have found a few risk factors that make a person more likely to develop STS and those include radiation and certain family cancer syndromes which will be discussed briefly, a damaged lymph system (lymphangiosarcoma [a malignant tumor that develops in lymph vessels] is a very rare complication of chronic lymphedema) and exposure to certain chemicals. To note, injury and lifestyle factors such as smoking, diet, and exercise are not linked to the risk of STSs.

Family cancer syndromes can contribute to an increased risk of developing STSs. Family cancer syndromes are disorders caused by genetic mutations that a patient can be inherited with or spontaneously occur. Some of these syndromes include neurofibromatosis (NF) (also known as von Recklinghausen disease) which is caused by a NFI gene mutation; Gardner syndrome, caused by a mutation in adenomatous polyposis coli gene which is associated with familial adenomatous polyposis. Furthermore, Li-Fraumeni syndrome is an inherited TP53 gene mutation (a tumor suppressor gene), these individuals are more prone to the cancer-causing effects of radiation exposure. Retinoblastoma, a defect with the RBI gene, cancer that develops in the eye and bone (osteosarcoma). Werner syndrome, mutation within *RECQL2* gene, children develop problems that the elderly are at increased risk for such as cataracts, skin changes, arteriosclerosis, and increased risk of STSs. Few more to note: Gorlin syndrome (increased risk of getting fibrosarcoma and rhabdomyosarcoma) and tuberous sclerosis (increased risk of rhabdomyosarcoma).^[7]

The more common malignant retroperitoneal STSs include liposarcoma, leiomyosarcoma, fibrosarcoma followed by rhabdomyosarcoma, malignant fibrous histiocytoma, gastrointestinal stromal tumor, and synovial tumor.

In addition, genetic studies [Table I] have contributed to the development of these sarcomas which can provide therapeutic advancements in the future.^[8] Other genetic studies for STSs are expressed in literature. Zhao *et al.* demonstrated that increased PRUNE2 protein expression was found to be associated with a good prognosis in patients with leiomyosarcoma. These data suggest that increased PRUNE2 protein expression may serve as a favorable prognostic marker in STSs. One genetic

Table 1: Genetic alterations in retroperitoneal tumors

Tumor	Aberration	Gene (S) involved
Alveolar rhabdomyosarcoma	t (2;13) (q ³⁵ ;q ¹⁴)	<i>PAX3-FKHR</i>
Myxoid/round cell liposarcoma	t (1;13) (p ³⁶ ;q ¹⁴)	<i>PAX7-FKHR</i>
ALT/WDLPS	t (12;16) (q ¹³ ;p ¹¹)	<i>TLS-CHOP</i>
Dedifferentiated liposarcoma	Supernumerary ring chromosomes; giant marker chromosomes	Amplification of region 12q14-15, including <i>MDM2</i> , <i>CDK4</i> , <i>HMG2</i> , <i>SAS</i> , <i>GL1</i>
Sporadic gastrointestinal stromal tumor	Same as for ALT/WDLPS Activating kinase mutations	Same as for <i>ALT/WDLPS</i> <i>KIT</i> or <i>PDGFRA</i>

Malkowicz SB. Retroperitoneal tumors. Campbell-Walsh Urology. Ch. 52. p. 1506-15.e3. ALT/WDLPS: Atypical lipomatous tumor/well-differentiated liposarcoma

marker that can help with the outcome of the patient is the over expression of *MED12* gene mutation. This has been studied in a sample of patients, and this mutation within the sarcomas can be an indicator of poor prognosis.^[9-11] If our patient presented with a family history of pertinent cancers, it would be advisable to suggest multi-gene testing. The recent introduction of multi-gene testing for hereditary forms of cancer has rapidly altered the clinical approach to test at-risk patients and their families. However, there are limited data on the degree of cancer risk, and there are no clear guidelines on risk management for carriers of mutation. Not all genes included on available multi-gene tests are necessarily clinically actionable.^[12]

Morphological diagnosis based on microscopic examination of histological sections remains the gold standard for sarcoma diagnosis. Diagnostic imaging is imperative to delineate the anatomic limits of the lesion and assess the integrity and function of adjacent organs.

According to the National Comprehensive Cancer Network guidelines for our patients based on staging of the tumor [Table 2]; unresectable or Stage IV/metastatic disease, retroperitoneal STSs, in which a biopsy was performed; palliative options include chemotherapy, radiation therapy, surgery for symptom control, supportive care, and observation, if asymptomatic.^[12] The current treatment regimen for the patient in this case study is a combination of chemo (temozolomide for palliative treatment) and external beam radiation therapy. In addition, a surgical resection was performed for symptomatic control.

Temozolomide is a promising agent in soft tissues sarcomas. A study demonstrated two partial responses, two mixed responses, and three patients with stable disease that lasted >6 months, for an overall objective response rate of 8%. At a median follow-up of 13.2 months, the median

Table 2: Classification and staging of retroperitoneal tumors

		Anatomic stage/prognostic groups				
		Stage	T2b	N0	M0	G1, GX
Primary tumor (T)						
TX	Primary tumor cannot be assessed	IIA	T1a	N0	M0	G2, G3
T0	No evidence of primary tumor		T1b	N0	M0	G2, G3
T1	Tumor ≤5 cm in greatest dimension*					
T1a	Superficial tumor	IIB	T2a	N0	M0	G2
T1b	Deep tumor†		T2b	N0	M0	G2
T2	Tumor >5 cm in greatest dimension†					
T2a	Superficial tumor	III	T2a, T2b	N0	M0	G3
T2b	Deep tumor		Any T	N1	M0	Any G
Regional lymph nodes (N)		IV	Any T	Any N	M1	Any G
NX	Regional lymph nodes cannot be assessed					
N0	No regional lymph node metastasis					
N1	Regional lymph node metastasis					
Distant metastases (M)						
M0	No distant metastasis					
M1	Distant metastasis					
Histologic grade						
GX	Grade cannot be assessed					
G1	Grade 1					
G2	Grade 2					

Malkowicz SB. Retroperitoneal tumors. Campbell-Walsh Urology. Ch. 52. p. 1506-15.e3, *Superficial tumor is located exclusively above the superficial fascia, †Invasion of the fascia; deep tumor is located exclusively beneath the superficial fascial, superficial to the fascia with invasion of or through the fascia, or both superficial yet beneath the fascia

progression-free survival and the median overall survival were 2.0 months (95% confidence interval [95% CI], 1.7–2.3) and 13.2 months (95% CI, 4.7–31.1), respectively. Temozolomide at the dose schedule employed in the current study was well tolerated and had modest activity against previously treated, unresectable, or metastatic leiomyosarcoma of both uterine and nonuterine origins.^[13,14] However, meta-analysis suggests a slight advantage of 4% overall survival for the use of adjuvant doxorubicin therapy to decrease the risk of death and recurrence in patients with high-grade lesions, and doxorubicin is the foundation for chemotherapy in advanced sarcoma.^[15] The only single agents that are consistently associated with response rates of more than 20% in metastatic STSs are doxorubicin, epirubicin, and ifosfamide. Even for these agents, the range of objective activity between various small, and even larger trials, is impressive.^[16]

For patients with STS, the lungs are the most common sites of metastatic disease. Approximately, 20% of patients with soft tissue retroperitoneal sarcoma will present with metastatic disease. Although pulmonary metastases most commonly arise from primary tumors in the extremities, pulmonary metastasis may arise from almost any histology or primary site, such as the pelvis. To date, resection of disease has been the only effective therapy for metastatic sarcoma. Patients in whom metastatic disease develops after a disease-free interval of >1 year and can be completely resected are most likely to be long-term survivors. Surgical excision of lung metastases from STSs is well accepted and should be considered as a first line of treatment if preoperative evaluation indicates that complete clearance of the metastases is manageable.^[17]

CONCLUSION

This patient presented to us from a small outside facility, to a well-known urologist in a small town. Even though the patient has been doing very well after surgery (free of urinary retention and voiding as expectedly) along with the current treatment regimen, our approach could have been slightly different. In this patient, surgery was done prior to PET/CT scan and then referred to a high-volume institution medical center for further treatment which I believe was the pitfall in our approach. I would have suggested that this patient should have been referred to a main medical center initially (based on a few studies presented below), performed a PET/CT scan prior to surgery, discussed at tumor board about different approaches regarding management based on the pathology finding from the FNA, CT scan, PET/CT, and symptoms of the patient. Considering the relative rarity of retroperitoneal sarcomas, it is reasonable to consider if such lesions should be exclusively treated at high-volume centers. In a review of 260 STSs treated over a 3-year period, 86 were treated at one center whereas the remainders were managed at 38 other centers. The rate of local recurrence was 19% at the specialty/high-volume center and 39% in aggregate at the other hospitals. Survival was significantly different between groups for larger (>5 cm) and high-grade lesions. Similarly, in a registration study of over 4000 STSs treated at more than 200 centers in Florida, 68.1% were treated at low-volume centers and the remainder at seven other sites. There were significant differences in 30- and 90-day mortality and improved survival for high-grade lesions, lesions larger than 10 cm, and retroperitoneal sarcomas (39 vs. 31 months, $P=0.011$). On multivariate analysis, center

effect was a significant independent predictor of improved survival (odds ratio = 1.292, $P = 0.047$).^[8] On a side note, a testicular physical examination should be performed which is warranted for all retroperitoneal STSs prior to its diagnosis.

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Conflicts of interest

There are no conflicts of interest.

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